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Weight in infancy and prevalence of coronary heart disease in adult life

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Abstract

***Objective*—To determine whether low birth weight and low weight at 1 year are followed by an increased prevalence of coronary heart disease in adult life.**

***Design*—A follow up study of men born during 1920-30 whose birth weights and weights at 1 year were recorded.**

***Setting*—Hertfordshire, England.**

***Subjects*—290 men born and still living in East Hertfordshire.**

***Main outcome measure*—The prevalence of coronary heart disease, defined by the Rose/WHO chest pain questionnaire, standard electrocardiographic criteria, or history of coronary artery angioplasty or graft surgery.**

***Results*—42 (14%) men had coronary heart disease. Their mean birth weight, 7·9 lb (3600 g), was the same as that of the other men. Their mean weight at 1 year, 21·8 lb (9·9 kg), was 1 lb (454 g) lower (95% confidence interval 0·1 to 1·8, P=0·02). Percentages of men with coronary heart disease fell from 27% in those who weighed 18 lb (8·2 kg) or less at 1 year to 9% in those who weighed more than 26 lb (11·8 kg) (P value for trend=0·03). This trend occurred in both smokers and non-smokers and within each social class.**

***Conclusion*—These findings add to the evidence that coronary heart disease is "programmed" during early growth.**

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Introduction

Recent findings suggest that the pathogenesis of coronary heart disease begins in fetal life and infancy. Among 10 141 men born during 1911-30 in Hertfordshire, England, whose birth weights and weights at 1 year had been recorded, men with the lowest birth weights and weights at 1 year had the highest death rates from coronary heart disease.[1 2] The association with weight at 1 year was stronger than that with birth weight, though both were significant. Reduced growth in utero and during infancy has also been shown to be associated with an increased risk of hypertension and non-insulin dependent diabetes and higher concentrations of low density lipoprotein cholesterol and fibrinogen in adult life.[3-6] These findings have led to the hypothesis that coronary heart disease originates from early programming whereby undernutrition during sensitive periods in early life permanently changes the body's structure and physiology.[7 8]

The Hertfordshire study was based on diagnosis of coronary heart disease on death certificates.[2] We now present data on disease in living subjects. using validated methods we have measured the prevalence of symptomatic and asymptomatic coronary heart disease in a sample of 290 men born and still living in East Hertfordshire.

Methods

In Hertfordshire from 1911 onwards each birth was notified by the attending midwife, and a health visitor saw the child periodically throughout infancy. The child's birth weight and weight at 1 year of age were recorded.[1] We used these records to trace 5654 men who were born as singletons in the six districts of East Hertfordshire between 1911 and 1930 and who had both birth weight and weight at 1 year recorded to determine mortality from cardiovascular disease.[1] Of the total, 1186 men had died, 434 of them from coronary heart disease.[1] We subsequently approached the 1157 men who were born in East Hertfordshire between 1920 and 1930 and still lived there.[3] Of these, 845 men agreed to be interviewed at home. Their current occupation or their occupation before retirement and their father's occupation at the time of their birth were used to determine socioeconomic class currently and at birth.[9] Their blood pressure was measured.[3] After the interview men were asked if they would be willing to attend a local clinic to have blood samples taken, and 468 men agreed. Serum concentrations of lipids and concentrations of plasma clotting factors, glucose, and insulin were measured, and the results have been reported.[3 4 6]

For the study reported here, we reapproached the 370 men who had complete measurements on all blood samples. Of the 370, seven had died and 11 had moved away. Of the remaining 352, 290 (82%) took part. The men were visited at home by a nurse who asked for details of current smoking habits. After the interview the subjects were asked to come to a local clinic where the Rose/WHO chest pain questionnaire[10] was administered and standard 12 lead electrocardiography carried out according to the 1982 Minnesota protocol.[11] Height was measured with a portable stadiometer and

weight with a Seca scale. Waist and hip circumferences were also measured. Electrocardiograms were Minnesota coded independently in duplicate by two trained coders who were blind to all other data for the men.

Coronary heart disease was defined as the presence of one or more of the following: angina according to the questionnaire on chest pain; electrocardiography Minnesota codes 1-1, 1-2 (Q and QS codes)[11]; or a history of surgery for coronary revascularisation, either coronary artery bypass graft or coronary angioplasty. Our criteria did not include a history of heart attack because of possible error of recall or diagnosis.

STATISTICAL ANALYSIS

We analysed the data using tabulation of means, two sample *t* tests, and logistic regression. Multiple logistic regression was used to assess the combined effects of early weight and potential confounding variables such as smoking and social class on prevalence of coronary heart disease. P values were calculated by using the variables as continuous when appropriate.

