Birth weight and blood pressure

No evidence for a U shaped relation

EDITOR,—Lenore J Launer and colleagues claim “a distinct U shaped relation between birth weight and blood pressure.”¹ We have re-examined data from the Brompton study of 2000 children followed up until the age of 10.^{2,3} We found no evidence for a U shaped relation; that birth weight seems to be weakly associated with blood pressure at age 4 years and later; and that the main influence of birth weight seems to be indirect.

We believe that the statistical analyses of Launer and colleagues are misleading. Firstly, they imply that a U shape has been established despite observing a P value of only 0.06. They declare in the methods section that $P < 0.05$ will be interpreted as significant. Thus it is curious to assume proof of a U shape after obtaining $P < 0.06$ at 4 years of age. Their claims for a U shaped relation are not substantiated by the data presented but are speculations based on non-significant results.

Secondly, exploratory studies of this nature examine many potential relations. P values should be interpreted cautiously when many significance tests are being made. Most authors guard against false positive results by demanding smaller P values before regarding a relation as significant; this is advocated by the *BMJ*'s own guidelines.⁴ $P < 0.01$ is commonly used. Thus $P = 0.06$ gives little support to the suggestion of a relation; the observed data quite probably arise by chance alone.

Thirdly, a quadratic term in a regression equation does not necessarily provide evidence that a U shape is present; it might suggest non-linearity of the relation between weight and blood pressure but does not indicate the precise positions of the non-linearity. Possibly a quadratic term fits better than a linear one while the “true” curve is some totally different function. For example, a quadratic regression could arise from non-linearity in high values without providing information about low weights.

Fourthly, even a highly significant term would not indicate the magnitude of the relation. Significance does not imply clinical importance. The 95% confidence intervals for the quadratic term are extremely large and include zero (table II). The figure (c), despite a superimposed bold curve, shows that a U shaped relation is at best tenuous; there is considerable scatter about the curve, and the plotted points provide little support for a U shape. Even if a P value had confirmed a significant effect there still seems to be at most only a slight tendency towards a U shape.

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Authors' reply

EDITOR,—Our study was planned to examine the relation between birth weight and blood pressure prospectively in children. This was in response to findings based on retrospective cohort studies of adults that birth weight is inversely related to hypertension and other adverse cardiovascular outcomes.¹ We found support for a U shaped relation, albeit a modest one.

Our conclusions regarding the tenability of the model were also based on other evidence from the literature and evidence that emerged from the analysis of the relations between birth weight, weight, and blood pressure, as described in the discussion. The pattern of development of blood pressure by birthweight group was particularly interesting to us because it provides us with clues regarding the putative relations between prenatal and postnatal events. Because we realise that the exact nature of the association may be difficult to establish on the basis of this one report, we noted that the sample was small and further investigation was needed.

Although Peter M Fayers and Michael de Swiet do not agree with our interpretation of the data, it does not follow that we presented the results misleadingly. Although our P value just missed the 0.05 level, would it not be more misleading to ignore the finding because it did not fall under this cut off point? Furthermore, the data are presented for full evaluation by readers. We do not present only the results of the multiple regression equations and P values but also scatterplots and mean blood pressures by weight and weight gain categories to gain better insight into what drove the results derived from the model.

The clinical relevance of the quadratic term cannot be ascertained on the basis of one report. Further studies are needed to elucidate the role of birth weight and related factors in the development of blood pressure. We hope that our report spurs such investigations.

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Intrauterine growth and serum cholesterol

Link may be spurious

EDITOR,—Studies of associations between birth variables and adult morbidity such as that by D J P Barker and colleagues are of epidemiological interest, but the results need to be interpreted with caution.¹ Even within the limitations of 50 year old records the authors' main conclusion—that raised cholesterol concentrations in adult life are associated with impaired growth during late gestation—is difficult to accept on the basis of the data presented.

It is difficult to infer growth retardation from any single measurement such as abdominal circumference, which Barker and colleagues have found is correlated with raised serum cholesterol concentrations in adults. This variable is not a standard measure for assessing neonatal nutritional status, which is more usually estimated from the ponderal index, skinfold thickness, or ratio of the mid-arm circumference to the head circumference.²

Weight and abdominal circumference at birth are also related to several non-pathological variables, the most important of which is gestational age.^{3,4} Even if the woman recalls the last menstrual period with certainty there may be considerable dating error, which tends heavily towards an overestimation of gestational age.⁵ Regrettably, Barker and colleagues do not give the distribution of estimated gestational ages at birth; a number of preterm deliveries may have been included. The raw values of abdominal circumference are presented as a U shaped distribution, whereas the distribution should be near normal at term. The observed excess of values recorded at the lower

extreme could be due to prematurity, constitutional smallness, or growth retardation. Furthermore, an overestimated gestational age at birth would result in a falsely low value for abdominal circumference adjusted for gestational age. Any or all of these factors could be responsible for the observed correlation between neonatal abdominal circumference and adult low density lipoprotein concentration.

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Authors' reply

EDITOR,—Max Mongelli and Jason Gardosi confuse severe intrauterine growth retardation, which is important in paediatric practice, with the much commoner but less severe forms of reduced growth which are found among babies of average birth weight and lead to cardiovascular disease. We have shown that adult serum cholesterol concentrations are specifically associated with abdominal circumference at birth across the whole range of its distribution, which our scattergram showed to be normal and not U shaped. Serum cholesterol concentrations are therefore associated with the size of the infant liver, which synthesises and excretes cholesterol. We have shown that this association is strengthened by adjustment for gestation, which was recorded for all except 29 of the babies, and cannot be attributed to premature delivery. To distinguish constitutional smallness from growth retardation merely begs fundamental questions about the contribution of genetic and environmental influences to normal fetal growth.

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Minimally invasive surgery

More invasive than it looks

EDITOR,—In the article on future developments in minimally invasive surgery J E A Wickham falls into the trap of confusing personal desire with accurate prediction and novelty with science.¹ Most anaesthetists would query the term “minimally invasive.” Certainly such surgery entails “minimal access” but it remains to be seen how invasive minimal access surgery really is. Evidence is emerging, for example, that laparoscopic surgery is indeed quite a severe cardiovascular stress, and other “invasions” remain to be discovered.