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I INFECTION
POEMs



**BEST PRACTICE
ADVOCACY CENTRE**
The key to success in health care

Infection POEMs

Patient Oriented Evidence that Matters

Developed by the Best Practice Advocacy Centre
Level 8, 10 George Street
PO Box 6032
Dunedin
Phone 03 4775418
Fax 03 4772622

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Contents

SUMMARY	1
UPPER RESPIRATORY TRACT INFECTIONS	2
ANTIBIOTICS ARE FREQUENTLY NOT APPROPRIATE	2
Rhinitis	3
Acute Bronchitis	3
Sinusitis	4
Pharyngitis	4
Acute Otitis media	5
<i>Acute Otitis Media Guideline Summary</i>	5
<i>Keep antibiotics for otitis media with systemic features</i>	5
<i>Analgesia</i>	6
<i>Patient information</i>	6
ANTIBIOTIC RESISTANCE	7
DELAYED PRESCRIPTIONS	8
Delayed prescriptions reduce antibiotic use for the common cold	8
Even when an antibiotic is thought necessary only 45% are filled	8
A delayed prescription must be supported with good information	9
Guide to writing a delayed prescription	9
SYMPTOMATIC TREATMENT FIRST LINE	10
Pain, fever, headache, body aches	10
Cough	10
Nasal congestion	11
Runny nose & sneezing	11
COMPLEMENTARY MEDICINES	12
Vitamin C may reduce cold symptoms by half a day	12
Zinc appears to be effective for cold symptoms	12
Echinacea possibly effective for early treatment but not prevention of colds	13
Other herbal ingredients	13
ACUTE UNCOMPLICATED URINARY TRACT INFECTION (CYSTITIS)	14
ACUTE UNCOMPLICATED CYSTITIS IN WOMEN	14
Susceptibility patterns	14
Interpretation of resistance rates	15
Norfloxacin	16
Nitrofurantoin	16
Conclusion	16
QUICK REFERENCE CHARTS	17
REFERENCES	19

All information is intended for use by competent health care professionals and should be utilized in conjunction with pertinent clinical data.

Summary

1. Antibiotics are not needed for most upper respiratory tract infections. For most healthy adults the best treatment for colds, acute bronchitis, sinusitis and pharyngitis (sore throat) are symptomatic treatments.
2. In about 80% of children an episode of acute otitis media will resolve without antibiotic treatment. Evidence that routine antimicrobial treatment improves the course of outcomes after acute otitis media is weak. Antibiotics have no effect on pain in the first 24 hours. It is important to give full doses of analgesia before bedtime. If antibiotics are used then target them to those children presenting with systemic features such as fever.
3. There is no good evidence for or against the effectiveness of many of the over-the-counter cough and cold medicines. Rest, plenty of fluid and regular analgesics form a common sense approach. Products should be selected on the basis of symptoms.
4. Three of the more popular complementary medicines used in the common cold are vitamin C, echinacea and zinc. There is inconsistent evidence for their effectiveness. Vitamin C may reduce cold symptoms by half a day. Echinacea may be effective for treatment but not prevention of cold symptoms. Zinc lozenges may be effective for cold symptoms, but a suitable formulation is not available.
5. It is important to understand the interpretation of the available susceptibility data from laboratories. Susceptibility data is likely to overestimate rather than underestimate resistance due to the way it is collected.
6. Trimethoprim is the preferred therapy for uncomplicated acute cystitis. The fluoroquinolones e.g. norfloxacin, should not be regarded as first line therapy because of concerns regarding the promotion of quinolone resistance.
7. Effective patient education is an important aspect of reducing inappropriate antibiotic use.

Upper Respiratory Tract Infections

Upper respiratory tract infection involves inflammation of the respiratory mucosa from the nose to the lower respiratory tree, but not including the alveoli. In addition to malaise, it causes localised symptoms that constitute several overlapping syndromes: sore throat (pharyngitis), rhinorrhoea (common cold), facial fullness and pain (sinusitis), and cough (bronchitis).

Each year, children suffer about five such infections and adults two to three infections. Infective agents include over 200 viruses (with 100 rhinoviruses) and several bacteria. Transmission is mostly through hand to hand contact with subsequent passage to the nostrils or eyes rather than, as commonly perceived, through droplets in the air (Del Mar & Glasziou 2002).

Upper respiratory tract infections are usually self limiting. Although they cause little mortality or serious morbidity, upper respiratory tract infections are responsible for considerable discomfort, lost work, and medical costs. In addition to nasal symptoms, half of sufferers experience sore throat and 40% experience cough. Symptoms peak within 1-3 days and generally clear by 1 week, although cough often persists (Del Mar & Glasziou 2002).

Antibiotics are frequently not appropriate

Most upper respiratory tract infections are viral therefore the potential benefit from antibiotics is limited. Antibiotics do not have clinically important effects on colds and are therefore not recommended. Systematic reviews have found a minimal to modest effect of antibiotics in people with acute bronchitis, sore throat, and sinusitis. Antibiotics can prevent non-suppurative complications of β haemolytic streptococcal pharyngitis, but in industrialised countries such complications are rare (Del Mar & Glasziou 2002).

