

in comparisons with coresidents but not with people living alone. Further studies are under way to identify whether intervention can help to prevent depression in carers.

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## Fetal growth and cardiovascular risk factors in Jamaican schoolchildren

Terrence E Forrester, Rainford J Wilks, Franklyn I Bennett, Donald Simeon, Clive Osmond, Mureen Allen, Andrene P Chung, Paul Scott

### Abstract

**Objective**—To determine relation between schoolchildren's blood pressure, glycated haemoglobin level, and cholesterol concentration and their anthropometry, socioeconomic status, and birth measurements.

**Design**—Retrospective cohort study.

**Setting**—27 schools closest to University Hospital of the West Indies, Kingston, Jamaica.

**Subjects**—2337 children aged 6-16 years who were born at university hospital were recruited, and their birth records were recovered: 1610 had suitable records, 659 had records including birth length, and 610 of these were prepubertal.

**Main outcome measures**—Blood pressure, glycated haemoglobin level, serum cholesterol concentration, anthropometry at birth, current anthropometry, and socioeconomic status.

**Results**—Multiple regression analysis showed that children's systolic blood pressure was inversely related to their birth weight ( $P < 0.0001$ ) and directly related to their current weight. Glycated haemoglobin level was higher in children with thicker triceps skinfolds ( $P < 0.001$ ) and who had been shorter at birth ( $P = 0.003$ ). Serum cholesterol concentration was inversely related to current height ( $P = 0.001$ ) and to length at birth ( $P = 0.09$ ) and was directly related to triceps skinfold thickness and higher socioeconomic status ( $P < 0.001$ ).

**Conclusions**—Blood pressure in childhood was inversely related to birth weight and directly to current weight. Glycaemic control and serum cholesterol were related to short length at birth, height deficit in childhood, and childhood obesity.

### Introduction

Hypertension and diabetes mellitus contribute substantially to cardiovascular mortality in the Caribbean. Fetal growth retardation has recently been added to the list of established risk factors for these diseases.<sup>1-8</sup> Thus, blood pressure in adults was inversely related to birth weight, blood glucose concentration after an oral glucose challenge was inversely related to birth weight and to weight at 1 year, and serum cholesterol concentration was inversely related to abdominal circumference at birth.<sup>4-8</sup>

The underlying mechanisms are largely unknown. Continued exposure to risk factors associated with poor socioeconomic circumstances might explain associations between weight and proportions at birth and disease in adulthood.<sup>9</sup> Alternatively, poor maternal nutrition might curtail fetal growth and thus affect the control of blood pressure and concentrations of blood glucose and serum lipids in later life.<sup>10</sup> In Caribbean communities the prevalence of hypertension and diabetes is high, and both social deprivation and poor maternal nutrition are common. Describing how social deprivation and "fetal programming" affect the prevalence of hypertension and diabetes is important for public health.

Retardation of fetal growth has been linked with blood pressure in adults and children.<sup>4,6,11-13</sup> However, there are few data for glycated haemoglobin and serum cholesterol concentrations in childhood.<sup>14</sup> In this study we determined how blood pressure, glucose tolerance (glycated haemoglobin level), and serum cholesterol concentration in Jamaican schoolchildren were related to socioeconomic status, body size and composition, anthropometry at birth, and maternal blood pressure and anthropometry.

Tropical Metabolism Research Unit, University of the West Indies, Mona, Kingston 7, Jamaica  
Terrence E Forrester, director  
Rainford J Wilks, lecturer  
Franklyn I Bennett, senior lecturer  
Donald Simeon, lecturer  
Mureen Allen, research fellow  
Andrene P Chung, research fellow  
Paul Scott, research fellow

Medical Research Council Environmental Epidemiology Unit, University of Southampton, Southampton General Hospital, Southampton SO9 4XY  
Clive Osmond, statistician

Correspondence to: Dr Forrester.

