Birth weight and blood pressure in adolescence

Studies may be misleading

EDITOR,—Jean W A Matthes and colleagues found that the blood pressures of 165 adolescents who had had low birth weight were no different from those of a similar number of controls and they concluded that this does not support a link between retarded fetal growth and hypertension.¹ Their findings contrast with eight published studies in pre-adolescent children and four in adults which show that birth weight is inversely related to blood pressure. Differences associated with birth weight are small in childhood but are progressively amplified through life.² Blood pressure is known to track from childhood through into adult life,³ but tracking is perturbed during the adolescent growth spurt.⁴ For this reason studies of adolescents are unlikely to contribute importantly to our understanding of the long term effects of fetal growth on blood pressure.

D J P BARKER
Director
C M LAW
Epidemiologist

MRC Environmental Epidemiology Unit,
Southampton General Hospital,
Southampton SO9 4XY

- 1 Matthes JWA, Lewis PA, Davies DP, Bethel JA. Relation between birth weight at term and systolic blood pressure in adolescence. *BMJ* 1994;308:1074-7. (23 April.)
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- 3 Labarthe D, Eissen M, Varas C. Childhood precursors of high blood pressure and elevated cholesterol. *Ann Rev Public Health* 1991;12:519-41.
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Findings could be influenced by stage of puberty

EDITOR,—Jean W A Matthes and colleagues are to be congratulated on adding to the data about the relation of birth weight and blood pressure that form their carefully designed study, but they do not draw attention to the considerable differences in height and weight between their cases and controls, the former being shorter and "fatter." They state that it was thought "inappropriate" to measure pubertal status, presumably on ethical or practical grounds, but the differences in height

suggest that their cases may not have completed their pubertal growth spurt and this could account to some degree for the negative findings regarding blood pressure. These data are also interesting in themselves in supporting the concept that babies small for dates at term, like runted piglets, may end up shorter and fatter than those of normal birthweight—a habitus that goes with hypertension.

JOHN A DAVIS
Professor

Great Shelford,
Cambridge CB2 5JE

- 1 Matthes JWA, Lewis PA, Davies DP, Bethel JA. Relation between birth weight at term and systolic blood pressure in adolescence. *BMJ* 1994;308:1074-7. (23 April.)

Authors' reply

EDITOR,—We agree with John Davis that the pubertal status of the two groups may be different in the results we report, although we are unaware of studies that show differences in later pubertal development in infants small for dates. If any difference was large enough to be considered important then "age at puberty" would become yet another proxy or even putative causal factor to explain differences in later life. Recognising differences in size between cases and controls, in our linear regression model we adjusted for height, weight, and body mass index. We judged in our study that it would be inappropriate to ascertain pubertal status: the delicate nature of the physical examination required could well have jeopardised recruitment into our study, let alone have posed ethical problems. Initially, details of menarche were collected but the information was very unreliable, most girls having already passed menarche. Similarities with runted piglets are intriguing but we doubt their relevance as our cases were shorter and lighter and had a lower body mass index.

Any perturbation of blood pressure tracking during the adolescent growth spurt would be expected to apply equally to both groups. This would add variation to the data; we took account of this in the study design in the selection of the standard deviation of the sample size calculation. Barker and Law have to argue that there is bias in the perturbation between the two groups for it to be an important factor. They have also to appreciate that, at the age of examination (15.6 years for cases, 15.8 years for controls) the puberty growth spurt has been largely completed, especially in girls (who have an earlier growth spurt), who outnumbered boys in our study by nearly 2:1.

Ours is the first population based, comparative study to investigate the incidence of low birth weight on later blood pressure by using carefully matched cases and controls. For the reasons we have given we believe our study of adolescents is important to the understanding of links between the fetal environment and blood pressure.

JEAN W A MATTHES
Senior registrar in child health
PETER A LEWIS
Senior lecturer in health informatics

D P DAVIES
Professor of child health
JACQUELINE BETHEL
Clinical databases manager

University of Wales College of Medicine,
Cardiff CF4 4XN

Nocturnal ambulatory blood pressure measurement

EDITOR,—We disagree that the findings of R J O Davies and colleagues should be taken into account as part of clinical and epidemiological interpretation.¹

The authors assume that the "aroused" ambulatory blood pressure is less accurate than the true physiological pressure. This is self evident but has no clinical relevance, as physiological pressure can never be measured in clinical practice. They also assume that the arousal response is an artefactual source of error. However, recent evidence suggests that such a rise is associated with poor outcome.² Indeed an increased vascular reactivity depends on this arousal. Furthermore, arousal by ambulatory measurement is likely to be less than arousal induced by conventional measurement, because serial measurements will remove the "white coat" effects.

