

Approaches to The Management of Common Infections in General Practice

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Introduction

We welcome the opportunity to write this booklet. It assumes a basic knowledge and hands on general practitioner experience of managing infections in the community. It is predominantly about antibiotic selection and use but it is not a mini text book. It does not go into infinite detail. It does not tell you "what to do". It is unequivocally slanted in the direction of conservative antimicrobial use, i.e. endeavouring to minimise antibiotic use to when it's genuinely needed.

We are both essentially hospital based clinicians with consultancies with Diagnostic Medlab, though Rod Ellis-Pegler has a private consulting infectious disease practice as well. Both of us have taught and listened to medical students, general practitioners and many others in the health service for many years. Much of what appears here is because of questions asked of us over these years. Some questions come up repeatedly. Somehow some things never seem to stick. Other points are made because we think, from our experience, they might be helpful to you.

We welcome comments, be they positive or negative. After all, we all learn more from our mistakes than our successes.

Rod Ellis-Pegler

Mark Thomas

Antimicrobial Resistance

- Generalisations about resistance are dangerous. There are lots of exceptions. Nevertheless, here goes!
- Broadly, the greater the weight of antimicrobials used in a community, the greater the resistance. Thus an overall reduction in antimicrobial use should help reduce resistance. There are some data supporting this.
- About 40% of antimicrobial use in New Zealand is in agriculture. The Ministry of Agriculture and Forestry are making genuine legislative and educational efforts to improve agricultural use of these agents.
- The greatest consumption of antimicrobial drugs in human medicine has been for otitis media. New strategies to manage this disease, using antimicrobial drugs less often, are familiar to all general practitioners and some of this change has been driven by this issue of resistance.
- The evolutionary drive towards resistance development comes from both appropriate and inappropriate antimicrobial use. It is common sense therefore to stop the inappropriate use while acknowledging we simply have to live with the problem when we use them appropriately.
- Like voting, when no single vote seems to make a difference, no one believes their antimicrobial prescription contributes to resistance. But, like voting, when it is all added up, it does.
- There are data accumulating that short course, high dose regimens are associated with less subsequent resistance than longer lower dose regimens.
- While acknowledging the Pharmac data are not beyond criticism, there has nevertheless been a steady and genuine reduction in the total amount of antibacterial use in New Zealand over the last four years. We are doing well.

Common Cold

Presentation:

- Colds are common – on average six to eight per year in children, two to four per year in adults.
- They usually last one week but persist for two weeks in about one in four patients.
- Mucopurulent nasal discharge does not indicate bacterial infection. It occurs in almost 50% of patients by the fifth day of illness and reflects the presence of desquamated epithelial cells and neutrophils.

Investigations:

- Sinus involvement is the rule, not the exception. When some enthusiastic researchers in the United States performed CT scans in otherwise healthy, adult patients with colds, they found abnormalities in the maxillary sinuses in 90%, the ethmoid sinuses in 60% and the frontal sinuses in 10% of patients.

Microbiology:

- Bacterial pathogens (*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*) are present in the nasal mucus from about one in five patients. These patients cannot be distinguished clinically from those whose mucus lacks these organisms. Swabbing nasal discharge for culture is not recommended.

Treatment:

- Despite the evidence that antibiotic treatment does not affect the duration or severity of symptoms and does not prevent secondary bacterial infections, patients who visit their doctor for a cold are still quite often prescribed antibiotics. The consequences are entirely negative – gastro-intestinal side effects, selection of resistant bacterial flora in the naso-pharynx and gut, unnecessary drug expenditure.
- The presentation of a patient with a cold should be used as an opportunity to emphasise the lack of effective therapy, the potential for symptoms to persist for more than one week, and the expectation of full recovery without complications.
- Time is the ultimate cure for all colds.

