asthma need to be appraised critically. For example, the number of admissions to hospital is often used as evidence of bad care of asthma in general practice. Admission to hospital may, however, often be appropriate. If we can remove the stigma attached to admissions for acute asthma generated by general practitioners junior hospital doctors may take our referrals for admission more seriously.

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AUTHOR'S REPLY,—I did show an increase in the number of peak flow recordings obtained post-clinic, although these were well short of the agreed standard of 100%. We hope to achieve our agreed standard before the audit cycle is repeated.

The clinic is run by a trained asthma nurse. We now prescribe peak flow meters for all our asthmatic patients, but this was possible only after the clinic had started. We are educating our patients about how to manage an acute attack on the basis of their own serial peak flow readings.

I did not include a definition of asthma in my paper as it was adequately defined in one of my references, and this is the working definition that we use.[1] The term known asthmatic patients diagnosed in 1989 refers to those patients identified as asthmatic by one of the doctors in our practice at some previous time, based on commonly accepted criteria in the history and physical examination but not necessarily on more objective measurements such as serial peak flow readings and reversibility tests. The increased proportion of asthmatic patients entered in the computer post-clinic largely represents previously known asthmatic patients not clearly identified as such before the asthma clinic was started.

Finally, the numbers of admissions to hospital that I recorded pre-clinic and post-clinic are too small for any worthwhile comment to be made on that aspect of the audit, although I agree that no general practitioner should hesitate to recommend admission for patients with acute asthma if in his or her clinical judgment this is appropriate.

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Site for immunising infants

SIR,—I do not agree with Angus Nicoll about the accepted site for immunising infants in general practice.[1]

I and colleagues conducted a most thorough search of published reports, both clinical and medicolegal, and consulted every leading authority during a dispute that we had with our local health authority over this matter in 1984.[2] Paediatricians advised us that this was not a matter for specialist pronouncement but one in which general practitioners had most experience. The Medical Defence Union, after giving a knee jerk warning against using the buttock, consulted its records for instances of injury. It reported 22 cases: 17 injuries to the radial nerve and five to the sciatic nerve, none of which had occurred in infants. Baraff *et al* showed that local reactions, notably pain and swelling, were more common after immunisation in the thigh.[3] Bergeson *et al* stated that the most common serious complications of intramuscular injections in children were muscle contractures and nerve injuries,[4] most of which were radial nerve palsies. Some children have required excision of fibrous tissue and lengthening of the triceps.

How did the strong fear of the sciatic nerve arise? Gilles and French showed from studies on young animals that penetration of the sciatic nerve did not cause palsy.[5] Nor was palsy due to ischaemia from interruption of the vascular supply or to intraneural haemorrhage. The final conclusion reached was that substances injected, such as streptomycin, antitoxins, bismuth, and quinine, were neurotoxic. But measles, mumps, and rubella vaccine is not neurotoxic, and in any case the sciatic nerve cannot be reached with the 16 mm needle used now, even in a test on a stillborn infant weighing 2000 g.

The infant prone across the mother's lap provides the most stable position for mother, baby, and doctor. Most important, the child does not observe the assault.

Finally, with regard to Nicoll's comment about effective absorption, we were given expert advice against rapid absorption: the child's immune system is immature, and, unlike a brush antigen without cells like hepatitis B vaccine, diphtheria, tetanus, and pertussis vaccine needs to be absorbed slowly. I hope that the buttock will become the preferred site for injections before the age of 1 year.

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High dose triazolam and anterograde amnesia

SIR,—In the context of the controversy surrounding the safety of the hypnotic benzodiazepine triazolam[1-5] we report the findings of an unpublished study performed in 1977, which support a relation between the dose of triazolam and the incidence of anterograde amnesia.

We studied 44 psychiatric patients admitted to the emergency psychiatric department of Liège University Hospital with symptoms related to personality disorders (n=26), psychoses (n=10), and adjustment disorders (n=8). There were 20 men and 24 women aged 17-66 (mean (SD) 35·4 (12·8) years). With their informed consent patients received triazolam 2 mg at bedtime for their acute insomnia for 1-19 days (mean 4·2 (3·6) days). No other psychotropic drugs were given. The patients' behaviour at night was observed by the psychiatric resident on call (P-FP or DS) as well as by the nursing staff. An independent resident interviewed the patients the next morning to assess their memory of the behaviour observed during the night.