Until rapid identification of those people likely to benefit from antibiotics is possible, the modest effects seen in trials must be weighed against the adverse effects, costs, and potential for inducing antibiotic resistance.

Rhinitis

In the case of a cold, sore throat is usually the first symptom to appear, followed by runny nose, sneezing, nasal congestion and cough. Headache and sinusitis may also be experienced.

Guidelines specifically recommend against using antibiotics to treat rhinitis and emphasise that even mucopurulent rhinitis does not benefit from an antibiotic (Snow *et al* 2001).

At best the benefits from antibiotics in acute purulent rhinitis may range from no benefit to a one in 10 chance that they will work. If the patient is prepared to wait, their purulent rhinitis is likely to get better without them needing to be exposed to antibiotics (Arroll & Kenealy 2002). A Cochrane review on purulent rhinitis lasting 10 days or more found a benefit from antibiotics with a number needed to treat of 6 (Morris 2000).

Given the limited benefit of antibiotics it is appropriate to offer patients symptomatic treatments such as analgesics and decongestants, it is not appropriate to offer antibiotics.

Acute Bronchitis

In the United States during 1998, uncomplicated acute bronchitis was removed as an indication for randomised controlled trials (RCTs) of antimicrobial therapy, preventing ethical approval for any new studies. Since then, three meta-analyses have been published; all reported no impact of antibiotic treatment on illness duration, activity limitation, or work loss; and all concluded that routine antibiotic treatment of adults with acute bronchitis is not justified (Snow *et al* 2001).

Two RCTs found that β agonists reduce the duration of cough in acute bronchitis compared with placebo or erythromycin (Hueston 1991 & 1994). The second RCT compared inhaled salbutamol with erythromycin, it found that more people using salbutamol were cough free at 7 days (39% versus 9%; NNT 4). Limited evidence from a third RCT suggests that this beneficial effect may be only in people with bronchial hyper-responsiveness, wheeze, or airflow limitation (Melbye *et al* 1991).

Cough is the most troublesome symptom of acute bronchitis and in many patients will persist for several weeks. It is important to advise patients about the long natural history of cough and that they should not be unduly concerned about cough that is resolving and that it is likely to take a few weeks to fully settle (Macfarlane *et al* 2002).

Sinusitis

Acute bacterial sinusitis does not require antibiotic treatment, especially if symptoms are mild or moderate. Symptomatic treatment or reassurance is the preferred initial management strategy (Snow *et al* 2001).

Patients with severe or persistent moderate symptoms and specific findings of bacterial sinusitis, such as chronic purulent rhinorrhoea that is culture positive, should be treated with antibiotics. (Note: take culture from the nasal cavity, not the vestibule).

In most cases, antibiotics should only be used for patients with specific findings of persistent purulent nasal discharge and facial pain or tenderness who are not improving after 7 days or those with severe symptoms, regardless of duration (Snow *et al* 2001). Narrow spectrum antibiotics are first line agents. On the basis of clinical trials amoxicillin, doxycycline, or co-trimoxazole for 7 days are the preferred antibiotics, occasionally up to 14 days may be required.

Pharyngitis

Pharyngitis caused by Group A β -haemolytic streptococcus (GABHS) is predominantly a disease of children aged 5 to 15 years. It has a prevalence of approximately 30% in paediatric pharyngitis but only 5% to 15% in adult pharyngitis in nonepidemic conditions.

Physicians should limit antibiotic prescriptions to patients who are most likely to have GABHS. Patient history and physical examination are useful in the diagnosis of strep throat. Clinical criteria can be used to guide management (McIsaac *et al* 2000).

Clinical criteria:

- history of fever or measured temperature higher than 38°C
- absence of cough
- tender anterior cervical adenopathy
- tonsillar swelling or exudate
- age younger than 15 years

Management recommendations:

- for 4 or more clinical criteria consider empiric antibiotics
- for 3 (or perhaps 2) clinical criteria perform a culture
- for only 1 clinical criteria withhold culture and antibiotics

GABHS are highly susceptible to penicillins. Penicillin (phenoxymethylpenicillin or penicillin V) is the drug of choice. Penicillin treatment may need to continue for ten days even though patients usually feel better within the first two to three days. Penicillin can be given with food as it affects the absorption of penicillin by less than 20%.

Acute Otitis Media

Evidence from systematic reviews suggests that antibiotics for the treatment of acute otitis media (AOM) provide only marginal benefit. In about 80% of children an episode of AOM will resolve without antibiotic treatment and serious complications are rare (Froom *et al* 1997). A poor outcome is unlikely if the child is not vomiting or has a temperature less than 38.5°C (Little *et al* 2002). Pain relief such as paracetamol is important along with observation for lack of improvement.

