Birth weight, current body weight, and blood pressure in late adolescence

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Abstract

***Objective*—To study the effect of birth weight and body weight on blood pressure in late adolescence.**

***Design*—Analysis of data on weight, height, and blood pressure at age 17 of subjects from the Jerusalem perinatal study, according to their birth weight. Data for men and women were analysed separately.**

***Setting*—Jerusalem, Israel.**

***Subjects*—32 580 subjects (19 734 men and 12 846 women) born in the three major hospitals in Jerusalem during 1964-71 and subsequently drafted in to the army.**

***Main outcome measures*—Correlations between birth weight and blood pressure at age 17 and weight and height at age 17 and blood pressure.**

***Results*—Diastolic and systolic blood pressures were associated with birth weight in both young men and young women, but the correlation coefficients were low. A high body weight at age 17 (>66 kg for women, >75 kg for men) rather than a low birth weight (<2500 g) was linked with higher systolic and diastolic blood pressures in both men and women ($p<0.01$).**

***Conclusions*—Intrauterine environment, as reflected by birth weight, has little effect on blood pressure in young men and women. Modification of factors which lead to excess weight during adolescence may have a major role in preventing hypertension in adults.**

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Introduction

Adverse intrauterine conditions have recently been related to ischaemic heart disease and chronic lung disease in adult life.[1,2] Raised blood pressure has been suggested as a possible link between an unfavourable intrauterine environment and the long term risk of cardiovascular disease.[2] Birth weight, a measure of intrauterine influences, has accordingly been found to be inversely associated with blood pressure in childhood,[3-5] as well as in adult life.[6-8] This observation, however, has not been confirmed by all studies.[9] Furthermore, in a recent study Hack et al reported lower blood pressures during childhood in children of very low birth weight.[10] Currently only three studies—among 77 young men in Sweden[6] and 3259[7] and 449[8] adults in Britain—have examined the role of birth weight in the epidemiology of hypertension in adulthood. As both birth weight and hypertension are common indicators of a population's health any association between these factors is of great interest.

We analysed data on blood pressure and physical measurements (weight and height) at age 17 years of 32 580 subjects from army records according to their birth weight obtained from the Jerusalem perinatal study, simultaneously adjusting for ethnic origin and socioeconomic factors.

Methods

The study population consisted of 33 545 subjects born in Jerusalem between 1964 and 1971. Birth weights recorded at the time of delivery as well as detailed antenatal and perinatal data were obtained from the computerised files of the Jerusalem perinatal study.[11,12] Blood pressure, body weight, and height measurements at 17 years of age were available from the Israel Defence Forces draft medical examination computerised records.[13] Complete information was available for 32 580 (97·1%) of the subjects. Blood pressure was measured in the sitting position in the right arm with a Bauman sphygmomanometer with appropriate cuff size. The end point for diastolic blood pressure was the disappearance of the Korotkoff sounds (phase V). The examiners were not aware of the perinatal data. Standing height was measured without shoes to the nearest centimetre. Body weight without clothes was determined to the nearest 100 g. The data for each subject were matched by using a seven digit identification number. The completeness of the match was confirmed by comparing sex and maternal identity number. Only 12 846 (38·3%) of our study population were women as women who declare themselves to be orthodox religious are exempted from military service.[13] The results are thus presented separately for men and women. Only a negligible minority (<2% of subjects) who were in hospital because of severe chronic and psychiatric disease and long term prisoners were not examined and consequently not included in our data.

A multiple linear regression analysis using the general linear models procedure of the SAS Institute software[14] was performed to control for the effect of the studied independent variables. The mean systolic or diastolic blood pressure was used as a continuous dependent variable. The independent variables in the analysis were body weight, height, and body mass index (kg/m^2) at 17 years of age; birth weight as a continuous variable; ethnic origin (defined according to paternal country of birth); area of residence (classified by municipal tax area into nine levels[12]; paternal educational attainment (0, 1-4, 5-8, 9-12, or ≥13 years of schooling); and birth order (categorised to avoid dubious assumptions about linearity). All variables that were significant at the $p<0.05$ level were added to the regression model. Separate models were estimated for men and women. The Pearson correlation coefficient was used to determine relations among the main variables.

A mutiple logistic regression analysis with the Logist procedure of the SAS Institute software was performed

by a stepwise method for blood pressure as a dichotomous variable, to adjust for the effect of the studied independent variables. High systolic blood pressure (>140 mm Hg) and high diastolic pressure (>85 mm Hg) were dependent variables. The results of the logistic regressions are presented as adjusted odds ratios and their 95% confidence intervals (that is, $e^{b \pm 1.96s}$, where b is the logistic regression coefficient and s is its estimated standard error). The estimates presented are based on the exclusion of cases with missing values (2·9%).

Results

The mean diastolic and systolic blood pressures at 17 years of age correlated with body weight, height, body mass index, and birth weight for both sexes (table I).