Pharyngitis

Presentation:

- Two questions need to be answered when assessing a patient presenting with a sore throat:
 - (i) what is the likelihood that the pharyngitis is due to *Streptococcus pyogenes* vs the viruses which are the more common causes?
 - (ii) what is the likelihood that *S. pyogenes* pharyngitis, in this patient, would be followed by acute rheumatic fever?
- Approximately 30% of episodes of pharyngitis in children and 5-15% of episodes of pharyngitis in adults are due to *S. pyogenes*.
- The chance of developing rheumatic fever following an episode of *S. pyogenes* pharyngitis may be as high as 50% in a child with a past history of rheumatic fever. It is approximately 1% in a child without such a history.
- Useful features from the history and examination:

	Viral	<i>S. pyogenes</i>
History	Cough Rhinorrhoea Hoarseness Diarrhoea	Fever
Examination	Conjunctivitis	Tonsillar exudates Tender anterior cervical lymph nodes

- A child with history of fever but not of cough, who has tonsillar exudates and tender cervical lymphadenopathy has an approximately 50% likelihood of *S. pyogenes* infection.

Investigations:

- Approximately 90% of episodes of rheumatic fever occur in Maori and Pacific Island children aged 5-15 years old. Therefore these patients comprise the group where the greatest effort should be expended on diagnosis and treatment.
- There is little to be gained from diagnosing and treating *S. pyogenes* pharyngitis in an adult European patient.
- To increase diagnostic accuracy the throat swab should be swept across the tonsils and posterior pharyngeal wall, and not across the soft palate and uvula.

- Remember that *S. pyogenes* colonises the pharynx of approximately 10-20% of school aged children, and a smaller proportion of adults. The isolation of *S. pyogenes* from pharyngeal swabs does not therefore necessarily imply that it is the cause of the pharyngitis.

Treatment:

- Antimicrobial treatment of *S. pyogenes* pharyngitis provides trivial benefit in the duration or severity of sore throat.
- The only reason to treat such infections is to prevent rheumatic fever.
- The evidence for prevention of rheumatic fever is derived from the treatment of pharyngitis with intramuscular benzathine penicillin.
- Oral penicillin, taken twice or three times a day, on an empty stomach, for 10 days, eradicates *S. pyogenes* infection and is presumed to be of similar efficacy in the prevention of rheumatic fever.
- Rates of eradication of *S. pyogenes* infection are less (approximately 70%) with treatment durations of 5-7 days.
- Treatment can be delayed for up to nine days after the onset of symptoms and still be effective in the prevention of rheumatic fever. Therefore it is usually feasible to delay treatment until throat swab results are available.

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Acute Otitis Media

Presentation:

- Acute otitis media usually follows a viral upper respiratory tract infection.
- Diagnosis sometimes is easy, e.g. when there is a bulging red or yellow tympanic membrane.
- However diagnosis is often less certain. It depends on accurate identification of fluid in the middle ear of a child who has signs or symptoms of acute otitis media, e.g. ear pain and fever.
- Detection of middle ear fluid is very unreliable unless pneumatic otoscopy or tympanometry is used. Use of a standard otoscope provides diagnostic accuracy that is "little better than a coin toss".
- Excessive diagnosis of otitis media is the most common reason for overuse of antibiotics in childhood.

Investigations:

- Swabs of nasal discharge are not helpful for identifying the cause of otitis media.

Microbiology:

- *Streptococcus pneumoniae* is the most common cause of acute otitis media. *Haemophilus influenzae* and *Moraxella catarrhalis* are less common.

Treatment:

- Most children will make an uncomplicated recovery without antimicrobial therapy. Meta-analyses show that it is necessary to treat 17 children to benefit one.
- Selection of the antimicrobial treatment for acute otitis media is primarily influenced by its ability to eradicate *Streptococcus pneumoniae*, the organism which is least likely to resolve spontaneously, and most likely to cause complications.
- A steadily increasing proportion of *Streptococcus pneumoniae* are resistant to penicillins, cephalosporins and other antimicrobials.
- Relatively poor penetration of antimicrobials into middle ear fluid increases the risk of treatment failure.
- When “standard dose” amoxicillin (10-15mg/kg TDS) is used the concentration of amoxicillin in middle ear fluid (MEF) is less than the minimum inhibitory concentration (MIC) of amoxicillin for many penicillin resistant strains of *Streptococcus pneumoniae* (Figure 1).
- About 30% of cases of otitis media due to these penicillin resistant strains will not be cured by standard amoxicillin doses. When “double dose” amoxicillin (25-30mg/kg TDS) is used the concentration of amoxicillin in MEF is greater than the MIC of the resistant strains and treatment failure is rare. Amoxicillin should thus be given in twice the usual dosage when used to treat otitis media.
- The MICs of cefaclor for penicillin resistant strains of *Streptococcus pneumoniae* are much higher than the MEF concentrations which can be achieved with this drug. When cefaclor is used to treat otitis media the microbiological failure rate for penicillin resistant strains is approximately 40%. Cefaclor should thus no longer be used for the treatment of otitis media (Figure 2).
- Resistance of *Streptococcus pneumoniae* to penicillins is not due to beta-lactamase production. Therefore use of amoxicillin with clavulanate will not provide increased activity against *Streptococcus pneumoniae*.