Acute Otitis Media Guideline Summary (NZGG 1997, www.nzgg.org.nz/library/gl)

Evidence from meta-analyses (Rosenfeld 1996, Del Mar 1997)

- antibiotics do not influence resolution of pain at 24 hours.
- early use of antibiotics reduced the risk of pain at 2-7 days by 40%. Only 14% of children still have pain at 2-7 days, therefore benefit is to 5.6% of all children with AOM (NNT 17).
- antibiotic use reduced contralateral AOM (NNT 17). Antibiotic use did not influence subsequent AOM or incidence of otitis media with effusion (OME).
- antibiotics increased the incidence of vomiting, diarrhoea and rash in children - for every child benefiting from reduced pain, another will suffer antibiotic induced side effects.
- broad spectrum β -lactamase covering antibiotics conferred no advantage over drugs such as amoxicillin or co-trimoxazole.
- aggressive use of β -lactamase drugs will cause bacterial resistance.
- these results do not apply to children with serious underlying disease, otitis media with effusion, concomitant illness other than viral upper respiratory tract infections or co-existing disorders requiring antibiotic therapy.

Keep antibiotics for otitis media with systemic features

Secondary analysis of a RCT has shown that antibiotics are only likely to benefit children with otitis media if they have fever or present with vomiting (Little *et al* 2002). The study set out to examine which children with acute otitis media were at risk of a poor outcome (e.g. an episode of distress or night disturbance by day 3) and whether or not these children might benefit from immediate antibiotics. In all, 315 children aged six months to 10 years with acute otitis media were randomised to receive antibiotic treatment immediately or 72 hours later.

The parents of all children in the trial used diaries to record the children's symptoms - severity of pain, episodes of distress, number of paracetamol doses used and temperature. Parents also noted the presence of cough, vomiting, rash and diarrhoea.

Children who had high temperatures or were vomiting were more likely to have a poor outcome by day three. Of the children who had high temperature or vomiting, distress by day three was less likely among those given immediate antibiotics compared with those whose antibiotics were delayed (32% vs 53%, NNT 5), as was night disturbance (26% vs 59%, NNT 3) (Little *et al* 2002).

The small minority of children presenting with fever or vomiting represent the simplest way to target antibiotics in acute otitis media.

In children without higher temperature or vomiting, immediate antibiotics made little difference to distress by day three (15% vs 19%, NNT 25) or night disturbance (20% vs 27%, NNT 14).

Primary analysis of the RCT found that immediate antibiotic prescription provided symptomatic benefit mainly after the first 24 hours, when symptoms were already resolving. Overall there was no significant difference in mean pain scores, episodes of distress, or absence from school between those receiving immediate or delayed antibiotics (Little *et al* 2001).

If an antibiotic is required amoxicillin is generally regarded as the antibiotic of choice. Five days of oral antimicrobial therapy is effective treatment for uncomplicated acute otitis media in children (Kozyrskij *et al* 1998).

Analgesia

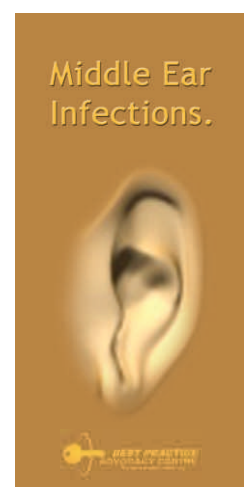
Adequate analgesia is important in producing symptom relief. Particular attention should be paid to advising parents about giving full doses of analgesia before bedtime to reduce night disturbance.

Explain to parents the importance of giving full doses of analgesia before bedtime.

Patient information

Information outlining the minimal role of antibiotics in the treatment of AOM will help educate parents. When antibiotics are expected or demanded consider a delayed prescription and explain that watchful waiting for 48-72 hours before starting antibiotic therapy in previously healthy children is appropriate due to the high spontaneous recovery rate (80%). Follow up is essential.

By prescribing early for a self limiting illness, doctors fuel expectation and encourage the cycle of re-attendance. Effective patient/parent education is essential.



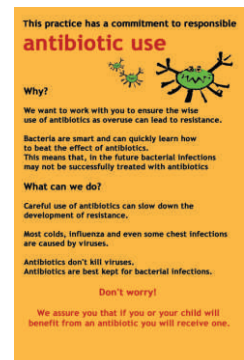
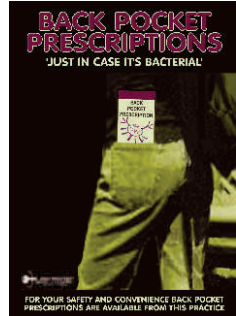
Available from BPAC

Antibiotic resistance

Excessive or inappropriate use of antibiotics is a major factor for selecting antibiotic-resistant bacteria. In general practice, the greatest benefit in preventing resistance must arise from the area of greatest misuse of antibiotics - treatment of respiratory tract infections (Ellis-Pegler 2000). In this context, it is worth remembering that antibiotics offer little or no benefit in most cases of rhinitis, sore throat, acute sinusitis, acute bronchitis, and acute otitis media.

