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Drs Rascher and Linderkamp comment:

Dr Anthony and Professor Levene have raised important questions concerning the blood volume method used in our study. They point to the following possible pitfalls: (1) the method of red cell mass measurement may not be reliable. We used a method described by Phillips *et al* (that is, dilution of fetal haemoglobin by transfused adult red blood cells).¹ Phillips *et al* report a maximum coefficient of variation of less than 3.6%.¹ In 20 double measurements of fetal haemoglobin we found a mean variability ($V = [A-B]/[A+B]/2$) of 3.4%. This variability may have caused a mean error of a single red cell mass determination of 7%. This is in the range of other red cell mass methods.^{2,3} The variability of fetal haemoglobin measurement and thus the error of red cell mass increases with decreasing fetal haemoglobin. (2) the microfuge packed cell volume has to be corrected for trapped plasma. Trapped plasma is about 2% for neonatal and adult red cells⁴ and can thus be neglected. (3) the whole body packed cell volume differs from the venous (central) packed cell volume. In adults, the body:venous packed cell volume ratio is about 0.91. In full term neonates ratios of 0.87⁵ and 0.90² have been reported, and in severely ill preterm infants ratios of 0.82 to 0.89 have been determined.³ The use of a mean body:venous packed cell volume ratio derived from another study merely changes the blood volumes by a constant factor. The maximum error for blood volume calculation from red cell mass and packed cell volume using a constant ratio of 0.855 for preterm infant is 4%.

As plasma volume measurements may be associated with an error of 6%,⁶ a double label technique using a red cell and a plasma indicator probably does not appreciably increase the reliability of whole blood volume estimation. On the other hand, we agree with Dr Anthony and Professor Levene that the use of a plasma protein label would have been more reliable for plasma volume measurement. However, determination of plasma volume was not the primary purpose of our study. Moreover, Evans blue is no longer commercially available and radioactively labelled proteins are not used any more in newborn infants for ethical reasons.

We conclude that the fetal haemoglobin dilution technique is a reliable method for red cell mass measurement and whole blood volume estimation. As blood volume did not change during transfusion, the increase in red cell mass was certainly associated with a decrease in plasma volume. A simple measurement of a change in packed cell volume would not have been as informative as the estimation of blood volume from red cell mass and packed cell volume.

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Non-invasive assessment of pulmonary arterial pressure in healthy neonates

SIR,—We read with interest the study by Skinner *et al*.¹ We would however, take issue with the statement that the method we used in our study to assess pulmonary artery pressure,² the inverse relationship with the ratio of the time to peak velocity (TPV) of pulmonary artery flow and the right ventricular ejection time (RVET), is less suitable for study of the newborn. The advantage of TPV:RVET ratio as a means of studying physiological changes is that we obtained quantitative data in 100% of our studies. Using tricuspid regurgitation, Dr Skinner *et al* obtained quantitative data in only 22% of term studies and 45% of preterm studies.

Our data suggested that pulmonary artery pressure falls slightly but significantly more slowly in healthy preterm than in term infants.² Dr Skinner *et al* did not find this difference and suggested that factors other than pulmonary artery pressure which can affect TPV:RVET might have influenced our results. We do not believe that to be the case for the following reasons, taking each of these factors in turn. Firstly, that the positioning of the pulsed Doppler sample is critical. We used a constant site in the centre of the artery distal to the pulmonary valve, not technically difficult in early life. Secondly, myocardial function, which if poor will prolong TPV. All infants in the study referred to were healthy and had good myocardial function. Any reduction in contractility resulting from lower gestational age would cause the difference which we found between preterm and term infants to be an underestimate. Thirdly, tricuspid regurgitation, here Dr Skinner *et al* have misread the reference cited. Kitabatake *et al* could find no statistically significant effect of tricuspid regurgitation on the relationship between TPV and pulmonary artery pressure.³ Finally, heart rate, which will slightly reduce TPV:RVET as it increases.⁴ The term babies in our study had a mean heart rate of 129 compared with 143 in those preterm. From the regression analysis provided by the data of Akiba *et al*,⁴ this difference would cause a change in TPV:RVET of 0.005, not likely to affect the significance of our data. For example, between 25 and 36 hours after birth mean TPV:RVET was 0.36 in the term infants compared with 0.29 in the preterms. In addition the difference in heart rate between the two groups remained constant through the study period while the differences in TPV:RVET did not.

Tricuspid regurgitation is a good method for estimating pulmonary artery pressure, so why did Skinner *et al* not find the same differences? While lack of longitudinal data may be part of the problem, the important information missing from this paper is the distribution of gestation within the wide range quoted (28 to 35 weeks) and even more

importantly the gestation of the seven infants in whom longitudinal quantitative analysis was possible. Healthy infants of less than 31 weeks are not common, this tends to bias the selection of infants in this type of study towards higher gestations. Thirty seven percent of the preterm infants in our study were of less than 31 weeks, this may be why we were able to demonstrate a difference.

Tricuspid regurgitation, when present, and TPV:RVET are both good methods for non-invasively assessing pulmonary artery pressure. Like all Doppler methods they both have limitations. Within the practice of paediatric cardiology, where both methods were developed and validated, tricuspid regurgitation has advantages particularly in children with large intracardiac left to right shunts. However, we would argue that a method which allows data collection in only a minority of normal subjects may not be the best for describing physiological changes.

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Dr Skinner *et al* comment:

We thank Drs Evans and Archer for their comments. There are now three Doppler techniques for assessing neonatal pulmonary arterial pressure: the TPV:RVET ratio, regurgitant tricuspid flow, and the analysis of ductal flow.¹ The TPV:RVET ratio can be measured serially in all infants, but is it as accurate a measure as that provided by tricuspid regurgitation when present and measurable?

If the TPV:RVET ratio is influenced by pulmonary arterial pressure only and it is valid to compare subjects of different size, absolute values can be obtained by imposing Evans' ratios on Kitabatake's regression from adults, which correlates TPV:RVET with pulmonary arterial pressure. However, Evans' ratio of 0.2:1 in preterm infants at six hours implies a mean arterial pressure of 100 mmHg; almost three times average systemic pressure! Similarly, the lower ratios seen in the preterm babies imply higher pressures than in term babies.

As aortic TPV is shortened by mitral regurgitation,² Kitabatake postulated that pulmonary TPV might be shortened by tricuspid regurgitation, and found nine of 11 adult patients with tricuspid regurgitation had TPV values below the regression line for the whole group. Although the regression for patients with tricuspid regurgitation did not differ significantly from this regression, a third of the whole group had tricuspid regurgitation. No comparison was reported between those with and without tricuspid regurgitation.

Serial measurement is clearly the best way to assess the speed with which pulmonary arterial pressure falls, and we presented our serial data on seven preterm babies graphically. They were the same mean gestational age