Figure 1 Relationship between amoxicillin MIC and middle ear fluid concentration for *Streptococcus pneumoniae*

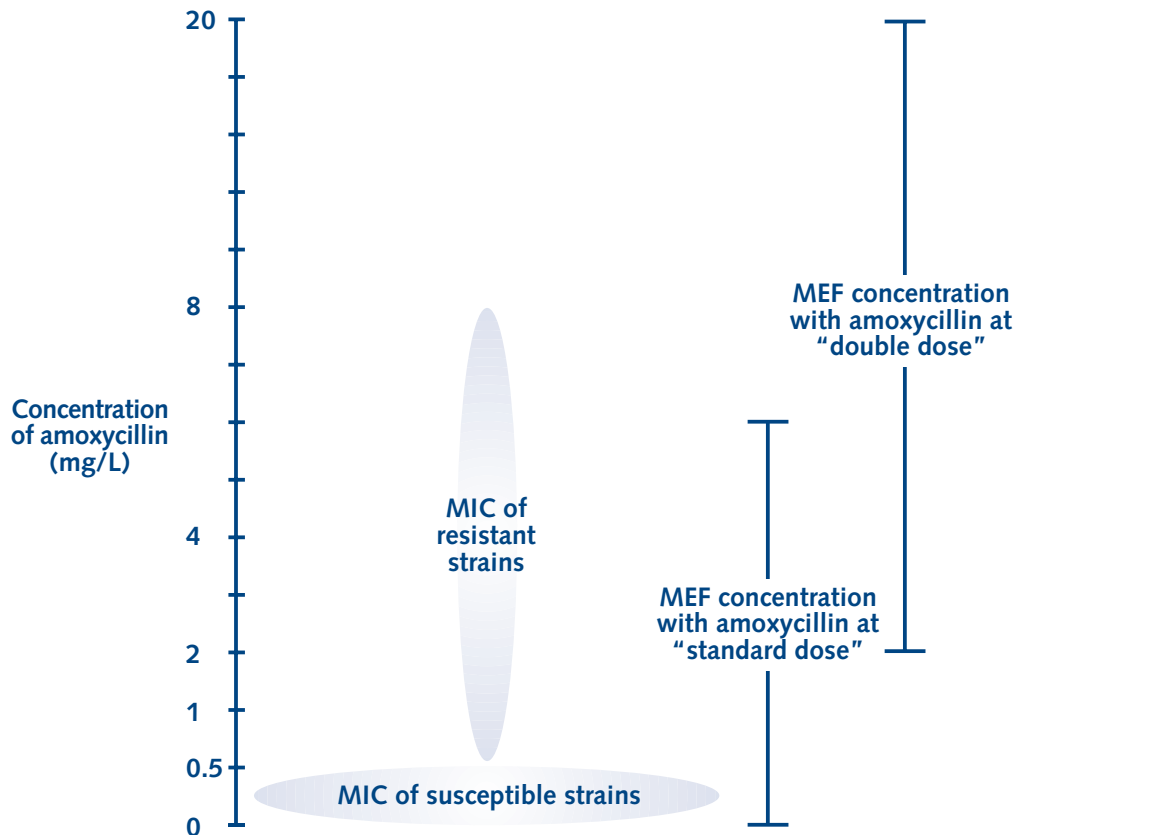
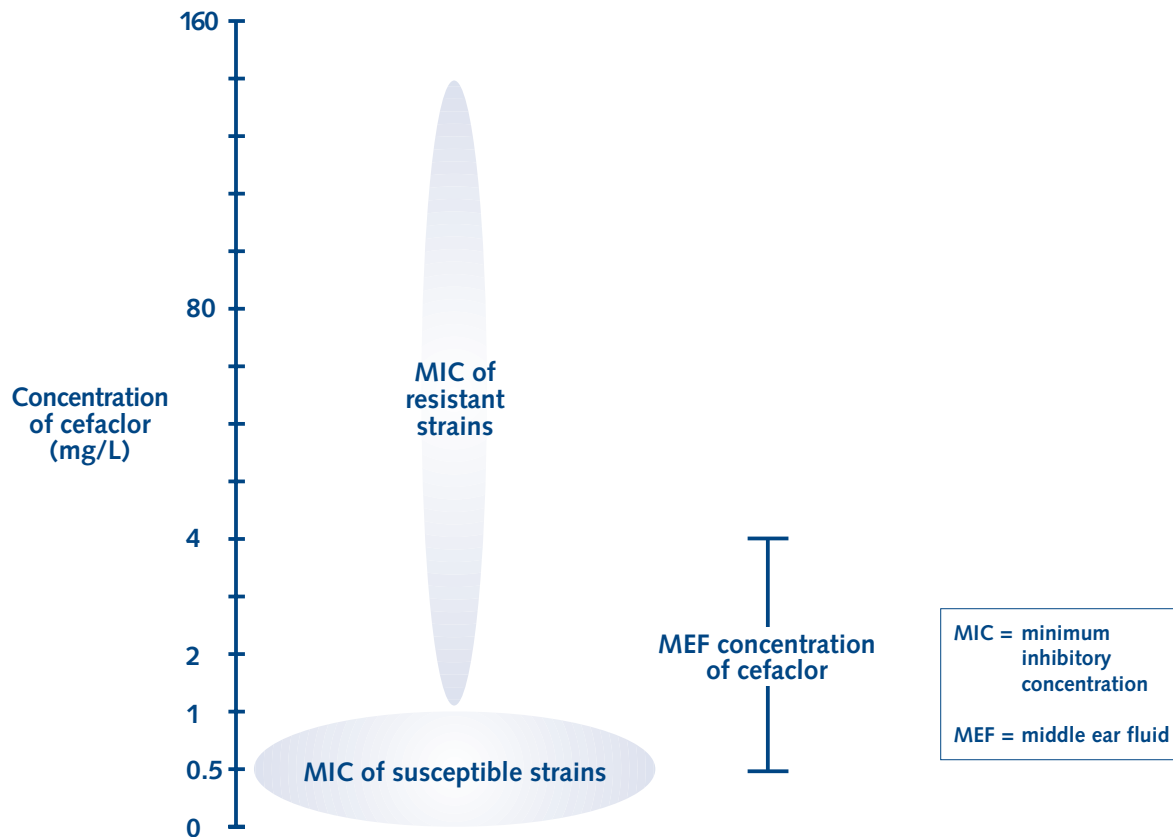