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## Methods

### SUBJECTS

Schoolchildren born in the University Hospital of the West Indies, Kingston Jamaica, were eligible for entry into the study, and we took a sample from the 27 schools nearest to the hospital. Attendance at school for children aged 6 to 16 is mandatory in Jamaica, and actual attendance is 83.5% in Kingston. Five of the 27 schools were primary or preparatory, and 22 were secondary or high schools. Two of the five primary schools were private, but all the secondary schools were state financed.

Parents identified those children in school who were born at the hospital, and we invited children to participate in the study after we had obtained their oral consent and parental written consent. The study was approved by the medical ethics committee of the University of the West Indies.

### MEASUREMENTS OF CHILDREN

The children were studied in school.

**Blood pressure**—Each child was seated for 10 minutes before blood pressure was measured by one of two observers with an oscillometric sphygmomanometer (Dinamap 1846SX<sup>15</sup>). Five measurements were taken a minute apart, and the fourth and fifth measurements were averaged to give the blood pressure. Middle upper arm circumference dictated cuff size.

**Anthropometry**—Two trained nutritionists measured each child's weight, height, middle upper arm circumference, triceps and subscapular skinfold thicknesses, and waist and hip circumferences.<sup>16</sup>

**Blood tests**—Venous blood was drawn after measuring blood pressure and anthropometry. Haemoglobin concentration was measured with a Coulter haemoglobinometer. Total serum cholesterol concentration and glycated haemoglobin level represented lipid status and usual blood glucose control respectively. Cholesterol concentration was measured enzymatically,<sup>17</sup> and glycated haemoglobin was measured by affinity chromatography.<sup>18</sup> The coefficient of variation for the cholesterol assays was 9.8% at a concentration of 4.5 mmol/l, while for the glycated haemoglobin assay it was 10.6% at 6%.

**Socioeconomic status**—Two observers conducted structured interviews to determine socioeconomic status while the children were seated awaiting measurement of blood pressure. Equal ratings from data on family possessions, utilities in the house, and school materials were used to compute a socioeconomic index that was directly related to wealth. As a guide to the accuracy of the responses, a random sample of 10% of the 1610 children enrolled in the study was chosen and one parent (head of household) was asked to answer the same questionnaire. Responses of parents and children were compared with scores for socioeconomic status. Each parent's score was subtracted from their child's score to obtain the difference. The mean of the differences (-1.4) provided a measure of bias, and the standard deviation (2.3) gave a measure of precision. The mean difference was not significantly different from zero.

### QUALITY CONTROL

Observers were trained and the techniques used were standardised before the study began. Two observers administered the questionnaire, and two others measured blood pressure and anthropometry. Estimates of variability within and between observers were obtained by testing 20 subjects before the study began and then again at points marking 25%, 50%, and 75% completion of the study. Bias and precision were calculated for test-retest differences. On each occasion collection of data was not resumed until measurements

within and between observers had a correlation coefficient of 0.9 or greater. For blood pressure, the Dinamap sphygmomanometer was calibrated weekly against a mercury manometer and tested for leaks every day.

### INFORMATION ON FETAL DEVELOPMENT

After children were enrolled, maternal hospital records were located to obtain data on mothers' weight, height, and blood pressure throughout pregnancy and on the children's birth and placental weights, crown-heel length, crown-rump length, and head circumference. While birth and placental weights were routinely recorded, lengths were not recorded for many of the older children.

### STATISTICAL ANALYSIS

Data analysis was confined to the 1610 children who were born after 28 weeks' gestation and had suitable records. Of these, 659 had complete records including measurements of head circumference and crown-heel length.

Descriptive data for the population are based on the total sample (1610). Multiple regression techniques were used to determine associations between children's current blood pressure, glycated haemoglobin level, cholesterol concentration, and anthropometry and their birth weight and placental weight, placental to birth weight ratio, and maternal anthropometry in the first trimester.