It is incorrect for the authors to infer from their work that "the blood pressure recorded by ambulatory machines at night may underestimate to variable degrees the reduction in the blood pressure during sleep." The absolute measurement during sleep may be lower, but the reduction may not be underestimated. This is because an equal, if not greater, arousal to blood pressure measurement could occur during the day. If it can be assumed that arousal caused by a measurement is greater when awake than when asleep, the nocturnal reduction during sleep will be overestimated when absolute blood pressure is considered.

Outcome data to date is based on awake conventional blood pressure measurements. It may be that night reading will be a better predictor of outcome as they allow as near a basal state as is practical by reducing the arousal response to a minimum. Until large studies relating nocturnal readings to outcome are performed the best time to take a blood pressure will remain unknown.

ANDREW SHENNAN
Lecturer in obstetrics and gynaecology
MICHAEL DE SWIET
Consultant physician

Institute of Obstetrics and Gynaecology,
Royal Postgraduate Medical School,
Queen Charlotte's and Chelsea Hospital,
London W6 0XG

AIDEN HALLIGAN
Lecturer in obstetrics and gynaecology
Department of Obstetrics and Gynaecology,
University of Leicester,
Leicester Royal Infirmary,
Leicester LE2 7LX

- 1 Davies RJO, Jenkins N, Styrdling J. Effect of measuring ambulatory blood pressure on sleep and on blood pressure during sleep. *BMJ* 1994;308:820-3. (26 March.)
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Racial differences and hypertension

EDITOR,—In their clinic based study of hypertensive patients, Jamil Mayet and colleagues conclude that people of black African descent have more left ventricular hypertrophy than white people for a similar degree of hypertension.¹ They state that reported duration of hypertension was similar in black and white people, but do not fully

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address the issue of selection bias in their study population. Hypertension in black people may be diagnosed at a more advanced stage than in the general population, and referrals to a specialist clinic may also differ by ethnic group. This would mean that the true degree of hypertension was greater in the black people studied.

These selection biases can be overcome by a population based study. In such a study we showed that average resting systolic blood pressure is 6 mm Hg higher in men of black African descent and 17 mm Hg higher in women of black African descent than in the general population.² Further, we showed that the nocturnal fall in blood pressure is less in black than white people, even when resting blood pressure is taken into account. The overall burden of hypertension for a similar blood pressure would therefore be greater in black than in white people.

People of black African descent have a greater mortality from stroke,³ more left ventricular hypertrophy,⁴ and more renal damage⁵ than white people. Racial differences in cardiac structure alone cannot account for this. A more plausible explanation is that ethnic differences in hypertensive load are inadequately characterised by current methods of blood pressure measurement.

N CHATURVEDI
Research fellow
M G MARMOT
Professor

Department of Epidemiology and Public Health,
University College London,
London WC1E 6EA

P M McKEIGUE
Senior lecturer

Department of Epidemiology and Population Sciences,
London School of Hygiene and Tropical Medicine,
London WC1E 7HT

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(3750 g) 260 g higher than previous British birth-weight standards, which are based on menstrual dates and show considerable flattening at term.²

We have since examined our accuracy of gestational dating by ultrasound measurement of the fetal biparietal diameter using Campbell and Newman's dating tables.⁴ We studied 19 consecutive singleton, normal term pregnancies resulting from assisted conception by in vitro fertilisation or intrauterine insemination booked at our hospital. All had the usual detailed ultrasound examination at 18-19 weeks by ultrasonographers who were not aware of the precise gestational age at the time of measurement. Gestational age derived from the biparietal diameter⁴ was compared with the true gestational age as determined from the date of fertilisation. The mean error (age estimated on ultrasonography minus true gestational age) was -0.57 days, with a standard deviation of 2.96 days and normal distribution.

We then looked at the possible effect of constitutional variation shown by the measurement obtained from the dating scan on the subsequent birth weight. There was no significant correlation between biparietal diameter centiles, adjusted for gestational age, and birth weight for gestation centiles ($r=0.256$; $P=0.37$). Furthermore, there was no significant difference in average birth weight for gestation centile between the two groups of babies that had the largest and smallest biparietal diameters (average of centiles, 47 v 40).

Thus the 95% confidence interval for ultrasound dating by biparietal diameter is -5.9 to 5.9 days in our unit. In contrast, as we previously reported,⁵ "certain" menstrual dates (routine ultrasound dates being used as a reference) have a heavily skewed distribution of error of -9 to 27 days (95% confidence interval). This inclination for menstrual dates to overestimate the true dates can lead to birth weights being plotted against gestational ages that are too advanced. We believe this to be the reason for an artificial flattening of the birthweight curve, emphasizing the need for dates of determined on the basis of ultrasound scans to be used to derive accurate birthweight standards.

