

airway obstruction and not against its causes will not be beneficial.

I AMIRAV
Paediatric Department,
Rebecca Sieff Government Hospital,
13100 Safed,
Israel

- 1 Skoner DP, Fireman P, Davis HW, Wall R, Caliguini LA. Increases in plasma concentrations of a prostaglandin metabolite in acute airway obstruction. *Arch Dis Child* 1989;64:1112-7.

Drs Skoner and Fireman comment:

In response to Dr Amirav: (1) Persistence of post treatment rises of the measured prostaglandin $F_{2\alpha}$ metabolite were not unexpected, as this metabolite is stable in plasma and may be detectable for hours after the release of prostaglandin $F_{2\alpha}$, which has a relatively short half life. (2) All of the infants in group II (infants after treatment) had residual signs of airway obstruction. (3) Pulmonary function testing would certainly be superior to clinical parameters in assessing the degree of airway obstruction, but this methodology was unavailable and may be unreliable in infants. (4) Inflammatory mediators are released either as a primary event causative of a disease process or as a secondary event, which may not be related to pathophysiology. In either case, the relationship of the mediator to the pathophysiological process is very complex, as inflammation is likely an orchestrated response, with release of multiple mediators simultaneously and synergism or antagonism between various mediators in provoking pathophysiology. Additionally, the desired human pathophysiological response may be inaccessible to direct measurement. As such, absolute proof of a causal relationship between a mediator and a pathophysiological process is frequently lacking and rests on a body of indirect rather than direct evidence.

Three criteria for implicating a mediator in disease pathophysiology are generally accepted: (1) recovery at or near the site of active disease; (2) reproduction by exposure to the mediator; and (3) attenuation or prevention by pretreatment with a mediator antagonist. The results of our study indicate that a metabolite of prostaglandin $F_{2\alpha}$ was detectable in plasma during acute airway obstruction and satisfy criteria (1). Other investigators have documented that inhaled prostaglandin $F_{2\alpha}$ can cause bronchoconstriction (criteria 2).¹ This evidence, although suggestive, is insufficient to prove a causal relationship. In situations such as this, clinical trials with specific antagonists (criteria 3) can provide confirmation that a given mediator participates in a pathophysiological process. For this reason, we believe that therapeutic trials using specific anti-inflammatory agents for the treatment of airway obstruction are warranted.

- 1 Mathe AA, Hedqvist P, Holmgren A, Svanborg. Bronchial hyperreactivity to prostaglandin $F_{2\alpha}$ and histamine in patients with asthma. *Br Med J* 1973;i:193-6.

Diagnostic accuracy of pH monitoring in gastro-oesophageal reflux

SIR,—Da Dalt and colleagues believe their data show that a pH study has 100% sensitivity and 94% specificity for the diagnosis of

gastro-oesophageal reflux.¹ In particular, in their discussion they make comment of the fact that they did not find any false negatives and conclude that a negative result must be thought of as being sufficient to rule out gastro-oesophageal reflux.

In order to comment about the sensitivity or specificity, a comparison must be made with a gold standard. In the study by Da Dalt and colleagues, the indication for 24 hour oesophageal pH study was a clinical suspicion of gastro-oesophageal reflux. If the pH study was negative, the children were followed up clinically for a period ranging from eight months to two years. On the basis of the observations made over this period of time, the authors decided none of these children had gastro-oesophageal reflux. I would be very sceptical that clinical follow up was sufficient to use as a gold standard and would be reluctant to accept that clinical suspicion would be used as an indication for a test on the one hand, and then subsequently as the confirmation that the test was accurate.

By contrast, the gold standard used for confirmation that abnormal tests were indeed abnormal was the combination of a barium swallow or oesophagoscopy, or both. Although no indication is made of what constituted a positive barium swallow examination or an oesophagoscopy, we can be more confident with the specificity of the test. It would be useful to know whether the oesophagoscopy included a biopsy.

Finally, I question the conclusion that pH monitoring should be used as the first line of investigation in the diagnosis of gastro-oesophageal reflux. A case may be able to be made for this suggestion in children admitted to hospital, but the extrapolation that the diagnosis of gastro-oesophageal reflux in a child who is an outpatient should involve his or her admission to hospital, is premature.

R L HENRY
The University of Newcastle,
Rankin Drive,
Newcastle, NSW 2308,
Australia

- 1 Da Dalt L, Mazzoleni S, Montini G, Donzelli F, Zachello F. Diagnostic accuracy of pH monitoring in gastro-oesophageal reflux. *Arch Dis Child* 1989;64:1421-6.

Drs Da Dalt, Mazzoleni, Montini, Donzelli, and Zachello comment:

We are grateful to Dr Henry for the comments on our paper and for the opportunity to clarify some aspects of our study.

We agree with the necessity of a gold standard but we would like to point out that neither barium swallow nor oesophagoscopy have got the characteristics to be a gold standard in the diagnosis of gastro-oesophageal reflux.¹

For that reason and for ethical considerations we decided not to perform these examinations on children with normal pH study and we thought that a clinical follow up would be sufficient. In fact in most of these children symptoms disappeared spontaneously because they were due, we think, to a physiological gastro-oesophageal reflux, which is not detected as abnormal by pH study and for which no treatment is necessary. Only in a few children, in whom symptoms were persistent, did we reach a different final diagnosis such as coeliac disease, anorexia, etc.