Innovative approaches to address the concern of growing antibiotic resistance have been tried, published and shown to work including (Ellis-Pegler 2000):

1. Delayed prescriptions are provided to the patients but they are advised not to fill them unless their condition worsens.
2. A second free consultation if the condition worsens after an initial 'no-antibacterial prescribed' consultation.
3. A written practice commitment to a 'low antibacterial-use practice' which offers a simple explanation and viral versus bacterial disease data.



Available from BPAC

All approaches should be undertaken in conjunction with effective patient education and information.

When antibiotics are indicated it is important to choose an antibiotic with the narrowest spectrum to cover the likely causative pathogen(s) as this will assist in limiting the development of resistance.

Some antibiotics, for reasons that are not clear, have a low resistance potential and do not induce resistance even when used in high volume over decades e.g. doxycycline, nitrofurantoin. While other antibiotics have a high resistance potential and may cause resistance with even limited use e.g. tetracycline, ciprofloxacin. It makes sense to preferentially select antibiotics with low resistance potential and the appropriate spectrum of coverage (Cunha 2003).

Delayed prescriptions

Whether to prescribe an antibiotic for a respiratory tract infection is a common dilemma in primary care. Physicians are uncomfortable about prescribing antibiotics when the evidence suggests little benefit, but they have concerns about not prescribing them for patients who might benefit. They also wish to maintain good relationships with patients who often expect an antibiotic (Becker 2002).

The “delayed prescription” along with a discussion of the pros and cons of antibiotics (both written and verbal) provide a useful approach. This technique invites patients to participate in the decision. Delayed prescriptions have shown to be effective strategies for reducing the use of antibiotics in colds (Arroll *et al* 2002), acute bronchitis (Macfarlane *et al* 2002), pharyngitis (Little *et al* 1997) and otitis media (Little *et al* 2001). Delayed prescribing is not only associated with a decrease in antibiotic use but it also changes patient perceptions about respiratory infections and decreases subsequent visits for uncomplicated respiratory illnesses.

Delayed prescriptions reduce antibiotic use for the common cold

In the study by Arroll *et al*, 129 patients presenting with the common cold who requested an antibiotic or whom their physician thought wanted an antibiotic were studied. They were randomised to either receiving a delayed prescription or being instructed to take antibiotics immediately. Patients given a delayed prescription were less likely to actually take at least one dose of the antibiotic (48% vs 89%, NNT 3 CI 2-5). No clinically significant difference was noted between groups in their temperature or symptom score at days 3, 7, or 10 (Arroll *et al* 2002).

Even when an antibiotic is thought necessary only 45% are filled

A study showed that for patients with acute cough for whom an antibiotic would normally be prescribed, a delayed prescription is picked up only 45% of the time (Dowell *et al* 2001).

The study by Dowell *et al* duplicates previous work but with a slight difference. The authors excluded anyone for whom the GP would not have considered an antibiotic and those patients with a strong preference for antibiotics. Patients presenting to their GP with acute cough as the primary complaint were randomly assigned (blind allocation) to receive an antibiotic immediately or to have a prescription held at the practice to be picked up after a week if required.

Approximately 45% of the patients in the delayed prescription group actually picked up their prescription. The rate of recovery was the same in each group. The overall satisfaction was high in each group. Nearly all of the GPs (41/47, 87%) found delayed prescriptions useful and intended to use this method in the future (Dowell *et al* 2001).

A delayed prescription must be supported with good information

A qualitative study looked at the experiences and attitudes of GPs and patients regarding the use of a delayed prescription in the treatment of upper respiratory tract infections (Arroll *et al* 2002). Seven primary themes were identified: value judgement of antibiotics, decreased antibiotic use, patient-centered factors, effects on the physician-patient relationship, patient convenience, adverse effects, and selectivity of use. GPs valued empowering patients to be more involved in decision making about their health care management more highly than patients. GPs generally viewed the strategy as giving patients reassurance and meeting their expectations for antibiotics. Both patients and GPs agreed that delayed prescribing is not appropriate for all patients. The following quote from a patient reflects this "delayed prescribing is good for me but not necessarily for everybody. Many people have a very poor understanding of medicines."

Patients need to understand the explanation of why antibiotics are not currently indicated and the instructions as to when they might be needed.

Prompt card for verbal information given to patients with cough/acute bronchitis

- "I have examined you and I am happy there is no sign of serious disease which definitely needs antibiotics today. Most chesty illnesses get better on their own, although the cough may take a long time to go completely.
- Antibiotics don't seem to make much difference to how quickly most people recover. However, if you feel you are getting worse after a while, considering taking antibiotics then would be reasonable.
- So, here is a prescription for an antibiotic for you to keep at home. You are quite likely not to need it, but use your judgment whether to get them in due course."