Twenty two patients did at least one thing at night that they could not remember subsequently. The most common event was nocturnal bulimia (n=13): patients ate some of their own sweets or took their neighbours' supply or emptied the unit's fridge. Other motor behaviour was observed in six cases, from simple walking in the corridor or making telephone calls to leaving the unit and, in one case, driving a car and returning several hours later. Six patients showed increased anxiety with typical panic attacks, and five patients verbalised suicidal thoughts, which did not appear in their history or in the assessment performed the previous day or the next morning. Suicide attempts were noted in four patients concurrently with the suicidal ideation, and heteroaggressive acts in two patients. None of the patients recalled these adverse events during the interview the next morning. The adverse events stopped in 21 patients when triazolam was stopped.

This study shows an extremely high incidence of amnesic adverse events associated with high dose triazolam. Amnesic bulimia at night was so common that we called it "the triazolam fridge syndrome." Triazolam was first marketed in Belgium in 1977. The normal recommended dose then was 0·25-1 mg; we gave 2 mg. The recommended dose now is 0·125-0·5 mg.

Several previous reports have described anterograde amnesia associated with triazolam at lower doses, but with a much lower incidence.[6-10] Our study suggests that the dose of triazolam is a crucial factor in the incidence of amnesic reactions.

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Monitoring lithium treatment

SIR,—R F Kehoe and A J Mander report serum lithium concentrations in excess of 1·05 mmol/l in 56 of 458 patients taking lithium during a one year period and note that in one third of these cases the doctor did not make any response within six weeks.[1]

These findings, while giving cause for concern, may in fact compare favourably with the practice in parts of the country where no lithium register is kept. Recently a lithium audit was carried out in the department of psychiatry, North Manchester General Hospital, a district general hospital serving a catchment population of 200 000. Of 201 patients identified as taking lithium, the case notes of 56 were selected at random for examination. Of 37 patients who had been taking lithium for three or more years, eight were found to have had, during the year of audit, a serum lithium concentration $\geq$1·3 mmol/l. In only five of these cases was there evidence in the case notes of the doctor having initiated any response.

Perhaps more worrying was the finding that, of the 31 patients who had been started on lithium within the previous five years, there was confirmation in the case notes of there having been a prior physical examination in 20, a medical history in 18,

and a review of systems in only seven. A clear statement of the indications for treatment with lithium was found in 18 of the notes, while an explicit treatment plan had been preserved in only five.

In none of the case notes was there a record suggesting that the patient had been informed of the possible side effects or toxicity of lithium, nor of the need to have regular blood tests and to maintain adequate fluid intake. Lithium is known to be a toxic drug and patients are undoubtedly given information about its use, but this should be recorded, particularly in view of recent medicolegal interest in the use of lithium.

Kehoe and Mander comment that certain aspects of lithium prescribing and monitoring habits give cause for concern; our audit suggests that this concern should also be extended to the period when lithium is first prescribed and to the recording of treatment and advice given.

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Is *Bordetella pertussis* clonal?

SIR,—M N Khattak and colleagues were right to finish their title with a question mark.[1] Although their elegant study shows the discriminatory power of genotype analysis by restriction enzyme digestion and pulsed field gel electrophoresis and its suitability for typing and epidemiological tracing, we do not agree with the conclusion that their results fail to support the hypothesis that this organism is essentially clonal.

The operational definition of clones provided by Ørskov and Ørskov describes them as "bacterial cultures isolated independently from different sources, in different locations and perhaps at different times, but showing so many identical phenotypic and genetic traits that the most likely explanation for this identity is a common origin."[2] Implicit in this concept is the requirement that the specific combinations of chromosomal genes coding for characters identifying clones are not rapidly broken down by recombination and mutation.[3] The authors' demonstration that six of the seven DNA types found in German strains—accounting for 22 of the 23 strains studied—were also found in the United Kingdom indicates to us that for these markers the rates of change caused by recombination and mutation are slower than the rates of spread of these organisms through western Europe, thus leading to the occurrence of statistically overrepresented, widespread, identical genotypes, a coincidence of features which is a strong criterion of clonality.[4] Our view is that rather than refuting the clonal concept for *Bordetella pertussis* the pulsed field gel electrophoresis data provide quite good evidence favouring the hypothesis that in genetic terms this organism has a relatively stable, and clonal, population structure.

