

Mrs Yudlin and Dr Dungar comment: Mr Bailey and Ms Voss do not appear to be challenging the results of our study but rather questioning whether the label 'children' in table 2 is appropriate. Their suggestion that the variance for significant premature 'children' in this table should be of the order of 15-20 cm² is, we believe, misleading. A variance of this size would relate to the actual heights of children, whereas we were concerned only with the variance in child 'biases'; that is, differences between measurements recorded by health visitor and auxologist.

Mr Bailey and Ms Voss have raised an interesting theoretical question, but our study design does not allow its resolution. The main point at issue is whether measurements made by a trained auxologist using the Harpenden stadiometer and applying traction are affected by the child's 'elasticity' as much as measurements made by a health visitor, using a Microtome or wallchart. Mr Bailey and Ms Voss suggest that they are, by their statement that "the effect due to a child is removed, in the analysis, by the differencing that occurs when the auxologist's measurement is subtracted from that of a health visitor". Our standpoint, on the other hand, is that the auxologist's measurement is the best available, and the purpose of our study was to examine how health visitor measurements compared with this best.

Prolonged low dose indomethacin for persistent ductus arteriosus

Sir,—We reviewed with great interest the article by Rennie and Cooke.1 The treatment of patent ductus arteriosus remains an important issue in the care of the premature infant. However, we would like to address several areas in order to clarify results achieved by the investigators. Certain specific descriptions were missing in the methods section that would be helpful in justifying prolonged low dose indomethacin as an effective treatment.

Our first concern is the basis for the diagnosis of the patent ductus arteriosus and its relapse. While clinical symptoms are important diagnostic parameters, they are subject to observer bias especially in a study spanning different institutions. Echocardiography, the preferred diagnostic method, would strengthen the initial diagnosis and the presence or absence of relapse.2 This improvement would have provided an important prospective diagnostic description to define the patient population more accurately.

Secondly, the many clinical factors that influence the patency of the ductus were excluded.3 There was no mention of important confounding variables such as fluid management, methods of ventilation, use of exogenous surfactant, or severity of the sepsis. In addition, the lack of serum indomethacin concentrations leaves an important question for the management of patent ductus arteriosus. Our experience with measuring concentrations of this drug confirmed the large and unpredictable variation noted by Brash et al.4 We were unable to establish a threshold at which clinical response was certain and felt that this was due to the fact that even low levels of indomethacin were associated with cessation of prostaglandin synthesis. This observation led to the present study as we felt, like Seyberth et al that resurgance of prostaglandin synthesis could be important in relapse.5

Dr S Rennie and Dr Cooke comment: We thank Dr Marino and his colleagues for their interest in our paper. We accept that echocardiographic diagnosis of patent ductus arteriosus would have provided more objective evidence on which to enrol and subsequently assess subjects, but at the time this study was started the technique was not available to us in either centre. We would obviously use this method in any future studies.

The problem of differences in management should have been taken into account in the conclusion that this study was randomised. Fluid management was fairly uniform, with fluid restriction to 120 ml/kg/24 hours in both centres being aimed for. During much of the time that this study was in progress we were also recruiting infants to a randomised surfactant trial. The problem of the severity of disease was partly discussed by the demonstration that by chance the long course group tended to be nursed in higher ambient oxygen at enrollment.

We would not agree that serum indomethacin concentrations are not important in the management of patent ductus arteriosus. Our experience with measuring concentrations of this drug confirmed the large and unpredictable variation noted by Brash et al.4 We were unable to establish a threshold at which clinical response was certain and felt that this was due to the fact that even low levels of indomethacin were associated with cessation of prostaglandin synthesis. This observation led to the present study as we felt, like Seyberth et al that resurgance of prostaglandin synthesis could be important in relapse.5