Results

Forty two men (14%) fulfilled one or more criteria for coronary heart disease. Twenty seven had typical angina, 15 had electrocardiographic evidence of myocardial infarction, and 12 had a history of coronary artery surgery. Their mean birth weight was similar to that of men without coronary artery disease (table I). Their mean weight at 1 year, however, was 1lb (454 g) lower. They were shorter and had higher concentrations of low density lipoprotein cholesterol. Differences in systolic blood pressure, plasma fibrinogen concentrations, serum concentrations of high density lipoprotein cholesterol, and rates of impaired glucose tolerance were in the expected direction but were not significant.

The prevalence of coronary heart disease showed no trend with birth weight (P=0·9) but fell progressively with increasing weight at 1 year (P=0·03; table II). In a simultaneous analysis of birth weight and weight at 1 year together, prevalence of coronary heart disease fell with increasing weight at 1 year (P=0·01) but showed no trend with birth weight (P=0·3). The odds ratio for coronary heart disease was 3·6 in men who had weighed 18 lb (8·2 kg) or less at 1 year when compared with men who had weighed more than 26 lb (11·8 kg).

Men currently in lower social classes had a higher prevalence of coronary heart disease (P for trend= 0·03; table III). Men born into lower social classes also tended to have a higher prevalence of coronary heart disease, but this trend was not significant (P=0·1). Table III shows that the trend of coronary heart disease with weight at 1 year occurred in each social class group, defined currently or at birth. Men currently in high social classes tended to have higher weight at 1 year. Mean values were 23·5 lb (10·7 kg) in social classes I, II, and IIIN; 22·5 lb (10·2 kg) in class IIIM; and 21·7 lb (9·8 kg) in classes IV and V. There were, however, no trends in weight at 1 year with social class at birth; mean values being 22·6 lb (10·3 kg), 23·2 lb (10·5 kg), and 22·4 lb (10·2 kg), respectively. The trend in coronary heart disease with weight at 1 year was seen in smokers, former smokers, and non-smokers (table III). Adjustment for birth weight and the three variables in table III in turn gave P values for the trend of coronary heart disease with weight at 1 year of 0·05 (current social class), 0·02 (social class at birth), and 0·01 (smoking status).

TABLE I—*Mean birth weight and weight at 1 year, related to variables in adult life for men with and without coronary heart disease*

Variable	With coronary heart disease (n=42)	Without coronary heart disease (n=248)	Difference (95% confidence interval)	SD
Birth weight (lb)*	7·9	7·9	0 (−0·4 to 0·4)	1·3
Weight at 1 year (lb)*	21·8	22·8	−1·0 (−1·8 to −0·1)	2·6
Measurements in adults:				
Age (years)	66·8	66·8	0·0 (−1·1 to 1·0)	3·1
Height (m)	1·70	1·73	−0·02 (−0·04 to 0·00)	0·06
Body mass index (kg/m²)	26·4	26·7	−0·3 (−1·5 to 0·8)	3·4
Waist:hip ratio (%)	93·8	93·7	0·0 (−1·7 to 1·8)	5·2
Systolic blood pressure (mm Hg)	165	163	2·5 (−4·9 to 9·8)	19
Low density lipoprotein cholesterol (mmol/l)	5·3	4·6	0·6 (0·3 to 1·0)	1·1
High density lipoprotein cholesterol (mmol/l)	1·18	1·23	−0·05 (−0·16 to 0·05)	0·3
Fibrinogen (g/l)	3·11	3·04	7 (−12 to 26)	58
Proportion (%) with impaired glucose tolerance	29	21	7 (−7 to 21)	
Proportion (%) of current or former smokers	83	83	0 (−12 to 12)	

*1 lb=0·454 kg.

TABLE II—*Percentages of men with coronary heart disease according to their birth weight and weight at 1 year*

Weight	No of men	Percentage (No) with coronary heart disease
Birth weight (lb)*:		
≤5·5	10	20 (2)
−6·5	38	21 (8)
−7·5	84	17 (14)
−8·5	94	6 (6)
−9·5	44	11 (5)
>9·5	20	35 (7)
Weight at 1 year (lb)*:		
≤18	15	27 (4)
−20	47	21 (10)
−22	86	14 (12)
−24	85	14 (12)
−26	35	6 (2)
>26	22	9 (2)
All	290	15 (42)

*1 lb=0·454 kg.

