parison with that from the environment and emphasised the capacity of the immune system to respond effectively to numerous simultaneous antigens.[8] Using data linkage, Miller et al found no evidence for an increase in admissions to hospital for serious bacterial infections following MMR vaccination. [9]

One disadvantage of giving vaccines in combination is that it may not always be clear which component is responsible for a particular adverse event. As important as safety is ensuring that combining antigens does not compromise the protection afforded by each antigen. In the study by Schmitt et al, no difference was found in subjects achieving protective concentrations of antibodies against diphtheria, tetanus, hepatitis B, and polio.[5] Concentrations of pertussis antibody were the same for both groups and comparable with those achieved in trials of DTaP alone. However, the concentrations of Hib polyribosylribitol phosphate (PRP) antibody were statistically significantly lower in those children receiving all the antigens mixed together. The clinical significance of this is uncertain.

One of the longest established combination vaccines is DTwP. Two Swedish vaccine trials found a significant difference in post-immunisation levels of diphtheria antitoxin depending on the presence and nature of any pertussis antigens in the vaccine.[10] The addition of an efficacious wholecell pertussis (wP) component to diphtheria and tetanus vaccine increased the geometrical mean titre of diphtheria antitoxin in the recipients, whereas the addition of acellular pertussis (aP) or a poorly efficacious wholecell pertussis vaccine produced lower concentrations than only diphtheria and tetanus vaccine. In a few children, the concentrations reached were considered non-protective, confirming the well known adjuvant effect of efficacious wholecell pertussis vaccines. DTwP vaccines can be combined with Hib vaccines with no clinically significant loss in immunogenicity, but when DTaP is used instead lower concentrations of Hib PRP antibodies have been observed,[11] and in some cases these are below protective levels. The clinical significance of this was unclear.

However, there has been a rise in Hib cases in fully immunised children in the United Kingdom. This is probably in part due to the use of a combined DTaP/Hib preparation.[12] Dagan et al reported that infants who were given a diphtheria-tetanus-pertussis-polio-Hib vaccine, in which the Hib component was conjugated to tetanus, simultaneously with a pneumococcal vaccine also conjugated to tetanus toxoid had lower Hib PRP antibody concentrations than infants who had received pneumococcal vaccine conjugated to diphtheria toxoid.[13] Furthermore, children who had received higher doses of pneumococcal tetanus conjugate had poorer responses. This implies that difficulties may arise in using simultaneous or combined vaccines that have conjugates in common.

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Management of bacterial meningitis in adults

Algorithm from the British Infection Society represents current standard of care

The treatment of bacterial meningitis represents one of the success stories of modern medicine, particularly antibiotics. In the pre-antibiotic era bacterial meningitis was almost always fatal, but the prompt use of appropriate antibiotics together with supportive care can undoubtedly reduce the morbidity and the mortality of this condition substantially. And yet just 10 years ago a large study of acute bacterial meningitis in adults found a mortality of 25%.[1] Why can't we do better than that?

Acute bacterial meningitis tends to present to non-specialist, and often inexperienced, junior doctors. It is not very common—there are about 1000 patients in the United Kingdom each year—and so individual doctors will not see many patients. These are exactly the circumstances in which a management algorithm can help. The British Infection Society has recently published such an algorithm for the initial management of adult patients with presumed bacterial meningitis,[2] and which represents an updated version of the evidence based recommendations published by the society four years ago.[3] Key to the success of algorithms such as this one is simplicity. The new guidelines recommend a third generation cephalosporin such as

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cefotaxime or ceftriaxone as the first line of treatment in most patients, with the addition of ampicillin for older patients (to cover the possibility of *Listeria* infection), and vancomycin with or without rifampicin in case of a serious risk of infection due to penicillin resistant pneumococci. Importantly, the society recognises that a good outcome depends on factors other than the choice of antibiotic alone. Awareness of the early clinical signs, and prompt attention to oxygen requirements and circulatory support are rightly stressed.

Algorithms are not intended to cover all circumstances. For example, in some parts of the world pneumococci remain predictably sensitive to penicillin, and this drug can remain a first line agent for presumed pneumococcal meningitis, but we do not know how long this will be true. Patients in special or high risk groups, such as immunocompromised people or small children, present particular problems, and expert advice needs to be sought immediately.

Some will argue with the detail. The authors state that a lumbar puncture should not be done in patients with septicaemic meningococcal disease and take a relatively conservative approach to lumbar puncture and the use of computed tomography scans in general. The evidence base for these assertions is not always clear. It needs to be acknowledged that because of a lack of systematic controlled clinical trials, many of the recommendations of the working party, including those on the use of antibiotics, are based on expert opinion and consensus driven guidelines rather than a secure evidence base. However, in the absence of better evidence most doctors accept that documents such as this generally represent the standard of care for a particular clinical condition. The problem is that despite this guidelines are often not followed. In a revealing study carried out in the Netherlands, van de Beek et al followed up 365 adult patients with bacterial meningitis.[4] A year before the study began, a multiprofessional group of Dutch experts drew up guidelines for the empirical treatment of bacterial meningitis. These were agreed at a national consensus conference and were subsequently widely disseminated throughout the country. During their study, van de Beek et al found that only a third of patients received treatment in compliance with the guidelines. In patients over 60 years and those with other risk factors who were arguably at greater risk of a poor outcome if treatment was suboptimal the compliance rate was as low as 17%.

Although de Beek et al could not show any obvious clinical detriment as a result of failure to comply with the approved regimen there are important lessons here. Clearly, there are many reasons why the uptake of such guidelines may be low. These include poor quality advice (for example, not evidence based or not practical), and poor dissemination of the information (targeting the wrong group of doctors, for example). Guidelines for the use of antibiotics are becoming increasingly popular as a means of improving the quality of care, but if they are to be effective they need careful consideration—not just of their content, but of how they are followed up and implemented.[5]

An additional but less obvious benefit of the publication of such guidelines is that they draw attention to changing practice in a rapidly moving field. At the time of the last leading article in the *BMJ* dealing with acute bacterial meningitis, just three years ago,[6] the management of penicillin-resistant pneumococcal infection was unclear and the role of corticosteroids debated. In the current recommendations from the society a combination of vancomycin and rifampicin is advised if resistance to penicillin is considered likely. Notably the use of adjunctive corticosteroids has changed after the recent publication of the European dexamethasone meningitis study, which showed a significant reduction in mortality in patients who were given dexamethasone 10 mg every six hours for four days and started just before or at the same time as the first dose of antibiotics.[7] However, though bacterial meningitis is a seemingly tractable infection, in this study the mortality from pneumococcal meningitis was still 14%, even in the group treated with steroids. There is still much to do.

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No-fault compensation systems

Experience elsewhere suggests it is time for the UK to introduce a pilot scheme

In 1978 the Pearson Commission in the United Kingdom rejected a no-fault system in dealing with clinical negligence. While declaring the existing tort system as costly, cumbersome, prone to delay, and too capricious in its operation to be defensible, the commission rejected no-fault compensation on grounds of the difficulty in overhauling the tort liability system and the perceived difficulties in causation judgments.[1] A general conservatism in the legal profession and opposition from the insurance industry were other factors. Much has changed in the NHS since then.

The long overdue white paper on the reform of the clinical negligence compensation system is much awaited. Reforms to be considered include fixed tariffs

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