Testing for associations between current blood pressure, glycated haemoglobin level, and cholesterol concentration and anthropometry at birth (including body length and head circumference) was restricted to the 659 children with complete records. Because tracking of blood pressure and serum lipids is lost at puberty,<sup>19-21</sup> which can obscure associations with birth measurements, we selected the 610 children with complete records who were prepubertal (aged  $\leq 10$  years) for these analyses.

In these analyses birth weight, placental weight, and crown-heel length were divided into groups and tested for trend in association with blood pressure, glycated haemoglobin level, and cholesterol concentration. The sample of 1610 children provided 80% power at the 95% level of significance to show a difference in blood pressure of 2 mm Hg between children in the highest and lowest quarters of the birth weight distribution (SD for blood pressure = 10 mm Hg).

## Results

### SUBJECTS

The 27 schools screened yielded 2983 eligible subjects, of whom 2337 were willing to take part in the study. The remaining 646 (302 boys, 344 girls) declined because of parental or personal objection. No further data were available on these 646 children. Of the 2337 children willing to take part, 1610 had sufficient records for inclusion in the study population and were born after 28 weeks' gestation (1409 were born at term, between 38 and 42 weeks' gestation).

Table 1 shows the group comparisons for the 610 children (309 girls, 301 boys) aged  $\leq 10$  years and the 1000 children (570 girls, 430 boys) aged  $\geq 11$ . Table 2 shows the birth measurements for boys and girls: boys were heavier than girls and had greater head circumferences, but placental weights were not different.

### BLOOD PRESSURE

For the whole sample of 1610 children, systolic pressure was inversely related to birth weight ( $b = -2.6$  mm Hg/kg ( $SE = 0.5$ ,  $P < 0.0001$ ) in a simultaneous regression analysis with age, sex, and current weight.

**Table 1—Comparison between younger children and older children. Values are means (SD) unless stated otherwise**

Variable	Children aged ≤ 10 years		Children aged ≥ 11 years		P value
	No of subjects	Mean value	No of subjects	Mean value	
<b>Maternal details</b>					
Age (years)	609	25.4 (5.6)	999	25.0 (5.4)	0.17
Parity	610	1.0 (1.5)	1000	0.9 (1.4)	0.09
Gravidity	610	2.3 (1.7)	1000	2.2 (1.6)	0.19
Height (m)	516	1.62 (0.07)	830	1.62 (0.06)	0.09
Body mass index (kg/m <sup>2</sup> )	584	19.7 (8.8)	864	20.0 (8.4)	0.64
Haemoglobin (g/l)	599	118 (8)	967	112 (11)	<0.001
Systolic blood pressure (mm Hg)	606	109 (9.7)	969	112 (10.3)	<0.001
<b>Neonatal details</b>					
Gestational age (weeks)	607	38.8 (1.9)	986	38.8 (5.3)	0.2
Birth weight (g)	610	3130 (500)	1000	3120 (480)	0.80
Placental weight (g)	584	550 (120)	931	570 (140)	0.002
Head circumference (cm)	505	33.8 (1.8)	154	33.7 (1.8)	0.50
Crown-heel length (cm)	503	50.8 (3.5)	151	50.3 (3.4)	0.10
Crown-rump length (cm)	476	32.3 (3.0)	115	33.0 (4.5)	0.06
Ponderal index (kg/m <sup>3</sup> )	503	24.2 (4.8)	151	24.8 (5.3)	0.20
<b>Childhood details</b>					
Blood pressure (mm Hg):					
Systolic	610	103 (9.8)	1000	108 (11.4)	<0.001
Diastolic	610	61 (6.5)	999	62 (6.9)	<0.001
Glycated haemoglobin (%)	582	6.0 (0.9)	977	5.8 (0.9)	<0.001
Serum cholesterol (mmol/l)	592	4.2 (0.8)	991	4.1 (0.8)	0.01
Socioeconomic status	602	11.3 (4.1)	997	13.0 (3.6)	<0.001