TABLE III—*Percentages of men with coronary heart disease according to their weight at 1 year and social class currently and at birth and smoking habits. Figures in parentheses are numbers of men*

Variable	Weight at age 1 year: ≤21 lb* (n=84)	−23 lb* (n=100)	>23 lb* (n=106)	All (n=290)
Current social class†:				
I, II, IIIN	21 (14)	13 (31)	7 (46)	11 (91)
IIIM	16 (43)	19 (48)	9 (44)	15 (135)
IV, V	26 (27)	14 (21)	13 (15)	19 (63)
Social class at birth‡:				
I, II, IIIN	11 (9)	8 (13)	8 (13)	9 (35)
IIIM	29 (17)	17 (35)	4 (47)	13 (99)
IV, V	19 (52)	19 (48)	15 (40)	18 (140)
Smoking status:				
Never smoked	38 (8)	11 (18)	9 (22)	15 (48)
Former smoker	20 (60)	19 (63)	9 (66)	16 (189)
Current smoker	13 (16)	11 (19)	6 (18)	9 (53)

*1 lb=0·454 kg. †Unclassifiable for one man. ‡Unclassifiable for 16 men.

Discussion

We have shown that men with symptoms and signs of coronary heart disease tend to have had low weight at the age of 1 year (table II). This is consistent with an association which has hitherto depended on studies of deaths from the disease. Coronary heart disease was defined by using validated methods and standard criteria. The 42 cases identified had the expected profile of cardiovascular risk factors, including short stature (table I). The overall prevalence of coronary heart disease in the men was 14%, comparable with results of British prevalence studies in this age group.[12,13] The threefold difference in prevalence between men who were small or large at 1 year (table II) is similar to the difference in mortality from the disease.[2]

Prevalence of coronary heart disease was not related to birth weight (tables I and II). In the Hertfordshire mortality studies based on 10 000 men death rates from coronary heart disease were inversely related to birth weight,[1,2] but the relation was weaker than with weight

Key messages

- Boys with low weight at 1 year have a high prevalence of coronary heart disease as adults
- This is consistent with the association between low weight at 1 year and increased death rates from coronary heart disease
- The association between low weight at 1 year and coronary heart disease occurs in smokers and non-smokers and in each social class
- This adds to evidence that influences acting before 1 year of age have an important effect on the risk of developing coronary heart disease

at 1 year. Perhaps our study was not large enough to show a relation between prevalence and birth weight.

Our study was confined to men born and still living in East Hertfordshire and willing to take part in the study. This introduces the possibility of selection bias. Our analysis, however, was based on comparisons within the sample, and bias would be introduced only if the relation between early weight and coronary heart disease were different in those studied and not studied. This seems unlikely.

Men in lower social classes were lighter at the age of 1 year. Low social class at birth, however, was not associated with low infant weight. Socioeconomic status at birth cannot therefore be used as an indicator of infant growth, which may explain the findings of a recent survey in Kuopio, Finland,[14] in which the prevalence of coronary heart disease was found to be less strongly related to social class at birth than to current social class. As expected[15] we found that men in the lower social classes had a higher prevalence of coronary heart disease. It has been argued that people with poor infant weight continue to be exposed to an adverse environment throughout childhood and into adult life and that it is this later environment that produces the effects being attributed to programming.[16 17] We have shown, however, that prevalent coronary heart disease is associated with low infant weight within each social class and in both smokers and non-smokers (table III). These findings add to the evidence that influences acting before 1 year of age have an important effect on the risk of coronary heart disease.

In previous studies we have shown that the major coronary risk factors—raised blood pressure, high cholesterol and fibrinogen concentrations, and impaired glucose tolerance—are all associated with impaired early growth independently of social class, smoking, alcohol consumption, and obesity. The strength of the associations between reduced early weight and coronary heart disease and its risk factors and the consistency of the associations in different populations[18 19] provide evidence that coronary heart disease is partly programmed in early life.

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ANY QUESTIONS

What is the upper age limit for surgical management of aneurysmal subarachnoid haemorrhage after the "herald" bleed? Does the anatomical site of the aneurysm have any bearing on age related criteria for surgical intervention?

Operations to clip a saccular (Berry) aneurysm that has caused a subarachnoid haemorrhage are prophylactic, intended to prevent the high morbidity and mortality associated with rebleeding. They are not a treatment of the haemorrhage itself. There are no nationally agreed criteria for the management of aneurysmal subarachnoid haemorrhage in Britain, and there are considerable differences between units—for example, in fluid replacement, the use of nimodipine, the timing of surgery, the craniotomy approach, and the type of aneurysm clip used.

Although in the past many units had an age limit of 65 for this form of surgery, most now look carefully at the risk features for any patient. Most surgeons are guided more by physiological age than by true chronological age. The position of the aneurysm is also a factor; anterior circulation aneurysms are much more favourable. Posterior circulation aneurysms or giant aneurysms, particularly those involving the skull base, are less likely to be accepted for surgical treatment in elderly patients. This observation might also apply to younger patients now that interventional neuroradiology has a part to play in management.—MICHAEL POWELL *is a consultant neurosurgeon in London*