The inability of simple electrophoresis of restriction fragments of whole DNA produced by *Eco* RI, *Sma* I, *Nci* I, *Bam* HI, *Ava* I and *Bgl* II to discriminate between strains suggests that they are very closely related. Whether these European strains are members of a single clone with pulsed field gel electropherotypes defining subclones, or whether these define clones in themselves, cannot be answered from the data to hand; information on the extent of linkage disequilibrium and further studies using other markers of genotype and phenotype would clarify this situation. It seems to us that the authors have answered the question posed by the title of their paper in the affirmative; the really important question that remains—albeit one that they have begun to address—is whether whooping cough in Britain and Germany is caused by one, or several, clones of *B pertussis*.

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AUTHORS' REPLY,—T H Pennington and K J Forbes suggest that the 17 distinct DNA types generated by pulsed field gel electrophoresis identify "subclones" and that *Bordetella pertussis* is essentially stable and clonal. It is unclear as to how they make the distinction between clones and subclones. Phenotypically *B pertussis* is not particularly stable. It shows striking colonial variation on repeated subculture;[1] changes in agglutinogen type occur both during infection and in response to vaccination;[2] and phase variation (loss of virulence factors) occurs at a frequency of one per 10^3 or 10^6 organisms.[1,3]

The types isolated by pulsed field gel electrophoresis that we describe were stable on repeated subculture and persisted after cross infection between siblings, yet they were clearly distinguishable in the four different pairs of siblings. In the light of these distinct, stable genetic differences it seems difficult to argue the case for clonality. Pennington and Forbes cite "the occurrence of statistically overrepresented, widespread, identical genotypes" as a strong criterion of clonality, yet we showed that the predominant genotype in the United Kingdom was not found among the 23 isolates examined from Germany.

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Physiotherapy intervention late after stroke

SIR,—In their paper on the effectiveness of physiotherapy on mobility late after stroke, Derick T Wade and colleagues went to great pains to develop a cross over study design which introduced blind assessment and controls.[1] This attention to design is not typical of research in stroke rehabilitation and the authors are to be congratulated. However, the results are ambiguous.

The study showed that mobility (as measured by time to walk 10 metres) decreased by about four seconds during the treatment phase but increased after treatment. This would be expected if the physiotherapy intervention was very active and required regular and specialised exercises. However, table II shows that much of the intervention was of an advisory and educational nature, including the provision of more appropriate aids. It is therefore worrying to note a decline in mobility in the period immediately after treatment in both groups (6·5 seconds in the early treatment group and 2·6 seconds in the late treatment group). The fact that these increases are not statistically significant is due to the acknowledged low power of the study.

These results strongly suggest that the improvement during treatment might be a placebo effect due purely to the attention given by the physiotherapist rather than the direct result of the interventions mentioned. The fact that the possible placebo effect was confined to changes in gait speed is probably a reflection of the lack of sensitivity to change of the other outcome measures, as is acknowledged by the authors.

A cross over design in drug treatment trials is invariably associated with the use of either a placebo or an alternative treatment. In such trials the differences in outcome between the treatment period and non-treatment period can be more confidently attributed to the treatment. In this study, because patients received no treatment or placebo in the non-treatment period it is impossible to disentangle the treatment effects of physiotherapy from any placebo effects.

Physiotherapy consists of more than direct physical treatment, also having a significant psychological component. Therefore the authors must be careful when they attribute the positive outcome to the more physical aspects of the intervention, for it is possible that a similar outcome could have been achieved by using other personnel such as well motivated and supervised volunteers, as has been shown in speech therapy after stroke.[2]

Although we recognise that finding placebos for physical and counselling interventions is much more difficult than in pharmacological areas, it is important that attempts are made to develop ways of controlling for placebo effects in an area where attention and care are likely to have significant beneficial effects on patients' performance.

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AUTHOR'S REPLY,—Trevor A Sheldon and his colleagues should reread the first sentence of our abstract: "To determine whether the intervention of a physiotherapist improved mobility. . . ." Rehabilitation is a problem-solving, educational process aiming to minimise handicap. Its reiterative components include assessment, planning (goal setting), intervention, and evaluation (reassessment) and each of these can be further subdivided. Few components of this process can be so isolated that effects can be attributed to one specific item. We were very careful to state throughout that the trial investigated the effect of being seen by a physiotherapist.

Next, if attention alone had caused improvement in gait speed why was no change seen in manual dexterity or mood? Why should attention specifically and only improve gait speed?

One cannot assume that volunteers might be as effective without further trials. The volunteers in speech therapy trials were given the results of assessments and were supervised by trained therapists. The equivalent would be for the first "assessment" visits to be undertaken by a trained therapist, followed by visits by volunteers with trained therapists supervising. As the average number of visits was four, this seems uneconomic.