Drs Skoner and Fireman comment:

In response to Dr Amirav: (1) Persistence of post treatment rises of the measured prostaglandin F2α metabolite were not unexpected, as this metabolite is stable in plasma and may be detectable for hours after the release of prostaglandin F2α, which has a relatively short half life. (2) All of the infants in group II (infants after treatment) had residual signs of airflow obstruction. (3) Pulmonary function testing would certainly be superior to clinical parameters in assessing the degree of airflow 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 pathophysiologic 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 pathophysiologies. Additionally, the desired human pathophysiologic response may be inaccessible to direct measurement. As such, absolute proof of a causal relationship between a mediator and a pathophysiologic 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 F2α was detectable in plasma during acute airflow obstruction and satisfy criteria (1). Other investigators have documented that inhaled prostaglandin F2α can cause bronchoconstriction (criteria 2). 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 pathophysiologic process. For this reason, we believe that therapeutic trials using specific anti-inflammatory agents for the treatment of airflow obstruction are warranted.

Diagnostic accuracy of pH monitoring in gastro-oesophageal reflux

Stir—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. 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 and the indication for pH study is diagnostically important. 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 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 would be 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 explanation that the diagnosis of gastro-oesophageal reflux in a child who is an outpatient should involve his or her admission to hospital, is premature.

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Drs Da Dalt, Mazzoleni, Montini, Donelli, 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.

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 improved whenever 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, anaemia, 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 in at least two episodes of spontaneous reflux were present in five minutes (according to Meyers et al). A biopsy was performed in all our cases 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 such as the 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.

A catabolic state in dexahemosone treatment of bronchopulmonary dysplasia

Stir—Dexamethasone treatment is being increasingly used in babies with bronchopulmonary dysplasia because of its benefit. 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 duc tus 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 eutaxate 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, septicemia, 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 only developed on commencing treatment, to our knowledge this has not been commented on in previous reports. Mean weight gain fell to ~5 g/week from one of about ~10 g/week the day before 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