(Macfarlane *et al* 2002)

Guide to writing a delayed prescription

1. Explain the difference between viral and bacterial infections. Emphasise that antibiotics are of no benefit in viral infections.
2. Ensure the patient understands that the prescription is only to be dispensed if they do not start to get well in the next few days (3-5 days).
3. Alert the patient to signs of deterioration.
4. Reinforce the beneficial effects of symptomatic therapies such as paracetamol, decongestants, steam inhalations, lozenges and gargles.
5. Advise the patient to rest and drink plenty of fluid.
6. Clearly write on the prescription a "dispense-by" date. After this date the prescription is not valid and the patient must return to the surgery for a new prescription.
7. Remind patients that the prescription must only be used for their current infection and that it may not be suitable for future infections or other members of their family.
8. Reassure the patient that if they are worried about how sick either they are, or their child is, they can return at any time.

Delayed prescriptions are a safe strategy for patients with an upper respiratory infection who do not need an antibiotic but who demand one. A delayed prescription should be accompanied by both verbal and written information (posters and patient information brochures are available from BPAC).

Symptomatic treatment first line in upper respiratory tract infections

There are a large variety of cough and cold products available to relieve specific symptoms. Care should be taken in selecting the most appropriate product. Not all combinations are logical e.g. a cough suppressant and an expectorant. There is no good evidence for or against the effectiveness of many of the over-the-counter (OTC) medicines, however many patients report a subjective benefit.

Pain, fever, headache, body aches

Paracetamol, NSAIDs and aspirin (not for a child) are effective analgesics and antipyretics. They reduce the aches and pains associated with the common cold, as well as reduce fever.

Cough

Non-productive coughs can be treated with a cough suppressant. There are three main categories:

1. Centrally acting e.g. pholcodeine (e.g. Actifed CC Dry Cough[®], Duro-Tuss[®]), codeine and dextromethorphan (e.g. Benadryl Dry Forte[®], Robitussin DX[®], Vicks Formula 44[®]).
2. Demulcents e.g. simple linctus and glycerin, lemon and honey (e.g. Lemsip Dry Cough[®])
3. Antihistamines e.g. diphenhydramine, promethazine and triprolidine

A cochrane review looked at a number of products used in acute cough (Schroeder & Fahey 2003). Five trials compared cough suppressants with placebo in adults. Codeine was no more effective than placebo in reducing cough symptoms. One study favoured dextromethorphan over placebo, whereas a second did not show an effect. Antihistamines act as cough suppressants, not through their action on histamine, but by reducing cholinergic transmission of nerve impulses in the cough reflex. Three trials compared antihistamines with placebo in adults. Antihistamines were no more effective than placebo in relieving cough symptoms (Schroeder & Fahey 2003).

Demulcents such as simple linctus and glycerin, lemon and honey, soothe and coat the pharynx. They have a pleasant taste and are particularly suitable for children and pregnant women because of their lack of active ingredients.

Productive coughs can be treated with an expectorant. Expectorants increase bronchial mucus secretion, resulting in increased liquefaction of the sputum, which can then be coughed up. The main expectorant ingredients include guaiphenesin, ammonium salts and ipecacuanha. Products containing guaiphenesin include Actifed CC Chesty Cough[®], Lemsip Chesty Cough[®], Robitussin EX[®].

Two trials compared guaiphenesin with placebo in adults. In the larger study, 75% of participants taking guaiphenesin stated that the medicine was helpful compared to 31% in the control group ($p < 0.01$, NNT = 2). In the second study, both groups showed improvement with respect to cough frequency and severity, with no statistically significant differences between groups (Schroeder & Fahey 2003).

Nasal congestion

Oral sympathomimetic agents e.g. ephedrine and pseudoephedrine are used in cough and cold remedies for both their decongestant and bronchodilatory actions. Oral decongestants may be limited by their side effects e.g. insomnia, tremor and anxiety. They should be avoided in those with cardiovascular disease, due to their potential to increase blood pressure, and by those taking monoamine oxidase inhibitors (MAOIs) or β -blockers. Topical decongestants e.g. oxymetazoline and xylometazoline are associated with fewer side effects, they should not be used for longer than 5 days to avoid rebound congestion (Mason 2002).

Runny nose & sneezing

Antihistamines are used in cold remedies because they suppress the production of mucus, providing relief for runny nose and preventing the post nasal drip that irritates the throat and causes coughing. Products containing sedative antihistamines are best avoided by people taking other sedative medicines e.g. benzodiazepines, and also by patients with narrow-angle glaucoma or prostatic hypertrophy.

OTC medication for the common cold	Symptoms
Paracetamol NSAID Aspirin (not in children)	Fever, headache, facial pain, body aches and sore throats.
Oral decongestant Intra-nasal decongestant Sedating oral antihistamine Less sedating oral antihistamine	Sneezing, runny nose, nasal congestion and possibly cough. Locally acting preparations reduce systemic side effects.
Intra-nasal normal saline	Nasal decongestion, generally ineffective.
Cough suppressant (antitussive)	Non-productive cough, generally ineffective.
Expectorant	Productive cough, guaiphenesin probably effective.
Mucolytic	Thick secretions, probably effective.
Gargle, lozenge (not zinc), throat spray	Sore throat, generally ineffective.
Zinc lozenge Vitamin C Echinacea	Prevention and treatment of symptoms, generally ineffective.
Patient Information	
Provide common sense advice	Rest, maintain fluids, steam inhalation.
Provide written information	Consider brochures on: <ul style="list-style-type: none"> • Colds & Flu • Middle Ear Infection

Complementary medicines

Vitamin C may reduce cold symptoms by half a day

Vitamin C appears to reduce the duration of symptoms in people with upper respiratory tract infections. However, the beneficial effect is small and may be explained by publication bias.