We also would like to point out that in

patients with an abnormal pH study we performed a barium swallow and/or oesophagoscopy especially in order to rule out structural anomalies; however, a radiological gastro-oesophageal reflux was diagnosed when at least two episodes of spontaneous reflux were present in five minutes (according to Meyers *et al*²). A biopsy was performed in all our oesophagoscopies and signs of oesophagitis were always present.

Finally we agree with Dr Henry that not all children who vomit need a pH study or other examinations, but we think that when a major clinical problem is present and an important gastro-oesophageal reflux is suspected, admission is to be considered. An alternative could be to perform an ambulatory 24 hour pH study; this has recently been attempted even in children.³

- 1 Sondheimer JM. Gastroesophageal reflux: update on pathogenesis and diagnosis. *Pediatr Clin North Am* 1988;35:103-16.
2 Meyers WF, Roberts CC, Johnson DG, Herbst JJ. Value of tests for evaluation of gastroesophageal reflux. *J Pediatr Surg* 1985; 20:515-20.
3 Sondheimer JM, Haase GM. Simultaneous pH recording from multiple oesophageal sites in children with and without gastroesophageal reflux. *J Pediatr Gastroenterol Nutr* 1988;7: 46-51.

A catabolic state in dexamethasone treatment of bronchopulmonary dysplasia

SIR,—Dexamethasone treatment is being increasingly used in babies with bronchopulmonary dysplasia because of reports of its benefit.^{1,2} We have reviewed the effect of treatment in the first nine infants we have treated. All were infants with bronchopulmonary dysplasia who had been ventilated from birth for respiratory distress syndrome. Gestation ranged from 25 to 30 weeks (mean 27.5) and birth weight ranged from 740 to 1510 g (mean 1050). Four babies had required surgical ligation of a patent ductus arteriosus. Dexamethasone was commenced between days 32 and 67, and the starting dosage varied between 0.46 and 2.13 mg/kg/day (mean 1.07). The infants' ventilatory requirement had been either static or deteriorating over the week before treatment. We found the treatment effective in the short term managing successfully to extubate all the infants within a week and seven of nine by the third day of treatment.

There has been concern over the incidence of side effects including hypertension, septicaemia, necrotising enterocolitis, hyperglycaemia, and the possibility of longer term adrenal suppression. In our patients infection, hypertension, and hyperglycaemia did not cause any real problem. Three of our nine patients, however, required prolonged courses in excess of five weeks to maintain the effect and appeared to exchange dexamethasone for ventilator dependence; this is of particular concern with regard to possible adrenal suppression.

We would highlight the fact that a pronounced catabolic state developed on commencing treatment, to our knowledge this has not been commented on in previous reports. Mean weight gain fell to -57 g/week from +190 g/week; only one infant gained any weight in the first week of treatment and all had previously been gaining weight. Blood urea concentrations averaged over the first week on treatment were 5.43 times those of

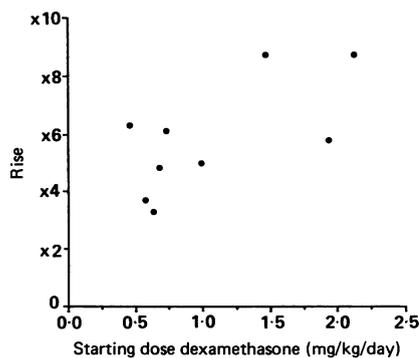


Figure 1 Weight change during first week.

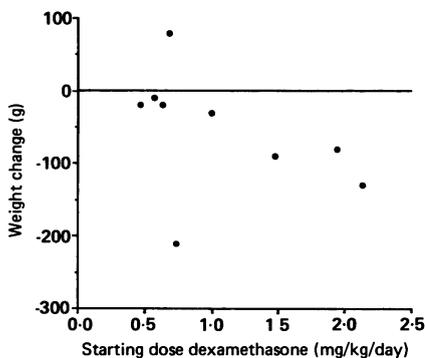


Figure 2 Rise in blood urea concentrations.

the week before treatment (before treatment mean 0.87 mmol/l and on treatment mean 4.73 mmol/l). This catabolic state appeared to be a dose related effect (see figs 1 and 2).

The importance of adequate nutrition in premature infants is well accepted and the likelihood of inducing a catabolic state should be borne in mind when considering dexamethasone treatment. Future studies of growth and nutrition in premature infants should take into account the use of dexamethasone, and further studies of the role of dexamethasone in bronchopulmonary dysplasia should include the effectiveness of lower dose treatment.

P D MACDONALD
P GALEA
L G ALROOMI
Glasgow Royal Maternity Hospital,
Rottenrow, Glasgow
G4 0NA

- 1 Mammel MC, Green TP, Johnson DE, *et al.* Controlled trial of dexamethasone therapy in infants with bronchopulmonary dysplasia. *Lancet* 1983;i:1356-8.
- 2 Avery GB, Fletcher AB, Kaplan M, *et al.* Controlled trial of dexamethasone in respirator dependent infants with bronchopulmonary dysplasia. *Pediatrics* 1985;75:106-11.

