New quinolones in clinical practice

Sir,

As discussed by Dr Masterton in his editorial (Vol 60(2), 1999, p.82). New quinolone antibiotics available in oral formulation and administered once-a-day are, or will soon be, available to treat community-acquired respiratory tract infection (RTI).

Grepafloxacin and levofloxacin are available now, while trovafloxacin should be available shortly and moxifloxacin, gatifloxacin and SB265805 are likely to be registered for oral therapy in the next few years. Intravenous forms of levofloxacin, trovafloxacin and moxifloxacin will be available for hospital use and another quinolone, clinafloxacin, may be available only in intravenous form for therapy of severe sepsis.

Given the unproven role of antibiotic therapy for many RTIs in the community, such as acute cough and many exacerbations of chronic obstructive pulmonary disease, it is unclear if such additional agents will be required. Most patients with chest infections treated by GPs receive amoxycillin and there is no evidence that this will change. However, penicillin and, more dramatically, macrolide resistance is increasing in *Streptococcus pneumoniae* in the UK and the ongoing use of cephalosporins to treat RTI in hospitals is contributing to the epidemic of *Clostridium difficile* infection.

While in the short term it is probable that there will not be a large market for these agents in the UK, they are likely to be useful drugs in denied patients. The challenge is to identify these patient groups, as resistance to these agents already occurs in rare strains of respiratory pathogens such as *S. pneumoniae* and *Haemophilus influenzae* and they are not without unwanted side effects.

AP MacGowan
Consultant Medical Microbiologist
Department of Microbiology
Southmead Hospital
Bristol BS10 5NB

Sir,

Masterton does well to summarize the current status of an increasingly complicated group of drugs. An advisory group of the Paul Erhlich Society has recently classified these agents into 4 groups (like the cephalosporins) and interested readers are referred to this document (Naber and Adam, 1998). Contrary to Mastertons' opinion, I believe toxicity is still an issue with the newer agents which will be the main reason for their individual success or failure.

The other major differences between them are in their individual pharmacokinetic and microbiological characteristics, with some approaching oral bioavailability of 100%, making them very good candidates for oral therapy, even in serious infection. The good activity against the gonococcus and *Chlamydia* spp make them tempting possibilities for treatment of urethritis and cervicitis and some even have indications for intra-abdominal infections but their major likely potential is for monotherapy of serious respiratory infections. Not only are all the major traditional pathogens likely to be covered (including penicillin resistant pneumococci) but also all the currently recognized atypical pathogens. The new quinolones seem to offer a real alternative to β lactam/macrolide combinations for such clinical problems.

They continue to be a paradox, however. Their excellent pharmacodynamic characteristics mean they are well suited to use in life-threatening infection and some argue they should be reserved for these. Although they may be less likely to select for resistant strains than older quinolones, they are subject to the same resistance mechanisms and these mechanisms are posing more of a clinical problem than was anticipated at launch of the earlier drugs. On the other hand, their good bioavailability, low gastrointestinal side-effect profile and broad spectrum mean they are popular choices in general practice where widespread success could compromise their use in more serious infections.

IM Gould
Consultant Microbiologist
Department of Medical Microbiology
Aberdeen Royal Infirmary
Aberdeen AB25 2ZD

Naber KG, Adam D (1998) Classification of fluoroquinolones. *Int J Antimicrob Agents* **10:** 255–7

Local anaesthetics: the debate continues

Sir,

I congratulate Drs Singh and Erwin for a concise description of the local anaesthetics (Vol 59(11), 1998, p. 880–3). It would have been even better if the authors had added the following points of practical significance. Under 'topical analgesia', amethocaine gel is gaining popularity because of its faster onset of action than EMLA. In addition, 4% lignocaine as a spray is commonly used in endoscopic procedures.

Although the authors have mentioned 'caudal blockade' for postoperative pain relief, epidural infusion of local anaesthetics is used for the same purpose. The doses mentioned in *Table 1* are for an average adult and cannot be applied to children.

S Kannan
Anaesthetic Registrar
Department of Anaesthetics
Altnagelvin Area Hospital
Londonderry BT47 1SB

Sir,

The letter from Dr Kannan updates our review by including Ametop (amethocaine 4% gel) and including the exact preparation (4% lignocaine) used in endoscopic procedures, and we thank him for this. However, we deliberately did not give a table for doses of anaesthetic drugs in children as the *route* of absorbtion is so important in determining toxicity, so only *maximum* doses are published in each route in adults.

Caudal infusions are no longer used even for chronic pain relief because of the imprecise level of blockade and the risk of infection.

D Erwin
Consultant Anaesthetist
Whipps Cross Hospital
London E11 1NR

Acute myocardial infarction: failed thrombolysis

Sir,

Sutton and de Belder listed tight coronary stenosis among the causes of failed thrombolysis (Vol 59(10), 1998, p.797), implying that, in some cases, 'myocardial necrosis was primarily related to an outstripping of the supply–demand relation for blood flow' (O'Neill, 1998), in the absence of intracoronary thrombus. The possibility that myocardial infarction could occur in the absence of coronary thrombosis, validated at autopsy by Roberts and Buja (1972), has recently received 'in vivo' confirmation. This was achieved by intracoronary aspiration thrombectomy which showed that aspiration yielded not only recent as well as organized thrombi, but also, in 30% of cases, a total absence of thrombotic material (Murakami et al, 1998).

This paradigm of myocardial infarction limits the therapeutic potential of thrombolysis, also raising the possibility that an analogous situation might exist in ischaemic stroke, where the recent enthusiasm for thrombolysis (Multicenter Acute Stroke Trial-Europe Study Group, 1996) might now need to be tempered with a degree of caution.

OMP Jolobe
Consultant Geriatrician
Department of Medicine for the Elderly
Tameside General Hospital
Ashton under Lyne OL6 9RW

Murakami T, Mizuno S, Takahashi Y et al (1998) Intracoronary aspiration thrombectomy for acute myocardial infarction. *Am J Cardiol* **82:** 839–44

O'Neill WW (1998) Coronary thrombosis during acute myocardial infarction: Roberts was right. *Am J Cardiol* **82:** 896–7

Roberts WC, Buja LM (1972) The frequency and significance of coronary arterial thrombi and other observations in fatal acute myocardial infarction. *Am J Med* **52:** 425–43

The Multicenter Acute Stroke Trial-Europe Study Group (1996) Thrombolytic therapy with streptokinase in acute ischemic stroke. *N Engl J Med* **335:** 145–9