Figure 2 Relationship between cefaclor MIC and middle ear fluid concentration for *Streptococcus pneumoniae*



MIC = minimum inhibitory concentration
MEF = middle ear fluid

Acute Bacterial Sinusitis

Presentation:

- Acute bacterial sinusitis usually follows a viral upper respiratory infection.
- The diagnostic challenge is to determine whether the patient's symptoms represent a relatively prolonged cold or bacterial superinfection of the inflamed sinuses.
- Colds commonly last about one week and approximately one quarter of patients with an uncomplicated cold will still have symptoms at 14 days. Furthermore involvement of the sinuses is the rule rather than the exception. Therefore most patients with sinusitis will not have a bacterial infection. This is especially so for patients who have been unwell for less than one week.
- Deterioration complicating recovery from a cold, purulent nasal discharge, maxillary tooth ache or facial pain, and unilateral sinus tenderness are helpful pointers to bacterial sinusitis.

Investigations:

- Investigations are rarely necessary for the management of patients with suspected bacterial sinusitis.
- If sinus Xrays or CT scans do not show mucosal thickening, an air-fluid level or complete sinus opacification, then bacterial infection is very unlikely. The presence of mucosal thickening alone does not help to discriminate between viral and bacterial infection, but the presence of complete sinus opacification or of an air-fluid level significantly increases the probability of bacterial infection.
- Raised ESR and/or CRP are suggestive of bacterial infection.
- Direct sinus puncture is the only reliable method to diagnose bacterial sinusitis and to identify the pathogen. About 60% of patients with radiological evidence of significant fluid in a sinus have large numbers of bacteria in the purulent sinus fluid. Sinus puncture and lavage is rarely indicated for treatment.
- Swabs of nasal discharge do not provide a useful guide either to the presence or the identity of bacterial infection in the sinuses.