Which routine test for kidney function?

SIR,—In a recent article Parkin, Smith, and Brocklebank studied some simple tests for assessing glomerular filtration rate in children with known renal disease.¹ One of the tests studied performed better than the others. It was a height:creatinine index, where a value below 2.1 indicated a low glomerular filtration rate with a sensitivity of 91%.

The calculations for the predictive values of the different tests, however, have also been calculated from the 80 samples in their study.

Table 1

	Test result	Plasma clearance of ⁵¹ Cr edetic acid		Total
		<80 ml/min	>80 ml/min	
Height:creatinine <2.1	+	20	100	120
	-	2	378	380
		22	478	500

Table 2

	Test result	Plasma clearance of ⁵¹ Cr edetic acid		Total
		<80 ml/min	>80 ml/min	
Height:creatinine <1.5	+	15	10	25
	-	7	468	475
		22	478	500

Twenty two of these were from patients with a low glomerular filtration rate. The prevalence of low glomerular filtration rate in this group is 28%. The prevalence of the disease, for which one is looking in the tested population, influences the predictive values for the test quite a lot. The only thing the reader of the article knows about these children is that they all have a renal disease, and that the physician caring for them has decided to measure their glomerular filtration rate by ⁵¹Cr edetic acid clearance. A prevalence of low glomerular filtration rate of 28% in this group means that the process of selecting these 72 children, who were tested, from all the others with known renal disease has been quite efficient. The authors now propose that this unknown procedure is to be replaced by using height:creatinine <2.1 as the selecting instrument for suspicion of low glomerular filtration rate. Let us see what happens. The prevalence of reduced glomerular filtration rate is low in the population. Let us presume that the general practitioners with an interest in paediatrics, who are the non-nephrologists the authors recommend the test for, will have to think about the renal function in at least 500 cases of renal disease before they will find 22 cases with low glomerular filtration rate. Using the sensitivity and specificity given in the article we can calculate the following table (see above: table 1).

From this table we can get the predictive value of a normal test to be 99%, but the predictive value of an abnormal test is only 17%.

The authors don't recommend the height:creatinine index <1.5 because its sensitivity is too low. What will happen if we apply it to the 500 children we are talking about with a renal disease and unknown renal function? (see above: table 2).

The predictive value of a normal test is still very good, 98%, and the predictive value of a pathological test is much better, 60%. But this test leaves one third of the group we are looking for undetected. So even if we only have to make 25 clearance tests to find 15 of the 22 with a low glomerular filtration rate compared with 120 clearance investigations to find 20 of them, the five we lose by this method can be quite important.

But both these calculations are based on the assumption that the risk for a low glomerular filtration rate is evenly distributed in the 500 individuals, and that the height:creatinine index will work in the same way in all cases. I don't think that is true. These children all had a known renal disease, and the risk of having a low glomerular filtration rate must be different between diagnosis. If, by using this information, one can reduce the group of 500 children to a more manageable lot of say 100, and then by applying the height:creatinine

index as the authors suggest and with the value <2.1, the whole procedure will work quite well. I think that is what the authors have done, but they must not keep the hidden part of the screening they have performed hidden from the reader.

S BLOMSTRAND
Department of Paediatrics,
Lasarettet, Box 850,
S-501 15 Borås,
Sweden

- 1 Parkin A, Smith HC, Brocklebank JT. Which routine test for kidney function? *Arch Dis Child* 1989;64:1261-3.

Drs Parkin and Brocklebank comment:

The purpose of the study was to help paediatricians to identify children with reduced glomerular filtration rate and then to decide when to refer those children to a specialist paediatric nephrology centre. We accept the analysis of Dr Blomstrand but the context of our investigation was not screening for reduced glomerular filtration rate in the general population. Given that the children have established renal disease, the decision as to which diagnostic test to use must be made. To this end we have identified normal ranges of β_2 microglobulin and plasma creatinine concentrations in children who have measured normal glomerular filtration rate and given some guidance about which is the most appropriate test to use.

We would agree that this is not an unscreened population and that the results in the general population might be different.

Neonatal purpura fulminans and transient protein C deficiency

SIR,—We present a unique case of an otherwise well neonate presenting with purpura fulminans due to transient protein C deficiency.

A 4310 g girl was born to unrelated parents after an uncomplicated pregnancy and delivery. There was no relevant family history. Vitamin K₁ was injected at birth and a routine examination showed a healthy infant. From 7 hours of age there was rapid development of areas of 'bruising' affecting the trunk and limbs typical of purpura fulminans. Her vital signs were normal. At 18 hours of age she had a right sided clonic convulsion. Oliguria was present with the serum creatinine concentration rising to 114 μ mol/l. Ultrasound of the heart and brain and a renal isotope scan were normal. The full blood count, prothrombin time, and activated partial thromboplastin time were normal. A septic screen was clear. The clinical picture was consistent with