TABLE I—*Pearson correlation coefficients of birth weight and weight, height, and body mass index at age 17 with systolic and diastolic blood pressure at age 17*

	Men (n=20 699)		Women (n=12 846)	
	Systolic	Diastolic	Systolic	Diastolic
Birth weight (g)	0·015*	0·025**	0·019*	0·007
Body weight (kg)	0·237***	0·175***	0·185***	0·149***
Height (cm)	0·100***	0·086***	0·072***	0·070***
Body mass index (kg/m²)	0·217***	0·153***	0·164***	0·125***

*p<0·05; **p<0·0005; ***p<0·0001.

However, the correlation coefficients for birth weight were low. To show the clinical importance of the associations mean blood pressure was determined for three birth weight and three body weight groups (upper 10th, lower 10th, and intermediate categories) (table II). Blood pressure was significantly (p<0·001) associated with body weight but not with birth weight for these categories. Table III gives the estimated partial correlation coefficients of a multiple linear regression analysis, using either diastolic or systolic blood pressure as the dependent variable.

A multiple logistic regression analysis undertaken to examine the association of birth weight group with high diastolic blood pressure (>90 mm Hg) or high systolic blood pressure (>140 mm Hg) showed no consistent relation. Only subjects with birth weight 3500-3999 g for women and 4000-4499 g for men were associated with a significantly (p<0·05) decreased risk of high diastolic blood pressure compared with those with birth weight 3000-3499 g (odds ratios, 95% confidence intervals 0·74, 0·59 to 0·93 and 0·80, 0·66 to 0·99, respectively). Women with birth weight 4000-4499 g had a significantly higher (p<0·05) risk of high systolic blood pressure compared with those with birth weight 3000-3499 g (2·59, 1·08 to 6·20). Body weight was significantly (p<0·02) related to high diastolic blood pressure and body weight and body mass index

TABLE III—*Partial correlation coefficients for systolic and diastolic blood pressures by multiple linear regression analysis according to birth weight and weight, height, and body mass index at age 17*

	Men (n=20 088)		Women (n=12 492)	
	Systolic	Diastolic	Systolic	Diastolic
Birth weight (g)	0·027**	0·010	0·051**	0·024*
Body weight (kg)	0·008	0·001	0·002	0·005
Height (cm)	0·007	0·014*	0·011	0·007
Body mass index (kg/m²)	0·011	0·014*	0·012	0·005

*p<0·01; **p<0·001.

significantly (p<0·02) linked with high systolic blood pressure in both men and women.

Discussion

Systolic and diastolic blood pressure at 17 years of age was related to birth weight in a population of 32 580 subjects. These results agree with those of Barker *et al*[7 8] and Gennser *et al*,[6] but contradict the results of Higgins *et al*.[9] Our results lend some support to the suggestion made by Simpson *et al* that the intrauterine environment might influence the genesis of both low birth weight and later high blood pressure.[3] However, the contribution of birth weight to the variation in blood pressure seems to be small. Furthermore, low birth weight (<2500 g) was not associated with significantly higher systolic or diastolic blood pressure.

Body weight and body mass index at age 17 were associated with blood pressure. The increased risk of raised blood pressure among overweight adolescents is well recognised.[15] As blood pressure in adults is correlated with change in weight from childhood to adult life[16] it seems that the major environmental effect on blood pressure is exerted during childhood, rather than over the intrauterine period.

Barker *et al* suggested that the geographic variation in cardiovascular mortality in Britain might be due to differences in the intrauterine environment linked with changes in blood pressure.[7] In contrast, Elford *et al* concluded that factors acting in adult life seem to be more important determinants of regional differences in blood pressure than the intrauterine environment.[17] Our results show a small contribution of intrauterine environment, as reflected by birthweight, to the variation in adult blood pressure. Nevertheless, overweight adolescents rather than low birthweight infants seem to be at risk of high pressure in adulthood. Therefore, the suggestion by Barker *et al* of improving the nutrition of pregnant women as a means of increasing their child's birth weight, thereby reducing the offspring's blood pressure in adulthood, should be reconsidered. However, the important role of weight control during adolescence in preventing adult hypertension is further emphasised.

TABLE II—*Mean (SEM) systolic and diastolic blood pressure (mm Hg) [number of subjects] at age 17 in women and men by birth weight and body weight (upper 10th, lower 10th, and intermediate categories)*