Microbiology:

- *Streptococcus pneumoniae* and *Haemophilus influenzae* are the most common pathogens. Anaerobic bacteria are present in about 5% of patients and usually reflect extension of a dental abscess.

Treatment:

- Antimicrobial therapy has minimal effect on the outcome of acute sinusitis. This is partly because a significant proportion of treated patients do not actually have a bacterial infection.
- Overall it is necessary to treat at least seven patients to see a reduction in illness duration in one.
- Doxycycline or amoxicillin, given for 10-14 days, are appropriate for those patients most likely to have bacterial sinusitis.

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Acute Exacerbations of Chronic Bronchitis

Presentation:

- Chronic bronchitis is usually the outcome of smoking more than 20 cigarettes per day for more than 20 years.
- Patients with chronic bronchitis typically experience one to four exacerbations of their illness each year. Each exacerbation usually lasts a couple of weeks.

Investigation:

- The results of sputum microscopy and culture are a poor guide to whether the patient is likely to benefit from antimicrobial therapy.

Microbiology:

- *Haemophilus influenzae*, *Streptococcus pneumoniae*, and/or *Moraxella catarrhalis* are commonly present in sputum whether the patient is "well" or is experiencing an acute exacerbation of their chronic bronchitis.
- Gram-negative bacteria, e.g. *Pseudomonas aeruginosa* may be found in sputum from more severely affected patients especially those who have recently been treated with steroids and/or an antimicrobial agent.
- The number of bacteria present in bronchial mucus increases during exacerbations of chronic bronchitis, but whether this change is a consequence, or a cause, of the exacerbation is not clear.

Treatment:

- There is sparse evidence of any significant benefit from antimicrobial treatment of acute exacerbations of chronic bronchitis.

- Antibiotic treatment of acute exacerbations provides a very small short-term benefit in lung function. Peak expiratory flow rate is increased by about 10 L/min in the week after treatment is started. The duration of symptoms is reduced by about one day. However antibiotic treatment does not reduce the need for further general practitioner consultations in the following month.
- Acute exacerbations of chronic bronchitis cause a temporary deterioration in lung function. However acute exacerbations do not appear to hasten the long term decline in lung function.
- It is hoped that treatment with an antibiotic, which provides a prolonged reduction in bacterial colonisation of the airways, might increase the duration between exacerbations, and hence perhaps reduce the need for general practitioner consultations and admissions to hospital. The evidence for this effect (seen best with quinolones) is still slim.
- In the absence of evidence for a significant beneficial effect, antibiotics should not be used in the majority of patients with an acute exacerbation of chronic bronchitis.
- In those patients with the most severe disease and those with severe associated conditions, e.g. congestive heart failure, a brief course (7-14 days) of amoxicillin 500 mg tds may provide a clinically useful short-term benefit.

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Influenza

Presentation:

- Annual winter epidemics usually start in May, peak in June, July or August and resolve during September.
- The striking features which help differentiate influenza from other, less severe, respiratory tract infections are : an abrupt onset and the presence of fever (approx. 75% cases), chills, headaches, and myalgia (each approx. 50% cases). Cough, sore throat, profuse nasal discharge, and anorexia (each approx. 50% cases) are common, while vomiting and diarrhoea are unusual. When general practitioners use these clinical criteria to diagnose influenza, their accuracy is very high $\approx 75\%$
- The fever usually lasts one to five days.
- Primary viral pneumonia presents early in the illness while secondary bacterial pneumonia (usually due to *Streptococcus pneumoniae*, *Haemophilus influenzae* or *Staphylococcus aureus*) usually presents about one week after the onset of influenza.

Investigations:

- Laboratory confirmation is rarely required. The virus can be grown from throat or nose swabs.
- A group of sentinel general practitioners collect samples at the beginning of the influenza season to ensure that the prevalent strains are identified each year.