**Table 2—Comparison between boys and girls in their birth details. Values are means (SD)**

	Boys (n=731)	Girls (=879)
Birth weight (g)	3178 (4891)	3077 (483)***
Placental weight (g)	570 (166)	563 (140)
Crown-heel length (cm)†	50.68 (3.54)	50.73 (3.43)
Head circumference (cm)‡	34.04 (1.81)	33.52 (1.73)***
Ponderal index (kg/m <sup>3</sup> )	24.7 (5.2)	24.1 (4.6)
Gestational age (weeks)	38.87 (1.92)	38.78 (2.09)

\*\*\*P<0.001.

†Data available for 309 boys and 350 girls.

‡Data available for 310 boys and 344 girls.

*Prepubertal children*—Table 3 shows that blood pressure was also inversely related to birth weight in the 610 prepubertal children. Placental weight was inversely related to systolic pressure after adjustment for age, sex, and current weight (test for trend, P=0.003). This relation became non-significant in a simultaneous regression with birth weight. There was no significant relation between the ratio of placental to birth weights and blood pressure. The associations between birth weight and blood pressure were independent of gestational age and of maternal blood pressure during pregnancy (test for trend allowing for maternal systolic blood pressure, P<0.001).

**GLYCATED HAEMOGLOBIN**

For the whole sample of 1610 children, glycated haemoglobin was directly related only to triceps skinfold thickness (P<0.001) in a simultaneous regression analysis with age, sex, and current weight.

*Prepubertal children*—Glycated haemoglobin level was non-significantly related to weight, ponderal index, and head circumference at birth in a simultaneous regression with age, sex, and current weight. However, table 4 shows that crown-heel length was inversely related to glycated haemoglobin level independently of gestation (test for trend, P=0.003). The ratio of placental to birth weights was not related to glycated haemoglobin level.

**CHOLESTEROL**

For the whole sample of 1610 children, cholesterol concentration was positively related to socioeconomic

status (P<0.001), triceps skinfold thickness (P<0.001), and first trimester maternal body mass index (P=0.002) and inversely related to current height (P=0.001) in a simultaneous regression analysis with age and sex.

*Prepubertal children*—Cholesterol concentration was not associated with birth weight in a simultaneous regression analysis with age, sex, and current weight. Cholesterol was, however, inversely associated with

**Table 3—Association between systolic blood pressure in 610 children aged ≤ 10 years and their birth weight (adjusted for age, sex, and current weight)**

Birth weight (g)	No of subjects	Mean systolic blood pressure (mm Hg)
≤ 2500	60	105.4
2501-2750	94	105.4
2751-3000	101	103.6
3001-3250	117	100.9
3251-3500	111	102.5
3501-3750	72	102.2
> 3750	55	101.8
Total	610	103.0 (SD 9.2)

Test for trend, P=0.0001.

**Table 4—Association between glycated haemoglobin level in 475 children\* aged ≤ 10 years and their crown-heel length at birth (adjusted for age, sex, and current weight)**

Crown-heel length (cm)	No of subjects	Mean glycated haemoglobin level (%)
≤ 46	43	6.19
> 46-48	74	6.14
> 48-50	96	6.13
> 50-52	107	5.94
> 52-54	88	5.86
> 54	67	5.88
Total	475	6.01 (SD 0.88)

Test for trend, P=0.003.

\*Those in whom all measurements (crown-heel length, crown-rump length, and glycated haemoglobin level) were made.

## Key messages

- Risk of hypertension, diabetes, and coronary artery disease in adulthood have been related to weight and proportions at birth
- In Caribbean communities the prevalence of hypertension and diabetes is high
- This study of Jamaican schoolchildren showed that their blood pressure was inversely related to birth weight, while their glycated haemoglobin level and serum cholesterol concentration were inversely related to length at birth
- These findings might relate to the different patterns of chronic cardiovascular disease that exist in Britain between people of West Indian origin in Britain and white people

crown-heel length (table 5), but this association was not significant in a simultaneous analysis with placental weight.

