Longitudinal study of cholesterol values in 68 children from birth to 11 years of age

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Abstract

Sixty eight children born in 1977 who were taking part in an unrelated study of childhood asthma were selected to have their serum cholesterol concentrations measured at birth, and at 4 months and 1, 2, 3, 4, 5, and 11 years of age. Concentrations of high density lipoprotein were measured at 5 and 11 years.

Cholesterol values increased rapidly from birth and plateaued at 1 year. There was a further small rise just before puberty. Tracking of values was seen after the age of 1 year, but did not become established until 4 years of age. The cholesterol concentrations in girls were marginally higher than those in boys. The mean (SD) values of cholesterol (mmol/l) for boys were: at birth, 1.7 (0.4); at 1 year, 3.9 (0.9); at 5 years, 5.2 (1.9); and at 11 years, 5.0 (0.7). For girls the corresponding figures were: at birth, 1.9 (0.6); at 1 year, 4.7 (1.0); at 5 years, 4.6 (0.7); and at 11 years, 5.1 (0.7). The mean (SD) high density lipoprotein concentrations (mmol/l) for boys were: at 5, 1.16 (0.35) and at 11, 1.51 (0.23). For girls they were 1.28 (0.30) and 1.56 (0.27), respectively.

The serum cholesterol concentrations in these children were high compared with published figures from north America.

Coronary heart disease and cerebrovascular disease remain major causes of morbidity and mortality. The World Health Organisation (WHO) report on the prevention of cardiovascular disease concluded that sufficient knowledge had accumulated to achieve a large reduction in its incidence and gave prominence to dietary factors.¹ In the United States there has been a decline in both saturated fat intake and mortality from coronary heart disease but in the United Kingdom change has been slow.² The reports of three expert panels (American, European, and British) agree that there is a need to instigate preventive measures in childhood, as they consider that atherogenesis has its origin in childhood and that life styles are also formed during this period.³

The present study, initially started to provide 'in house' reference values, may help to explain why British adult cardiovascular mortality remains high.

Patients and methods

A cohort of 68 children was recruited in 1977 as part of a prospective study of the development of atopy in a group of children all of whom had one atopic parent. No attention was paid to

the presence of familial coronary risk factors in this selection, which was made antenatally at the maternity outpatient clinic of Poole General Hospital. The study was approved by the hospital ethics committee. The cohort comprised 31 boys and 37 girls, all but one of whom were white. No attempt was made to modify the children's diet during the study. The social class of the families determined by the paternal employment when the child was aged 5 was: I—13%, II—36%, III—16%, IV—27%, V—6%, and 2% unclassified. This cohort represents the remaining children available for study at age 11 from an original cohort of 95.

The children were seen annually for the first five years of life and at the age of 11 when all except one girl were still prepubertal. Cord blood was obtained at birth and then blood samples were taken when the children were 4 months of age, annually at the time of their birthday during the first five years, and during the spring and summer of 1988. Blood was taken at least two hours after the previous feed; after infancy this was usually a four hour fast and at 11 the children fasted overnight. It was not possible to obtain blood from every child at each age. This was particularly apparent during the preschool period because of parental reluctance to submit their child to a venepuncture.

Cholesterol was measured on single samples by a cholesterol oxidase method at 37°C,⁴ using a commercial kit (Boehringer Mannheim, GmbH Diagnostica). At each age quality control against national standards was undertaken.

In the summaries of the Wellcome External Quality Assessment Programme published every six months for the period October 1980 to November 1988, this laboratory's bias for cholesterol did not exceed +0.18 mmol/l compared with the zero reference of all other methods, but tended to be negative for the period up to April 1986 and positive after that. The variation in our method for the period of these tests was not significantly different from that of other laboratories who were using the same method and who participated in the Wellcome Quality Assurance scheme. High density lipoprotein was measured after precipitation by phosphotungstate and magnesium chloride using the cholesterol enzymatic method with suitable standards.⁵ The blood had been frozen before assay.