	Systolic				Diastolic			
	Body weight (kg)			Adjusted for body weight	Body weight (kg)			Adjusted for body weight
Birth weight (g)	<47	47-66	>66		<52	52-75	>75	
				Women				
<2500	110 (1·1) [123]	114 (0·5) [535]	119 (2·2) [38]	114 (0·5) [696]	70 (0·8) [123]	72 (0·5) [532]	74 (1·7) [38]	72 (0·3) [693]
2500-3999	110 (0·4) [1078]	113 (0·1) [9 172]	119 (0·4) [1195]	114 (0·2) [11 445]	71 (0·2) [1077]	72 (0·1) [9 143]	75 (0·2) [1194]	72 (0·1) [11 414]
>4000	110 (1·0) [19]	112 (0·5) [494]	117 (1·1) [115]	113 (0·5) [628]	74 (1·7) [19]	72 (0·4) [491]	75 (0·7) [115]	73 (0·3) [625]
Adjusted for birth weight	110 (0·4) [1220]	113* (0·2) [10 201]	119* (0·4) [1348]		71 (0·3) [1219]	72* (0·2) [10 166]	75* (0·3) [1347]	
				Men				
<2500	115 (0·9) [142]	121 (0·4) [717]	130 (1·1) [74]	122 (0·4) [933]	72 (0·7) [142]	74 (0·3) [715]	76 (0·9) [74]	74 (0·3) [931]
2500-3999	117 (0·3) [1554]	120 (0·1) [14 421]	127 (0·3) [1789]	121 (0·1) [17 764]	72 (0·2) [1547]	74 (0·1) [14 383]	77 (0·2) [1781]	74 (0·1) [17 711]
>4000	115 (1·6) [46]	120 (0·3) [1 446]	125 (0·6) [367]	121 (0·3) [1 859]	71 (1·2) [46]	74 (0·2) [1 441]	77 (0·4) [367]	74 (0·2) [1 854]
Adjusted for birth weight	117 (0·3) [1742]	120* (0·2) [16 584]	126* (0·3) [2230]		72 (0·2) [1735]	74* (0·1) [16 539]	77* (0·2) [2222]	

*p<0·01.

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Neonatal screening strategy for cystic fibrosis using immunoreactive trypsinogen and direct gene analysis

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Abstract

***Objective*—To assess the effectiveness of a two tier neonatal screening strategy for cystic fibrosis, which combines estimation of immunoreactive trypsinogen followed by direct gene analysis in dried blood spot samples collected at age 5 days.**

***Design*—Prospective study of two tier screening strategy. The first tier of testing immunoreactive trypsinogen concentration was measured in dried blood spot samples from neonates aged 4-5 days. In the second tier direct gene analysis to detect cystic fibrosis mutations ΔF508 and ΔI506 was performed in those blood spot samples which produced the highest 1% of immunoreactive trypsinogen values. Direct gene analysis was also performed on blood spot samples from infants with suspected or confirmed meconium ileus, regardless of the immunoreactive trypsinogen value.**

***Setting*—The South Australian Neonatal Screening Programme, operating from the department of chemical pathology at Adelaide Children's Hospital.**

***Subjects*—All 12 056 neonates born in South Australia between December 1989 and June 1990. No selection criteria were applied.**

***Interventions*—All infants found to have two recognised cystic fibrosis mutations on direct gene analysis were referred directly for clinical management, and those with one recognised cystic fibrosis mutation were recalled for a sweat test; their families were given genetic counselling.**

***Main outcome measures*—Diagnosis or exclusion of cystic fibrosis by sweat testing of neonates identified as being at high risk of cystic fibrosis on screening and of those at minimum risk but whose subsequent clinical history raised suspicion about the disease.**

***Results*—Of the 12 056 infants screened, 11 907 (98·8%) were reported as "cystic fibrosis not indicated" on the basis of low immunoreactive trypsinogen values. Of the 148 (1·23%) infants with raised immunoreactive trypsinogen values and one (0·008%) with meconium ileus, 132 (1·09%) were reported as cystic fibrosis not indicated, four (0·033%) were identified as having cystic fibrosis, and 13 (0·108%) were recalled for sweat testing after direct gene analysis for the presence of the ΔF508 and ΔI506 cystic fibrosis mutations. No cases of affected infants are known to have been missed to date.**

***Conclusion*—The strategy of measurement of immunoreactive trypsinogen followed by direct gene analysis is a highly specific neonatal screen for cystic fibrosis, requiring only 2·8 families to be contacted for every case of cystic fibrosis diagnosed.**

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Introduction

Measurement of immunoreactive trypsinogen concentration in dried blood spot specimens taken at 4-5 days of age[1,2] has become the preferred primary neonatal screen for cystic fibrosis. However, some unaffected infants have raised immunoreactive trypsinogen values in the neonatal period, and an unacceptable lack of specificity exists in this initial measurement.[3] A screening strategy was consequently adopted[4] whereby all those infants with high values on initial blood spot testing are recalled for testing of a second blood spot specimen taken at age 4-6 weeks.[4] If the second immunoreactive trypsinogen value remains high the infant is again recalled, this time for a sweat test.[5-7] Such a strategy eventually reduces the false positive rate of the immunoreactive trypsinogen screen to an acceptable level, but in the intervening two to four weeks considerable anxiety is created for an appreciable number of families. Various authors have also reported affected infants who had normal immunoreactive trypsinogen concentrations on testing of the initial[5,7-9] and second[10] blood spot samples. This has resulted in uncertainty about the decision values to be applied to neonatal immunoreactive trypsinogen concentrations in blood spots in order to include most affected infants in the screen.[11]

Before neonatal screening for cystic fibrosis is unreservedly accepted a strategy of greater specificity and sensitivity is required.[12] To this end, interest has been shown in the use of direct gene analysis now that some of the mutations resulting in cystic fibrosis have been described.[13,14] A disadvantage of direct gene