**Table 5—Association between serum total cholesterol concentration in 485 children\* aged  $\leq 10$  years and their crown-heel length at birth (adjusted for age, sex, and current weight)**

Crown-heel length (cm)	No of subjects	Mean cholesterol concentration (mmol/l)
$\leq 46$	42	4.38
> 46-48	77	4.25
> 48-50	97	4.29
> 50-52	110	4.24
> 52-54	91	4.20
> 54	68	4.09
Total	485	4.23 (SD 0.84)

Test for trend,  $P=0.09$ .

\*Those in whom all measurements (crown heel length, crown-rump length, and cholesterol concentration) were made.

## Discussion

Our findings indicate that childhood blood pressure, glycated haemoglobin, and serum cholesterol concentration were related to weight and proportions at birth as well as to body size and proportions in childhood. The associations with length at birth were established in the 610 children with complete records who were aged 10 years or less. This analysis of 38% of the total sample might have introduced bias, but these children were similar to the total sample in their gestational age, anthropometry at birth, sex distribution, and maternal characteristics. They had lower blood pressure because they were younger and smaller.

## BLOOD PRESSURE

Our finding that systolic blood pressure was inversely related to birth weight is consistent with previous studies.<sup>4-6 10-13</sup> In adolescence tracking of blood pressure is disturbed and associations between blood pressure and birth weight are obscured.<sup>19-21</sup> As expected, systolic blood pressure was related to childhood weight and maternal blood pressure and the relation between birth weight and blood pressure was independent of maternal blood pressure.<sup>22-25</sup>

## GLYCATED HAEMOGLOBIN

A high level of glycated haemoglobin was related to shortness at birth as well as fatness in childhood. Thus, factors that influenced birth length were later associated with blood glucose control. The relation between glycated haemoglobin and skinfold thickness is not surprising given the known relation between obesity and insulin resistance and glucose intolerance.<sup>6 26-29</sup>

## SERUM CHOLESTEROL

Serum total cholesterol concentration in Jamaican children was related to shortness at birth as well as shortness in childhood. The relation between weight and serum cholesterol concentration has been noted before in children and adults.<sup>27-32</sup> The association between body length at birth and cholesterol might reflect abnormal intrauterine growth in which retarded trunk and visceral growth was associated with alterations in lipid metabolism. Abdominal circumference at birth, reflecting visceral growth, has been related to serum cholesterol concentration in adults.<sup>8 29</sup>

Antecedents of chronic cardiovascular disease track from childhood through to adulthood.<sup>30-39</sup> Tracking of blood pressure is evident by 1 year of age and becomes stronger with increasing age.<sup>33-36</sup> Serum cholesterol concentration also tracks.<sup>37-39</sup> This has been related to body composition and physical activity, but it might be related to metabolic programming accompanying restraint of fetal growth, which presents as shortness at birth.<sup>30-33</sup>

## SOCIOECONOMIC STATUS

Environmental forces acting throughout childhood and adult life are confounding variables, and familial microenvironments might influence birth weight.<sup>9</sup> In this study socioeconomic status was assumed to reflect social deprivation, an independent predictor of death from cardiovascular disease.<sup>9</sup> However, socioeconomic status had no independent association with blood pressure or glycated haemoglobin level. In addition cholesterol concentration was higher in the richer rather than the poorer children. Thus, fetal programming is perhaps more important than social deprivation in determining cardiovascular risk factors in children.

## CONCLUSION

Raised blood pressure in Jamaican children was related to lower birth weight independently of maternal blood pressure. Children who had been shorter at birth had raised glycated haemoglobin levels and serum cholesterol concentration. Shortness at birth probably identifies children whose growth was retarded in late gestation. Thus, retardation of intrauterine growth might be associated with the programming of glucose and lipid metabolism.