The data were not transformed before statistical analysis, as in larger series, cholesterol values have tended to follow a normal distribution. Correlation coefficients for tracking were obtained by comparing the ranking of measured values at each age and the corresponding rank-

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Table 1 Serum cholesterol values (mmol/l)

Age (years)	Girls		Boys		All children	
	No of children	Mean (SD) cholesterol value	No of children	Mean (SD) cholesterol value	No of children	Mean (SD) cholesterol value
Birth	25	1.9 (0.6)	22	1.7 (0.4)	47	1.8 (0.5)
0.3	26	4.4 (1.0)	23	3.9 (0.7)	49	4.2 (0.9)
1	26	4.7 (1.0)	17	4.5 (0.9)	43	4.6 (1.0)
2	22	5.0 (0.8)	17	4.3 (1.2)	39	4.7 (1.0)
3	18	4.5 (0.9)	14	4.5 (1.0)	32	4.5 (1.0)
4	30	5.0 (0.9)	21	5.0 (0.9)	51	5.0 (0.9)
5	27	4.6 (0.7)	22	4.8 (0.7)	49	4.9 (1.4)
11	36	5.1 (0.7)	30	5.0 (0.7)	66	5.1 (0.7)

Figure 1 Serum cholesterol values. Solid circles indicate boys, open circles girls, and divided circles total values. Vertical bars represent SD.

ing of those children's values at 11, using Spearman's rank correlation.

Results

The cholesterol values for the cohort are shown in table 1. The year by year variation in numbers is the result of some children declining venepuncture. The sample number, and the arithmetic mean (SD) are shown for different ages (fig 1). The values increased rapidly from birth to 4 months of age and plateaued at 1 year. The mean (SD) of individual changes in cholesterol were: from birth to 4 months 2.3 (0.9), from 4 months to 1 year 0.6 (1.3), from birth to 1 year 2.8 (1.1), from 1 to 2 years 0.1 (0.9), from 2 to 3 years -0.4 (0.8), from 3 to 4 years 0.5 (1.1), from 4 to 5 years -0.1 (0.7), from 5 to 11 years 0.3 (0.6), and from birth to 11 years 3.3 (0.8), respectively. The girls had a higher group mean than the boys. There was no difference in values between children who were atopic (n=35) and those who were not (n=33).

The frequency distributions of cholesterol values at 1, 5, and 11 years are shown in fig 2. A tracking phenomenon was seen for the higher values between the ages of 5 and 11. The children with the highest 10 values at 5 years of age have been picked out and their values at 1 and 11 highlighted. A similar phenomenon was found for the lowest values. The correlation coefficients of ranking among values at birth, 4 months, 1, 2, 3, 4, 5, and 11 years are shown in table 2. A correlation of 1 means that there was perfect tracking of results and 0 that there was none.

High density lipoprotein concentrations at 5 and 11 years are shown in table 3. The mean (SD) of individual changes of high density lipoprotein concentrations between 5 and 11 years was 0.31 (0.4) mmol/l. No tracking was observed between the limited values at 5 and

Figure 2 Distribution of serum cholesterol values for total cohort at (A) 1, (B) 5, and (C) 11 years. The open blocks in (B) represent the 10 highest values at 5 years.

Table 2 Rank correlation coefficients between cholesterol values in early childhood and those at the age of 11 years

Age (years)	Girls		Boys	
	Correlation coefficient	p Value	Correlation coefficient	p Value
Birth	0.04	>0.05	0.49	>0.05
0.3	0.31	>0.05	0.57	>0.05
1	0.57	>0.05	0.62	0.05
2	0.25	>0.05	0.47	>0.05
3	0.57	>0.05	0.12	>0.05
4	0.64	0.05	0.74	0.02
5	0.76	0.02	0.66	0.05

Table 3 Serum high density lipoprotein concentrations (mmol/l)

	Age (years)	
	5	11
All children:		
No of children	36	66
Mean (SD)	1.22 (0.33)	1.53 (0.25)
Boys:		
No of children	17	30
Mean (SD)	1.16 (0.35)	1.51 (0.23)
Girls:		
No of children	19	36
Mean (SD)	1.28 (0.30)	1.56 (0.27)

Figure 3 Comparison of cholesterol values in British and American children (British values plotted on American centile chart).⁹

those at 11 years (correlation coefficients 0.17, $p > 0.05$, for boys and 0.35, $p > 0.05$, for girls). The range of cholesterol:high density lipoprotein ratios at 11 years was 2.10:5.74 with an arithmetic mean (SD) of 3.36 (0.39)—boys 3.32 (0.82), and girls 3.4 (0.77), respectively.

