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'One for all' concerns regarding NICE antibiotic guidelines on suspected bacterial meningitis!

The most common bacteria causing meningitis include *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*. Guidelines issued by the National Institute for Health and Clinical Excellence (NICE) in regards to bacterial meningitis recommend administration of benzylpenicillin for children and young patients with suspected meningococcal disease in the pre-hospital setting. This is in accordance with existing advice issued by the chief medical officer.^{1,2} However, when the same patient comes in to hospital, the advice on the empirical antibiotic choice changes to third generation cephalosporins (with or without high dose amoxicillin depending on risk factors for *Listeria monocytogenes* infections) this means that, essentially, the same patient can be prescribed different antibiotics depending on where he or she is first seen!

At present there is convincing evidence suggesting an independent incremental association between 'delays' in administering 'the correct' antibiotics and mortality from acute bacterial meningitis.⁵ In addition, we know that delay in commencing adequate antibiotic therapy in septic shock cases is associated with higher mortality, and the use of inappropriate antibiotics is associated with higher mortality in blood stream infections.⁶⁻⁸ Penicillin resistant rates among UK *Haemophilus* species isolates is 17.7% and penicillin intermediate *S. pneumoniae* is 10.8%. In a Scottish study the prevalence of moderate penicillin resistant meningococci was 8.3%, the majority of isolates (52.2%) belonged to serogroup B,^{3,4} and according to the same NICE guidelines the prevalence of *Haemophilus* resistance to third generation cephalosporins is almost zero. There is currently a low prevalence of pneumococcal cefotaxime/ceftriaxone

resistance in the UK, with only 1.7% of strains reported to have intermediate or high resistance to cefotaxime between 2004 and 2007. Given these numbers it is unclear as to why NICE is still recommending benzylpenicillin.

Paul Erlich's '*Frapper fort et frapper vite*' statement is correct, however, in addition to 'hit hard and hit fast' we believe that in these cases we need to 'hit right' to achieve a more favourable outcome. Therefore, the choice of empirical antibiotic should be the same both in pre- and post-hospital settings, and benzylpenicillin in the doctors bag should be replaced with a third generation cephalosporin, for example, cefotaxime, to be administered to patients in a timely manner, unless of course there is history of true beta-lactam allergy or other contraindications.

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Response from NICE

We are grateful for the opportunity to provide some comment following the letter by Saeed *et al*¹ that points out an apparent discrepancy between NICE recommendations² for primary care antibiotic therapy (penicillin) and secondary care management (ceftriaxone) and makes a case for availability of a third generation cephalosporin in the GPs 'black bag'.

Unfortunately, the authors' arguments are based on a fundamental misunderstanding of the guidance as the population they discuss should not have been given antibiotic therapy in the first place. The only population for whom there is a recommendation for universal pre-hospital antibiotic therapy in this setting are those with suspected meningococcal disease (both meningococcal meningitis and septicaemia), that means patients who are ill with a non-blanching rash. The previous chief medical officer's (CMO's)³ advice and the NICE guideline² only refers to these patients. The arguments about *Haemophilus influenzae* type B meningitis and pneumococcal meningitis put forward by the authors, although microbiologically correct, are irrelevant as such patients with suspected meningitis and no rash should not receive pre-hospital antibiotics.

The reason for avoiding antibiotics in non-meningococcal meningitis is that such

patients should have investigations in hospital (for example, lumbar puncture) and important therapeutic interventions (for example, steroids) before or at the same time as they receive antibiotic therapy. At present such interventions are not available in most community settings. So for these individuals the priority is to provide rapid access to hospital and minimise the time from presentation to appropriate management. This is discussed in the full version of the NICE guideline where GPs are advised to send such cases to hospital urgently.²

The NICE guideline development group searched the evidence for the use of pre-hospital antibiotic use in meningococcal disease and concluded that there was insufficient high quality evidence to recommend antibiotic therapy in this setting (some studies indicated a worse outcome when antibiotics were used pre-hospital, and others implied improved outcomes but all were inadequate to draw firm conclusions) and, therefore, the NICE guideline has emphasised urgent transfer to hospital for children with a non-blanching rash. Despite the lack of supportive evidence, the recommendation to administer parenteral penicillin as previously recommended by the CMO³ was not rescinded as it was also considered that there was insufficient evidence to change the current practice. The NICE guideline therefore changes the emphasis for GPs seeing cases of suspected meningococcal disease. Where previously all such cases should have received penicillin prior to transfer to hospital, the emphasis is now on urgent transfer to hospital with opportunistic use of penicillin where this can be done without incurring any delay.

The appearance of antibiotic resistant bacteria in the community is a concern but is best managed by limiting antibiotic use rather than wider use of broad spectrum agents. With regard to the moderate penicillin resistance that the authors note was documented by Kyaw *et al*⁴ (and elsewhere), it is important to monitor through good surveillance (best achieved by obtaining blood and cerebrospinal fluid cultures in hospital) but, as Kyaw *et al* say in their paper, the clinical significance of moderate resistance among meningococci remains unknown.⁴

Meeting a case of meningococcal disease is thankfully a once in a lifetime experience for most GPs and, carriage of ceftriaxone over a GPs' career is unnecessary and wasteful, especially as we are still uncertain whether antibiotic

therapy outside a hospital environment even helps. We recommend that GPs continue to carry benzylpenicillin, at minimal cost, and to administer it if its use will not delay hospital admission.

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Methadone keeps people alive

We were surprised and disappointed to read Mike Fitzpatrick's review column 'Older addicts', as we feel it is inaccurate and ill-judged.¹ We have no problem with The Review articles being controversial but we do expect some attempt to justify controversial views with evidence.

Fitzpatrick makes sweeping statements about one of the therapeutic mainstays of drug dependency. The evidence base for methadone as an opiate substitution therapy is strong and recognised by the national guidelines and the recently published RCGP guidance.^{2,3} On an individual level a person on methadone is less likely to die, commit crimes, or get blood-borne viruses.⁴

In contrast, Fitzpatrick's piece is largely rhetorical and it is flawed rhetoric at that. He argues that because there are people who have been on methadone for many years, this 'confirms the spectacular ineffectiveness of the (methadone) treatment'. This is illogical, contrary, and is it not actually the reverse? The ageing demographic of those on methadone shows how well it has kept them alive, something that the RCGP's *2010 Research Paper of the Year* confirmed in a cohort of injecting drug users in Edinburgh.⁵ There is also little evidence that methadone maintenance increases the overall length of dependence.⁶

Fitzpatrick comments on 'the substantial mortality arising from methadone overdose (among the children of users as well as their parents)'. There are risks, as with any medication, but deaths in users on scripts are rare and often related to polydrug use. Only 0.1% of drug deaths are under 15 years.⁷ Careful attention to prescribing guidelines has mitigated the risk and, ultimately, methadone clearly reduces drug-related deaths.

Finally, Fitzpatrick stands in moral judgement of those on methadone with the pejorative comments that users have been consigned to 'lives of idleness and dependency'. He also suggests that medicalisation is 'robbing drug users of their dignity as well as their health'. We fundamentally disagree with Fitzpatrick's opinions, and it is utterly wrong and baseless to suggest methadone worsens health.

Many GPs have worked hard over many years to address the social exclusion and health inequalities of those with substance misuse health issues. It is perfectly reasonable to have a debate about medicalisation, and there is no reason why the prescribing of opiate substitution therapy shouldn't be included in that debate. However, we would prefer to see a debate that made some attempt to formulate opinions that go beyond a superficial kneejerk anti-methadone approach that has merely served to reinforce an ill-informed stereotype and deepen stigma.