A review (search date not stated, 30 RCTs) compared vitamin C versus placebo for prophylaxis and treatment of colds (Douglas *et al* 2001). Three RCTs used 1g daily or more of vitamin C taken at symptom onset. It found that in people taking vitamin C, the duration of symptoms was around half a day less (weighted mean difference 0.44 days/cold episode, 95% CI 0.23 to 0.64) representing about 15% fewer symptomatic days per episode.

There is some evidence that large amounts of vitamin C (greater than ~ 1g/day) confer no extra benefits. An RCT found that vitamin C doses in excess of 1g daily produced results that were no different to doses around the minimum recommended daily intake (Audera *et al* 2001). The recommended dietary allowance of vitamin C is approximately 60mg per day. Doses greater than 1g per day can lead to oxaluria, uricosuria, renal stones, diarrhoea and rebound scurvy.

Zinc appears to be effective for cold symptoms

A 1997 Cochrane review of seven trials (754 cases) revealed inconclusive evidence regarding the effects of zinc lozenges for treating the common cold.

A more recent RCT of 55 ambulatory volunteers taking either 1 lozenge of 12.8mg zinc (as the acetate) or placebo every 2 to 3 hours found that zinc lozenges were associated with a reduced duration (4.5 vs 8.1 days) and severity of cold symptoms, especially cough (Prasad *et al* 2000). Improvement of clinical symptoms with zinc treatment is believed to be related to a decrease in pro-inflammatory cytokine levels. The benefit appears to be maximal if the lozenges are started immediately after the onset of symptoms.

The formulation of lozenges also appears to be important because the addition of citric acid or tartaric acid may reduce efficacy, due to chelation of zinc ions. Common adverse effects include unpleasant taste, mouth irritation and nausea. Over-the-counter zinc lozenges are not available in the strengths used in the studies as they are classified as dietary supplements. The doses of zinc are low e.g. Strepsils Zinc Defence[®] lozenges contain zinc 3mg (as the gluconate) which is equivalent to 20% of the recommended daily dose and accordingly 5 lozenges are recommended daily. This daily dosage is not sufficient to treat cold symptoms.

Echinacea possibly effective for early treatment but not prevention of colds

Until the active constituents of echinacea are established, efficacy in the treatment or prevention of the common cold is difficult to determine. However, the majority of the available studies report positive results. It appears that echinacea may be helpful in the acute treatment of early upper respiratory infections (URIs), at the first sign of symptoms, but it is not useful in the prevention of URIs.

A systematic review included 13 randomised double-blind placebo-controlled trials with a total of 2416 patients (Barrett *et al* 1999). Four studied prevention, and although all showed a trend toward benefit, none were statistically significant. Nine studied treatment of acute URIs, and six showed benefit, two a trend, and one no benefit. All of the studies were limited by a lack of objective validated measures, all but one by the absence of a report of whether blinding was successful, and the one negative trial by insufficient dosing. As in many studies of naturaceuticals, different formulations and doses of echinacea purpura, echinacea palida, and echinacea angustifolia were used.

The safety of echinacea has only been evaluated over short term studies. It appears to be safe in people without autoimmune disorders or sensitivities to echinacea or its excipients. It should be avoided in pregnant or breast-feeding women due to the lack of evidence regarding its safety in these settings. An *in-vitro* study has shown the potential for immune suppression to occur with long term use of echinacea (<http://nps.org.au/Docs/pdfs/complementconsult.pdf>).

Other herbal ingredients

Many other herbal ingredients, particularly essential oils (e.g. peppermint, eucalyptus and pine oils) and herbal constituents (e.g. menthol, thymol) are ingredients of several over-the-counter cold products. Such products can lead to subjective improvements in cold symptoms (e.g. nasal congestion), but there is little objective evidence of this.

Acute uncomplicated urinary tract infection (cystitis)

A general rule of thumb is to define an uncomplicated urinary tract infection (UTI) as one occurring in a healthy young nonpregnant woman, and a complicated UTI as one occurring in anyone else.

Acute uncomplicated cystitis in women

- Trimethoprim is recommended as first line therapy. Nitrofurantoin can be used as an alternative to trimethoprim.
- Treatment with three days (trimethoprim 300mg daily or nitrofurantoin 50mg four times a day) is generally more effective than a single dose (trimethoprim 600mg or nitrofurantoin 200mg) and as effective as longer courses.
- Norfloxacin should only be used for proven resistant infections. There is concern that excessive use of norfloxacin will contribute to increased quinolone resistance.

