

experience and reports across the UK show that the ethnic minority population still remains at risk of vitamin D deficiency. Efforts to promote vitamin D supplementation as recommended by the Department of Health<sup>3</sup> need to be implemented and targeted at the risk group.

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## A vaccine scare in 19th century Northampton

The controversy regarding immunisation is longstanding. Records from 1806 concerning a vaccine scare in Northampton give a flavour of events, which strike a contemporary chord.

The revelation of Edward Jenner's 1798 seminal work meant smallpox mortality fell from 31% in unvaccinated children compared to 1.2% in vaccinated.<sup>1, 2</sup>

Northampton General Infirmary made cowpox vaccination a high priority and was proactive in its approach, with free cowpox inoculation being undertaken on the hospital premises from 1804 onwards.<sup>3</sup>

On 10 January 1806 the Board of Governors dealt with a growing vaccine scare concerning alleged vaccine failure and one in particular, leading to the death of a child, Peter Bell.

"Gentlemen, the public mind having been lately much agitated by reports of the insecurity of the vaccine inoculations, we have endeavoured to investigate those instances of failures we have heard of and have invariably found such reports to be arrived at either by error or misrepresentation."<sup>3</sup>

However, to defuse the situation an affidavit signed by the parents of Peter Bell denying these rumours was published in the *Northampton Mercury*:<sup>3</sup>

### Article from the *Northampton Mercury*, 10 January 1806

"Whereas a false and groundless report has been spread about this town and neighbourhood that our son Peter Bell died on the 6th instant of smallpox after having been inoculated for the cowpox by Dr Kerr and the Infirmary now we do hereby declare that neither the above named child nor our child Ann Bell ever had the smallpox or the symptom or appearance of smallpox whatever. Both our said children were inoculated for the cowpox by Mr. Mills and both of them came safely through the disease. The eldest of them has been ever since in

perfect health and Peter the youngest having been always a weakly child had better health after the cowpox than ever he had enjoyed before until he was seized with a violent complaint in his bowels of which he died on 20th December last." (Signed by William Bell, guard to the Defiance coach; Sarah Bell, his wife<sup>3</sup>)

The following week on 17 January the Board of Governors reported.

"The Governors...having adopted the resolution of permitting the poor to be inoculated for the cowpox as outpatients...do hereby certify that we know of no incidence of any person having had the smallpox who had been previously inoculated for the cowpox."<sup>3</sup>

A register was however established with the hope: "By these means the practice of vaccination and its merits as a complete security against the smallpox will be gradually be brought to the test of unprejudiced experience".<sup>3</sup>

One could regard this as common sense, which today would be described as "clinical governance".

Doctors beleaguered in the present time through similar "misrepresentations" regarding immunisations should take heart that this is not a new problem, but perhaps managers could learn from the more robust attitude taken by our medical forebears when dealing with the media in these matters.

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## More evidence is needed in the antibiotic treatment of *Pseudomonas aeruginosa* colonisation

In presenting various therapeutic approaches for the management of cystic fibrosis (CF), Smyth primarily considers evidence obtained from The Cochrane Library as either systematic reviews of randomised controlled trials (RCTs) or RCTs.<sup>1</sup> The antibiotic treatment of *Pseudomonas aeruginosa* (PA) when first isolated, is still an open question. When discussing this aspect, Smyth considers only the RCT by Valerius and colleagues.<sup>2</sup>

In our critical review of published clinical studies evaluating the early antibiotic treatment in asymptomatic PA colonised CF patients,<sup>3</sup> we identified three relevant RCTs (two versus placebo).<sup>2, 4, 5</sup> Our study also included eight cohort studies, two of which

were with historical controls. Overall, 309 patients (range 7–91) were recruited. There was a high variability between the individual studies for age, outcome measures, duration of follow up, and treatment (three studies: two RCTs; 1 cohort used only aerosol tobramycin, 1 colistin, 4 aerosol colistin plus ciprofloxacin, 1 intravenous treatment, and 2 miscellaneous therapy).

An overall critical evaluation indicated that early antibiotic treatment can reduce the rate of positive cultures and of anti-PA antibody titres. Long term benefit is expected but not yet proven. Moreover, we recently conducted an observational study which found that nearly all CF centres in Italy treat asymptomatic PA colonised patients in order to prevent or postpone chronic pulmonary infection (unpublished data). However, the adopted prescribing practice varies largely even within the same centre, highlighting the existing lack of formal consensus on this subject.

Several therapeutic options (aerosol therapy alone or oral therapy associated with aerosol inhalation) are available for the early treatment of PA colonisation, but no direct comparison has so far been made. Prospective multicentre randomised studies with relevant outcomes measures<sup>6</sup> are needed to investigate which of the different proposed antibiotic schemes has the best benefit/risk ratio and the best patient compliance.

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## Community needlestick injuries may still be dangerous

We read with interest the report by Makwana and Riordan on community needlestick injuries in children.<sup>1</sup> We do not believe, however, that the authors have presented sufficient data to support their conclusion that routine follow up after community needlestick injury is unnecessary.

In their study only 25 children had complete serological follow up. Their literature review cites three additional papers in which children were followed up after needlestick injury. Adding all of these children gives a total of 138 children who had

serological testing following needlestick injury. This is an insufficient number to allow one to conclude with confidence that the risk of transmission is low.