JASON GARDOSI
Director

THEO MUL
Research fellow

MAX MONGELLI
Research fellow

Perinatal Research and Monitoring Unit,
Department of Obstetrics and Gynaecology,
Queen's Medical Centre,
Nottingham NG7 2UH

MARK WILCOX
Visiting lecturer

Department of Obstetrics and Gynaecology,
Prince of Wales Hospital,
Shatin NT, Hong Kong

Ultrasound dating and birth weight at term

EDITOR,—Tine Brink Henriksen and Allen Wilcox' comment on our finding that the birth-weight curve in our study was steeper at term than that observed in other studies.² We ascribed this to our use of dates based on routine ultrasound scans instead of menstrual dates to derive our weight for gestational age standard.² They suggest that a constitutionally large fetus's gestational age is overestimated by the dating scan and that therefore bigger babies, with presumably larger birth weights at term, would selectively be plotted against later gestations, thus creating bias.

While it is true that the study they refer to showed variation in biparietal diameter between small (≤ 10 th centile) and large (≥ 90 th centile) babies,³ the difference between these extremes amounted to only about 1.5 mm at 18 weeks (figure 2 in reference 3). This difference is equivalent to less than one day's variation in gestational age⁴ and would translate at term to a difference in birth weight of under 20 g. In contrast, our mean birth weight at 40 weeks (3522 g) is about 120 g higher, at 41 weeks (3652 g) 167 g higher, and at 42 weeks

haemorrhage to avoid one major haemorrhage without regard to the possibility that we might endanger many more than one child. Because of the difficulty of investigating small risks of unspecified type, the treatment decision will eventually rely on prejudice concerning the likelihood of risks more injurious than the benefits. The point I made was that grosser risks can, and should, be excluded by clinical trial.

It is difficult to comment on doubts about the ethics of a randomised, controlled trial when it is not clear what treatment strategy is being proposed as more ethical. The options for infants at low risk of early haemorrhage seem to be to recommend treating all; to recommend treating none; and to recommend joining a clinical trial. Probably, with our present very limited state of knowledge, any of these would be ethical provided a clear statement of our uncertainty is made to the parents. The major advantage of the clinical trial is that it helps to reduce uncertainty in a way that none of the other options can. It is this property which makes me believe that it is the most ethical policy.

Doctors should be cautious about endorsing a policy of treatment for all. The argument that we know for sure that one very rare disease is eliminated by treatment is weak. If a child suffers a haemorrhage when untreated, both doctors and parents must suffer the pain of knowing that, with hindsight, this could have been avoided. However, avoidance of such personal pain is not a good reason for following a treatment strategy which may cause more suffering overall but allows us to remain ignorant of our causal role.

If non-treatment is recommended then Draper and McNinch's suggestion of making carers aware of the importance of warning bleeds should be followed, and it probably makes sense to suggest to breast feeding mothers who experience major difficulties during the early weeks that they consult a health visitor concerning supplementary feeding without delay.

JIM SLATTERY
Medical statistician

Department of Clinical Neurosciences,
University of Edinburgh,
Edinburgh EH4 2XU

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Thalidomide may be a mutagen

EDITOR,—The birth of two malformed children in England raises the question whether thalidomide, α -phthalimido-glutarimide, is a human mutagen as well as a potent teratogen. The fathers of both children are thalidomide victims.

CASE 1

In July last year a girl was born in Peterborough with no thumbs and only two digits on both hands. She has severe malformations of both legs, and the left leg is much shorter than the right. Both feet taper to one toe, neither of which has nails. Her father was born in 1960 with malformations of both hands and both legs. He was treated at the Hospital for Sick Children, Great Ormond Street, and his legs were amputated below the knee because of the severe malformations of both feet. He was assessed by the Thalidomide Victims' Compensation Panel and was awarded substantial damages and an annual pension for his severe disabilities. His mother, who is now dead, said that she had taken six to eight thalidomide tablets.

The affected child has two siblings, both boys, who are normal. Her mother was well during the pregnancy, had no bleeding in the early weeks of pregnancy, and took no medication. She had three ultrasound scans.

The x ray report of the child's limbs showed

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Vitamin K for neonates

EDITOR,—Whether vitamin K predisposes children to cancer certainly needs investigation. However, this issue was not central to my article,¹ as Gerald Draper and Andrew McNinch seem to suggest.² My question is whether any serious side effects exist for this drug and whether it is possible to justify treatment of 25 000 babies at low risk of