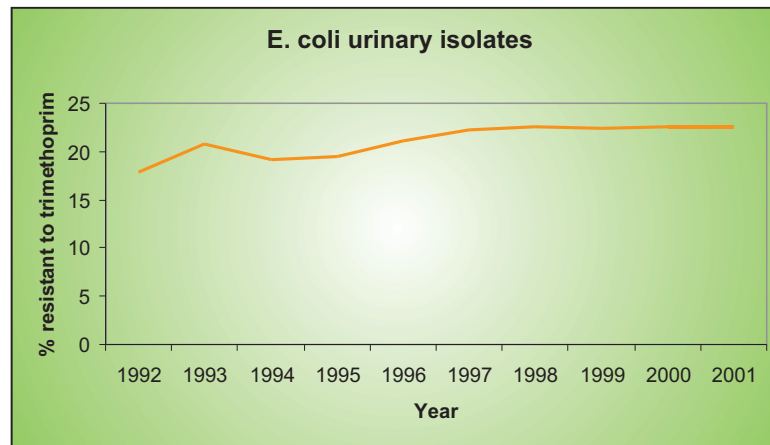
Urinary Tract Infection	Strength	Dose
Three day regimens		
Trimethoprim	300mg tab	1 daily
Nitrofurantoin	50mg tab	1 qid
Norfloxacin (max 6 tabs/script)	400mg tab	1 bd
Single dose regimens		
Trimethoprim (available on PSO)	300mg tab	2 stat
Nitrofurantoin	100mg tab	2 stat
Norfloxacin	400mg tab	2 stat

Simple urinary tract infection and bacteriuria in healthy women probably do not lead to kidney damage. Thus the main benefit of antibiotic treatment of cystitis is symptomatic relief (Leibovici 2002). Spontaneous resolution within 4 weeks may occur in up to 40% of patients, but antimicrobial therapy is usually indicated for amelioration of symptoms (Nicolle 2000).

Susceptibility patterns

Knowledge of the antimicrobial susceptibility profile of uropathogens causing uncomplicated UTIs in the community can be used to guide therapeutic decisions. However it is important to understand the interpretation of the available susceptibility data. Susceptibility data is likely to overestimate rather than underestimate resistance due to the way the data is collected. These data can then drive antibacterial decisions, shifting prescribing tendencies in directions that are neither immediately necessary nor in the long term, prudent (Ellis-Pegler 2000). An example of this is the increasing trend for prescribers to choose norfloxacin over trimethoprim for the treatment of uncomplicated UTI due to the proportion of *Escherichia coli* (*E. coli*) demonstrating resistance to trimethoprim.

Susceptibility data is collated by the Institute of Environmental Science and Research Limited (ESR). The following graph shows the susceptibility profile of *E. coli* urinary isolates to trimethoprim from 1992-2001.



Antimicrobial resistance trends in New Zealand. ESR, September 2002.

Interpretation of resistance rates

A Christchurch study by the Sentinel General Practice Network looked at the problems associated with interpreting cumulative resistance rates from local community laboratories (Richards *et al* 2002).

82 randomly selected GPs in Christchurch participated in the study (The Sentinel Network GPs). Midstream urine (MSU) samples were prospectively collected for standard microbiological analysis on all women between the ages of 16 and 50 years presenting with symptoms of dysuria and frequency and who had positive dipstick testing to either (or both) nitrites or leucocytes. MSUs were submitted for bacterial colony counts and resistance testing of isolates present in adequate numbers (Richards *et al* 2002).

374 specimens were collected. 299 fulfilled the inclusion criteria, of which 94 fulfilled criteria for significant infection. Overall trimethoprim resistance was found in 8 (8.5%) (95%CI 2.8, 14.2), with a resistance rate specifically for *E. coli* to trimethoprim of 11.9%. This compared with cumulative resistance rates from local community laboratories for *E. coli* to trimethoprim of 19%. For a woman in this age group presenting with symptoms of UTI it was estimated that her probability of having a trimethoprim resistant organism was 2.7% (8/299) (Richards *et al* 2002).

The actual level of trimethoprim resistant *E. coli* in the community is an important issue, however the study by Richards *et al* shows that it is not the key determinant of success on an intention to treat basis. Factors to consider include:

- A large number of patients presenting with symptoms of dysuria and frequency will not have an identifiable bacterial pathogen in the urine.
- Not all UTIs are due to *E. coli*. A significant number of organisms, particularly *Staphylococcus saprophyticus* may cause acute lower urinary tract infections and these are almost always sensitive to trimethoprim. Thus reporting resistance of *E. coli* to trimethoprim represents only a portion of the total bacterial isolates or species that cause cystitis and the resistance rate to trimethoprim is higher in *E. coli* than in other infecting organisms.
- Laboratory data are opportunistically collected and with increased empiric treatment of UTI based on symptoms and dipstick results, there is an increasing tendency for MSUs to be sent only when infection is complicated or treatment has failed. The reported results represent a population that is not confined to women with an uncomplicated UTI, but includes males, children, those with urological conditions and abnormal urinary anatomy.