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## Changing patterns of invasive *Haemophilus influenzae* disease in England and Wales after introduction of the Hib vaccination programme

Ruth M Hargreaves, Mary P E Slack, Anthony J Howard, Eileen Anderson, Mary E Ramsay

**Haemophilus Reference Unit, Oxford Public Health Laboratory, John Radcliffe Hospital, Headington, Oxford OX3 9DU**

Ruth M Hargreaves, senior registrar in microbiology  
Mary P E Slack, senior lecturer in microbiology  
Eileen Anderson, medical laboratory scientific officer

**Gwynedd Public Health Laboratory, Bangor, North Wales**

Anthony J Howard, director

**Public Health Laboratory Service, Communicable Disease Surveillance Centre, London NW9 5EQ**  
Mary E Ramsay, consultant epidemiologist

Correspondence to: Dr Hargreaves.

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Since 1990 we have been monitoring strains of *Haemophilus influenzae* referred to the Public Health Laboratory Service Haemophilus Reference Laboratories from all cases of invasive *H influenzae* disease from five English regions and Wales. Methods of reporting and participating laboratories have remained constant over this period, which allowed us to compare the incidence of infection before and after the introduction of vaccination against *H influenzae* type b in October 1992.

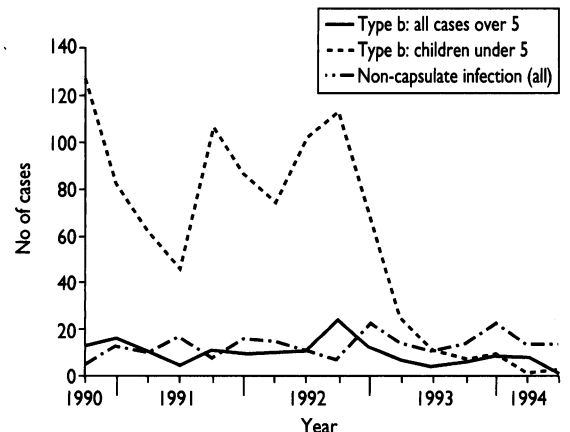
### Patients, methods, and results

The case definition was a systemic infection in which culture of normally sterile body fluid revealed *H influenzae*, or the organism was detected by antigen to *H influenzae* type b. Organisms were identified and typed at the reference laboratories using both type specific antisera and a polymerase chain reaction method.<sup>1</sup> Brief clinical details were also collected. The results for the first two years of the survey showed that most *H influenzae* infections were due to type b, presented as meningitis, and occurred in children under 5,<sup>2</sup> suggesting that mass vaccination of infants should achieve a rapid change in the pattern of invasive *H influenzae* infections.

Since October 1992 there has been a rapid reduction in the number of reported cases of *H influenzae* type b

disease, particularly in children aged under 5 (see figure). Annual attack rates for *H influenzae* type b disease in children under 5 (calculated using denominator populations) have fallen from 30.9 cases per 100 000 population in 1991-2 (369 cases recorded) to 2.0 per 100 000 in 1993-4 (24 cases), a reduction in risk of invasive disease from 1 case in 3200 to 1 per 50 000 children. Comparison of the rates of invasive *H influenzae* type b disease in children under 5 using log-linear regression showed a highly significant reduction ( $P < 0.001$  in 1993-4 compared with previous years).

Non-capsulate *H influenzae* isolates have shown an increase in annual attack rate (for all ages) from 0.25 cases per 100 000 population in 1990-1 (45 cases recorded) to 0.37 in 1993-4 (67 cases). The total number of recorded cases of non-type b infections (non-capsulate and other serotypes: 75 cases) exceeded the number of cases of *H influenzae* type b (50 cases) in 1993-4. These increases demonstrate a sustained trend, approaching significance for non-capsulate infections during 1993-4 ( $P = 0.066$ ), which has been most noticeable in people aged over 65 years.



Invasive *H influenzae* type b and non-capsulate infections by quarter