Treatment:

- Either zanamivir (Relenza) or oseltamavir (Tamiflu), begun within two days of onset of illness, will reduce the duration of illness by one to one and a half days. They reduce the rate of complications such as sinusitis, bronchitis and otitis media and might be expected to reduce the incidence of pneumonia.
- Most patients with influenza will present too late to benefit from these medications.
- Relenza (inhaled twice a day, \$66.00) and Tamiflu (one capsule twice a day, \$85.00) (neither is funded) each given for five days, should be considered for those most at risk of severe disease, e.g. the elderly and those with underlying chronic illnesses.

Prevention:

- Inactivated influenza vaccine contains the haemagglutinin (outer protein antigen) from three influenza strains similar to those that are expected to circulate during the winter.
- Vaccination provides a 30-40% reduction in the risk of days of illness, visits to the doctor, and admissions to hospital for respiratory illness.
- Mild soreness of the arm for a few days occurs in about one in four patients. Systemic effects occur at the same rate as with placebo.
- An annual influenza vaccination should be given, in March or April, to all patients over 65 years, and all younger patients with a chronic medical condition. Vaccine uptake in recent years has been about 50% in the elderly and about 20% in younger patients with chronic illnesses. We should be aiming to increase these rates significantly.

Urinary Tract Infections (UTI)

Presentation:

- About 50% of women presenting with clinical symptoms of UTI don't have UTI on testing. Contributions include "low count UTI", chlamydial disease, other sexually linked infections, vaginitis, non-infective causes and some causes we don't understand.

Investigations:

- There are actually a lot of patients who can wait for a result. Complications of cystitis are very rare.

Microbiology:

- *Staphylococcus saprophyticus* is the second most common bacterial cause of UTI in young women.
- Older men get cystitis (due to incomplete bladder emptying usually) from *S. epidermidis* as well as *Escherichia coli* and all the usual bacteria.
- If *S. aureus* is found in a urine specimen, beware invasive (bacteremic) *S. aureus* disease.

Treatment:

- Increasing general practitioner empiricism in UTI management means only those patients who fail treatment get their urine tested. Published resistance data are thus skewed. A recent Canterbury study of all women presenting to general practitioners with UTI symptoms, showed only about 12% overall resistance of UTI pathogens to trimethoprim.
- By and large, three day courses are optimal for "cystitis". Non beta-lactam drugs (e.g. trimethoprim) tend to do better than beta-lactams (e.g. amoxicillin-clavulanic acid) in these short course treatments. Trimethoprim, doxycycline, nitrofurantoin, amoxicillin-clavulanic acid, oral cephalosporin and pivmecillinam are all potential options of about equal, though of course not 100% efficacy. Try not to use norfloxacin as first-line treatment. Resistance rates to this important agent are increasing and have reached 10% in *Pseudomonas aeruginosa*.
- Elderly people without symptoms are best left with their infected urine (if by mistake you have discovered it!). Treatment uncommonly eradicates infection, causes side effects and truly does often lead to colonisation with another more resistant organism. The same is true for long term catheterised patients: they all have organisms in their urine specimens: leave them alone.

Acute Diarrhoeal Disease

Presentation:

- History and examination are generally poor predictors of causation.
- Bloody stools however argue for colonic inflammation, secondary to bacterial infection or “inflammatory bowel disease”.
- *Giardia lamblia* never causes bloody stools, macroscopically or microscopically.

Investigations:

- New Zealand general practitioners tend to test those with bloody stools, symptoms >5 days, recent travellers and campers, those in food, childcare and health related occupations and during an outbreak. This strategy produces a microbiological diagnosis in about 15% of cases.
- One stool is enough to test : the yield from further stools is low and certainly not cost effective.

Microbiology:

- *Campylobacter jejuni* is the predominant cause, surpassed by rotavirus in very young children. *Giardia lamblia* and *Salmonella* come next with *Cryptosporidium* and *Yersinia* uncommon and *Shigella* frankly rare.

Treatment:

- Management is about assessing fluid and electrolyte balance and wondering about the need to investigate the cause.
- Antimicrobial drugs contribute little useful to the outcome of common causes except for their clear role in giardiasis.
- Erythromycin and quinolones shorten *Campylobacter* excretion, but make virtually no difference to clinical symptoms. Quinolone resistance can develop within days in *Campylobacter* : don't use them.
- *Salmonella* excretion is prolonged by any antimicrobial and the clinical symptoms are unaffected.