Norfloxacin

The quinolones (e.g. norfloxacin) are effective in cystitis. However the resistance rate is likely to increase the more these drugs are used in the community. To help preserve the efficacy of the quinolones, norfloxacin should not be used as first-line therapy unless the urinary infection is complicated or caused by organisms known to be resistant to other antibiotics. Nitrofurantoin is a reasonable empiric choice in these situations.

Nitrofurantoin

The prevalence of resistance to nitrofurantoin among *E. coli* is less than 5 percent, although non-*E. coli* uropathogens are often resistant (e.g. most *Proteus* species, including *P. mirabilis*). The levels of resistance to nitrofurantoin have been steady over the years and resistant micro-organisms are rarely detected, even during long-term treatment.

Nitrofurantoin will rarely cause severe complications for example, pneumonitis, pulmonary fibrosis or hepatic failure. The rate of hospital admissions related to complications of nitrofurantoin was estimated as six per 10 000 defined daily doses (Hallas *et al* 1992).

Conclusion

Laboratory reported *E. coli* resistance rates to trimethoprim are at the level (over 20%) where an alternative first line antibiotic could be considered. However the study by Richards *et al* suggests that trimethoprim can still be confidently used as the antibiotic of first choice for empiric treatment of acute uncomplicated urinary tract infections despite the reported resistance rates. It is important to interpret carefully laboratory susceptibility profiles. Nitrofurantoin can be considered more generally as an alternative.

Quick Reference Charts

Acute bronchitis:

Common pathogens	First choice	Additional Information
Usually viral Secondary bacterial	Antibiotics are not indicated in viral disease.	Inhaled bronchodilators may be beneficial for selected patients with signs or symptoms of bronchial involvement. Other symptomatic treatments may be helpful (e.g. pain relief, hydration, cough preparations).

Acute bacterial sinusitis (severe & persistent moderate):

Common pathogens	First choice	Additional Information
S. pneumoniae H influenzae	amoxicillin	Treat for 7-14 days. Antibiotics are not indicated for mild infection.
less frequently: Moraxella catarrhalis S. aureus or anaerobes.	Alternative	
	doxycycline co-trimoxazole	

Pharyngitis (GABHS):

Common pathogens	First choice	Additional Information
Usually viral. Use antibacterials for proven streptococcal or other bacterial infection.	penicillin V	Antibiotics are not indicated for mild tonsillitis in communities at low risk of rheumatic fever. Treat for 10 days. Penicillin V can be given twice a day to treat streptococcal sore throat. Avoid amoxicillin due to high incidence of rash in infectious mononucleosis. Single dose IM benzathine penicillin may be used.
	Alternative	
	erythromycin	

Acute otitis media:

Common pathogens	First choice	Additional Information
Many are viral S. pneumoniae H. influenzae Moraxella catarrhalis	amoxicillin	Antibiotics are not recommended for most patients. 80% resolve without antibiotics. Poor outcome unlikely if no vomiting or fever. Duration of treatment is controversial. A 5 day course of antibiotics is generally effective. Consider 10 days in children under 2, where the ear drum is perforated, where the risk of complications is high. Adequate pain relief with paracetamol is essential.
	Alternative	
	Co-trimoxazole	

Acute uncomplicated UTI:

Common pathogens	First choice	Additional Information
E. coli S. saprophyticus P. mirabilis Klebsiella sp enterococci	Trimethoprim Nitrofurantoin	Three day treatment regimen preferred. Empiric treatment is appropriate. Urine dipstick can guide management. Perform culture and sensitivity only in treatment failure. Symptoms can be relieved by drinking more, analgesia and alkalinising the urine. Symptoms may persist for a short while even following effective antimicrobial therapy.
	Alternative Norfloxacin	

OTC medication for the common cold	Symptoms
Paracetamol NSAID Aspirin (not in children)	Fever, headache, facial pain, body aches and sore throats.
Oral decongestant Intra-nasal decongestant Sedating oral antihistamine Less sedating oral antihistamine	Sneezing, runny nose, nasal congestion and possibly cough. Locally acting preparations reduce systemic side effects.
Intra-nasal normal saline	Nasal decongestion, generally ineffective.
Cough suppressant (antitussive)	Non-productive cough, generally ineffective.
Expectorant	Productive cough, guaiphenesin probably effective.
Mucolytic	Thick secretions, probably effective.
Gargle, lozenge (not zinc), throat spray	Sore throat, generally ineffective.
Zinc lozenge Vitamin C Echinacea	Prevention and treatment of symptoms, generally ineffective.
Patient Information	
Provide common sense advice	Rest, maintain fluids, steam inhalation.
Provide written information	Consider brochures on: <ul style="list-style-type: none"> • Colds & Flu • Middle Ear Infection

Classification	Antibiotic
Narrow spectrum	Phenoxymethylpenicillin Flucloxacillin
Moderate spectrum	Amoxicillin Erythromycin
Broad spectrum	Amoxicillin with clavulanate Ciprofloxacin Co-trimoxazole Tetracyclines

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