If all of these needles contained HIV positive blood, applying the rule of threes<sup>2</sup> to the pooled data, we can say with 95% confidence that the risk of HIV transmission following community needlestick injury in children is less than 2%. The transmission rate in healthcare workers following HIV positive needlestick injury is around 0.35%. Their study, therefore, does not provide sufficient evidence to state that these children are at a lower risk of acquiring HIV following needlestick injury than healthcare workers in similar circumstances. Until such evidence becomes available, there seems to be no good reason to treat these children differently to healthcare workers following needlestick injury.

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## Authors' reply

We were interested to read this letter. The authors feel that children with community needlestick injuries should be treated the same as healthcare workers. This seems to miss the point of our paper. Hospital needlestick injuries are very different to out-of-hospital needlestick injuries: the blood is generally dry, so therefore less likely to be infectious;<sup>1</sup> the injuries are often superficial—again less likely to be infectious;<sup>1</sup> and, although the HIV status of the needlestick user is often unknown, the incidence outside of London is very low.

The risk of HIV transmission is estimated to be less than 1:100 000.<sup>2</sup> Our study was not designed to show the risk of transmission (which incidentally would need a study of more than 100 000 patients), but showed that only half those offered follow up returned for their appointment. Studies examining needlestick exposure and HIV seroconversion have shown that no children seroconverted despite not receiving HIV post-exposure prophylaxis.<sup>3–5</sup> Within this population of children were included those who sustained injuries from areas with a high prevalence of injecting drug use. Zamora and colleagues<sup>6</sup> evaluated HIV-1 proviral DNA from 28 discarded syringes of intravenous drug users and found no traces of the virus, concluding that the risk of HIV transmission in that setting was zero.

These children are therefore in a low risk group for transmission of infectious viruses, and together with the low rate of attendance for follow up, it is still reasonable, we feel, to offer follow up to those children who have high risk injuries or in whom parents have a high level of anxiety.

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## Interpreting immunogenicity data in UK studies

It has become increasingly clear that interaction between vaccines is an important consideration for immunogenicity studies. Only full information on all vaccines used in a particular population will allow correct interpretation of immunogenicity data.<sup>1</sup> This is particularly important where comparison is made to historical controls in a rapidly changing schedule such as that used in the UK, or where immunogenicity data obtained using vaccines that differ significantly from those currently in use are subsequently used to guide practice.

It also apparent that the “best” combination of specific vaccines, the effects of interactions of conjugate proteins, the optimal timing of the primary course, and the necessity for boosters within the UK schedule are all currently unclear. Certain groups of infants may require separate consideration, for example those born preterm or from specific ethnic backgrounds.

We therefore read with interest the data presented by Booy *et al* of responses to primary series immunisation in Asian infants born in the UK to a population of parents of whom “most” (88%) were born abroad.<sup>2</sup>

Based on the achievement of an anti-PRP GMT of 15 µg/ml, Booy *et al* are reassured that vaccination with PRP-T should protect this population from Hib meningitis. We are uncertain as to whether this confidence is justified. There is no clear description of the exact vaccines administered to their population, or of when the study took place. PRP-T and DTP were administered in separate limbs, but the nature of the pertussis component of the DTP (whole cell [DTPw] or acellular [DTPa]) is unspecified. Since DoH advice from 1996 was for combined single limb injection of PRP-T and DTP, we assume that the study predates 1996.<sup>3</sup> Given that DTPa was introduced in 1999,<sup>4</sup> we therefore also assume that the study DTP was DTPw. Separate limb administration of DTP, or using DTPw may result in a higher anti-PRP GMT in comparison to that achieved by infants receiving either combined vaccines<sup>5</sup> or an acellular DTP<sup>6</sup> (or a combination of this, as with the UK's new vaccine, Pediacel).

While Booy *et al* comment on their study as “descriptive and uncontrolled”, they do include a historical cohort of controls. Neither the original publication of the control

data,<sup>7</sup> nor this present publication clearly describe to the reader the actual (as opposed to planned) timing of important study interventions (vaccine administration, vaccine intervals, blood sampling in relation to vaccines), with the exception of acknowledging that the median time of primary course completion differed between the two groups. Clear descriptions of study timings would allow the reader to consider whether the populations are crudely comparable; alternatively a statistical analysis could have been performed that would take account of these differences. Without this the difference in GMTs is without context. Placing the data in context may help explain the otherwise very surprising finding that Asian infants appear to respond three times as well to PRP-T as Caucasians.

It would also be interesting to know the limits of detection for the anti-PRP assay, and how results above or below these limits were handled—the 28 (or 34) infants having surprisingly tight 95% confidence intervals around their GMT for such small numbers of infants.

Given the recurrence of Hib disease in the UK, the question of how well UK infants respond to PRP-T is clearly very important, as well as whether or not UK infants (like most others) should receive a fourth (booster) dose. Careful studies that help to address these questions are crucial. We would welcome the additional information from Booy and colleagues that would allow this current information to be more readily interpreted.

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## Car seat safety for premature and LBW infants

Recent advances in neonatal intensive care have resulted in improved survival rates of premature and low birth weight infants. These infants are frequently transported in the parent's own vehicle when discharged from hospital. Commercially available infant car seats are primarily designed for a typical