evaluating new asthma treatments. They provide no evidence, however, that long duration as against short duration asthma studies are any less subject to background variation in control of the patients' asthma: indeed this remains an area of controversy. There is much to support short duration studies in asthma as they avoid the effects of season and involve less interference with the patients' usual treatment. Also, as shown by one of our excluded patients, the child actually worsened on the placebo treatment. Extended studies are therefore not without hazard to our patients.

Studies with limited numbers of patients may run the risk of a type I statistical error,² which we guess is the point Dr Davies and colleagues are trying to make when they criticise the number of patients in our study. The risk of this sort of error can, however, be lessened by only accepting a significant result with a lower P value. If Davies and colleagues had carefully read our paper they would have noted only P values less than 0.01 were accepted, rather than the usual arbitrary but higher value of 0.05. Every experimental design must be efficient and having reviewed early workers' results³ we estimated⁴ that the critical size of our study should be 10 patients. Such estimates are more valuable than an arbitrary statement or decision as given by Davies and colleagues that the study was too small.

Their observations on the experimental design are unfortunately wrong. The study was completely double blind. There is no mention in our study that either patient or doctor knew when the patient was on active treatment. During the run in period for the placebo drug the tablet dose was adjusted randomly; blood was also taken from all patients for assay. As a result the active and placebo periods had matching behaviour for doctor and patient.

We do not agree that the paired *t* test is inadequate for our data. It is a test ideally suited for comparing two treatments given to the same patients, that is, where there is dependence between the two groups. They state without evidence that non-normality of distribution of data seriously invalidates our comparisons, however this is not true for either ANOVA or the *t* test, which is also based on ANOVA. They generalise, stating that all our data is non-normal, while if they had 'carefully' inspected the data such a criticism can only be justified for the frequency of awaking data and there it is not serious. As for the comment that variances in the groups differ, if they had cared to test for this using an F test they would discover that none were significantly different at a P value below 0.05. Davies and colleagues have fallen into a not uncommon error of failing to appreciate that fluctuations of sampling are commonly a cause of minor differences in variation. We suspect they would have leapt straight to a non-parametric test. Again this is not an uncommon mistake but should be avoided.

We finally come to their rather surprising 'juggling' with the data which enables them to conclude that 6 of our 13 children did not benefit from treatment. We reported that out of 10 patients with completed records, nine had increased morning peak expiratory flow rates and nine had reduced beta agonist usage. Perhaps we were 'too' honest in reporting all the patients studied. Two of the 13 could not be analysed as they failed to complete the diary records

and conclusion cannot be drawn from their incomplete data. One patient became so unwell on placebo that he required admission to hospital. This shows that far from not being ineffective, the patient had indeed benefited from the active treatment. Again this emphasises the risk of extended periods of placebo treatment.

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Urological diagnosis in utero

Sir,

In his survey on urological diagnosis in utero¹ Mr Thomas recommends that in neonates in whom an abnormality has been diagnosed antenatally but in whom ultrasound in the first days of life shows a seemingly normal urinary tract or only minimal dilatation, no further investigations should be performed. We have some doubts as to the correctness of this statement. We believe that by following this advice some functional abnormalities of the urinary tract which should be recognised early in life as they may benefit from prophylactic or corrective treatment will be missed. We recently observed a child in whom antenatal ultrasonography at 35 weeks showed pronounced bilateral dilatation of the renal calyces. A control ultrasound performed immediately after birth was normal. Cystourethrography at the age of 3 weeks showed massive grade IV vesicoureteral reflux in the left ureter and kidney. A control ultrasound at 3 weeks confirmed the noticeable dilatation of the left ureter and calyces. Ureterostomy was performed at the age of 6 weeks. Similar experiences have been reported by others.²

The fact that after the normal postnatal ultrasound we will assure the parents that no further investigations are needed will in all probability lead to further delay in the recognition of these functional abnormalities. We should also take into account the psychological impact of contradictory findings on the parents. We, therefore, would advise caution when interpreting ultrasonography during and immediately after pregnancy and we believe that radiological investigations should be performed when dilatation of the urinary tract is found, even if the postnatal ultrasound is normal.

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Mr Thomas comments:

Drs Roodhooft and Van Acker advocate a routine cystourethrogram for any neonate whose prenatal ultrasound scan has been equivocal—even though the initial postnatal scan shows an apparently normal urinary tract. This approach would certainly pick up the occasional child with unsuspected vesicoureteric reflux—but at the price of subjecting a large number of normal neonates to an unnecessary and invasive investigation. Until data becomes available to indicate the incidence of reflux in babies with ultrasonically normal upper tracts, I will continue to investigate only those with a degree of dilatation on the initial scan (or on a follow up scan at 1 or 3 months of age).

Much depends on the initial postnatal scan. In the case cited by Drs Roodhooft and Van Acker, it is perhaps surprising that the degree of dilatation associated with grade IV reflux was not detectable on the first scan when it had been visualised prenatally and later at 3 weeks of age. If the initial scan is, for any reason, technically unsatisfactory, it would certainly be prudent to repeat the scan at 1 month rather than the 3 months suggested in the annotation.

Clonidine and insulin tests for growth hormone deficiency

Sir,

The oral clonidine test has been recommended in the investigation of suspected growth hormone deficiency.^{1 2} While recognised that it may cause hypotension and drowsiness,³ it is thought to be preferable to the insulin tolerance test which is 'acknowledged to be unpleasant for the patient and potentially dangerous'.¹

We have, therefore, recently been using clonidine but have been concerned that the hypotension has sometimes been symptomatic. We should like to report the case of one child in which this was severe.

This girl was a growth retarded first twin who failed to match the growth progress of the second twin. While certain dysmorphic features were apparent we wished to

exclude remedial causes of growth failure including growth hormone deficiency. Two hours after an oral dose of clonidine (0.15 mg/m²) her blood pressure dropped from 115/70 to 85/40 (electronic doppler measurement using Dynamap, Critikon Ltd with appropriate cuff size), her pulse rising from 115 to 180/minute. She became pale and unresponsive with peripheral hypoperfusion, requiring resuscitation with intravenous plasma. Within half an hour she was well. The investigation showed her growth hormone response to be normal.

While recognising that this case is somewhat unusual, we do feel that it serves as a reminder that, like the insulin tolerance test, the clonidine test should not be undertaken lightly, requiring close patient monitoring and the immediate availability of resuscitative facilities.

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Pallid syncope

Sir,

Like a malingering teenager, a toddler may overbreathe, hold his breath, and faint. What happens next depends on his position. If he falls flat he usually recovers quickly; if his mother picks him up and holds him upright in her lap or over her shoulder, unconsciousness and bradycardia are prolonged, and he may jerk like the unfortunate patient who faints while in the dentist's chair. The appearance is similar to that of the child whose vagus over responds to a stubbed toe. As Dr Bower¹ emphasises, the history is important; and advice to hold or leave the child horizontal may sometimes be more appropriate than atropine.

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