Skin and soft-tissue infection

Presentation:

- Rapidly progressive cellulitis with lymphadenitis is due to *S. pyogenes*. Very occasionally it presents with impressive systemic symptoms 24-48 hours before the local limb cellulitis appears.
- Necrotising fasciitis is rare : it's extremely painful and that's often the clue.
- Deciding when a chronic ulcer (ischaemic, varicose, diabetic) is infected is very difficult. We probably all overstate and over respond to an "infected ulcer". Nevertheless, surrounding erythema, swelling, heat and tenderness extending for say two centimetres likely means cellulitis.

Investigations:

- There's rarely an opportunity for microbiological specimens in common limb cellulitis. Nevertheless, sampling a blister will often provide the cause.
- The need to routinely sample clinically obvious *S. aureus* focal skin sepsis is dependent on how much MRSA is found locally. At 10% prevalence (approached in South Auckland) the issue becomes a real one.

Microbiology:

- *S. aureus* and *S. pyogenes* are the overwhelmingly predominant causes of skin sepsis while Group G and C streptococci are occasional causes. Gram-negative bacilli are very uncommon.
- Impetigo is now often purely staphylococcal.
- The microbiology of the surface of chronic ulcers is usually a Gram-negative bacillary zoo and irrelevant to treatment decisions – which generally have nothing to do with antimicrobial drugs anyway. The presence of *Pseudomonas aeruginosa* does not necessarily mean it is causing disease.

Treatment:

- 20% of *S. aureus* are resistant to fusidic acid and 20% to mupirocin. Resistance to both is increasing. You can no longer prescribe these and expect a useful outcome without testing .
- Amoxicillin-clavulanic acid is grossly overused for ordinary skin sepsis. The choice, if there is one, is whether to use flucloxacillin or whether penicillin VK is adequate.
- There has been little critical evaluation of how to treat cellulitis around chronic ulcers. Flucloxacillin alone or amoxicillin-clavulanic acid are reasonable initial choices and are similarly appropriate for the infected diabetic foot.

- Ciprofloxacin treatment of infected chronic ulcers which have *P. aeruginosa* cultured from them is often followed by the rapid development of ciprofloxacin resistance. So beware.
- Remember that ciprofloxacin has poor activity against streptococci, was never a first line drug for *S. aureus* disease and *S. aureus* resistance to it is increasing.

Tips about infectious diseases from outpatient and private practice

- It is very uncommon indeed for a general practitioner to need to prescribe an antibiotic for an adult patient with a febrile illness that they cannot diagnose. The important corollary (except in the context of catastrophic febrile illness) is that giving an antibiotic to an adult when the diagnosis is unclear is universally pointless. Yes, I know you all know that but I have repeated it nevertheless.
- Ignore rigors (= “teeth chattering, uncontrollable shaking, can’t hold a beer without spilling it”, lasting for at least five minutes) at your patient’s peril. Yes, of course rigors sometimes usher in non bacteraemic illness, but they are a powerful predictor of bacteraemia (or malaria in travellers) and they always merit evaluation, investigation and re-evaluation.
- Glandular fever (due to EBV or very occasionally CMV) in adults can be atypical – no sore throat, no lymphocytosis but always cholestatic LFT abnormality and sometimes splenomegaly. It is not a rare cause in the adult who has been unwell for more than two weeks. Remember the laboratory tests (including the IM test) all measure antibodies which may take more than two weeks to become positive.
- Mild abnormalities of LFTs are extremely common in infective febrile illnesses, both those we define and those we don’t. Rarely do they merit ultrasound investigation unless there is some other clinical pointer to liver disease.
- Acyclovir is an overused medicine. The ointment is close to useless : it has no clinical benefit for either cold sores or genital herpes. The tablets are similarly clinically useless as treatment of recurrent genital HSV disease, even when used at the earliest suspicion of symptoms. Read the trials if you can’t believe any of this! The tablets however are an effective prophylaxis for frequent recurrences, but need to be dosed at least twice daily. They are also very effective treatment for primary genital HSV disease, if you ever see it.

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