Discussion

We know of no published long term longitudinal studies of cholesterol values in children in the United Kingdom. The few cross sectional studies give values in agreement with this study.^{6 7 8} When compared with studies from the United States^{9 10 11} and Australia¹² our values show similar tracking of values and a slightly higher mean cholesterol value for girls. Cholesterol values rise towards puberty, fall thereafter, and slowly climb to the pubertal values in late adolescence.^{13 14 15} One boy had a raised cholesterol value at the age of 5 of 13.2 (high density lipoprotein 1.58); this had been 2.6 at 2, 6.5 at 4, and became 6.3 at 11 (high

density lipoprotein 1.30) without treatment or dietary advice.

Our cholesterol values are higher than the normal values published in American series, although this cohort contains a preponderance of girls and an excess of higher social classes, both factors associated with increased values. When plotted on the centile chart from the Bogalusa study, which looked at the total child population in a Louisiana town in the 1970s, our group mean is raised (fig 3).¹¹ Similar results are obtained when plotted on the Federal Lipid Research Center study centiles.¹³ Our high density lipoprotein values are similar with those of the Lipid Research Center study. The ratio of cholesterol:high density lipoprotein is used as an index of risk in adults with a value above 4 causing concern. Our increased cholesterol values are not matched by a corresponding protective increase in high density lipoproteins.

The Lipid Research Center protocol for cholesterol measurement, which is the American standard, uses a non-enzymatic reaction on plasma extract, and is different from the method used in this study.¹⁶ There is always a danger when comparing results obtained using a different method, especially with lipid measurements which are among the most difficult and exacting of laboratory measurements. Our external quality controls are, however, well within United Kingdom standards and we consider comparisons can be made.

There is considerable debate about the concentration of cholesterol desirable for health. The evidence that atherosclerosis begins in childhood was established two decades ago,¹⁷⁻¹⁹ and it seems likely to be a problem of paediatric nutrition. Our cholesterol values would be considered raised by American standards, by which a cholesterol value of 5.18 mmol/l (200 mg/dl) has been suggested as a threshold above which dietary manipulations are indicated.²⁰ If this is applied to our cohort of 'normal' children 42% would require dietary treatment.

We consider that these differences in results are a cause for concern, and may explain some of the differences in adult mortality resulting from coronary heart disease. The previous position in this country of not recommending treatment limits and accepting raised concentrations in the general population needs to be reconsidered.²¹ It seems likely that our raised values are the result of dietary factors. Experience from the United States shows that adult eating habits can be beneficially altered by public education. We suggest that these measures should be applied to the whole family, including the children.

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Dexamethasone in meningitis

Dr McCracken and his disciples in Dallas have produced impressive evidence that locally acting mediators of inflammation do a fair amount of mischief in bacterial meningitis and their production can be suppressed by giving dexamethasone.¹ In a recent report (Mustafa *et al*, *American Journal of Diseases of Children* 1990;144:883-7) they showed that patients with bacterial meningitis treated with dexamethasone (89% due to *Haemophilus influenzae*) had, after 18 to 30 hours, lower cerebrospinal fluid concentrations of prostaglandin (PGE₂), interleukin 1 β , and lactate and subsequently fewer neurological sequelae.

The Committee on Infectious Diseases of the American Academy of Pediatrics has given recommendations (*Pediatrics* 1990;86:130-3). They conclude, however, that available data is insufficient to make recommendations about children under the age of 2 months or about bacterial meningitis not caused by *H influenzae*.

Dexamethasone should not be used in non-bacterial meningitis. For *H influenzae* meningitis the committee calls for more studies and sits on the fence—'dexamethasone *probably* reduces the likelihood of deafness' (my italics) and 'we recommend individual consideration of dexamethasone . . . after the physician has weighed the benefits and possible risks'. In other words, make your own mind up. If you're going to give it you have to give it at the start, it's illogical to give it after you've thought about it for a few hours, by then you'll have missed the boat, assuming that there is a boat to be caught. Published data suggest that children with a milder illness stand to benefit as much as those with severe disease so there seems to be no point in restricting dexamethasone to severely ill children only. Either you give it or you don't, but don't give it in viral meningitis.

ARCHIVIST

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