Annotations

Cholesterol and diet

Of recent years it has become increasingly apparent that the blood cholesterol concentration of a population is closely related to the prevalence of ischaemic vascular disease in that population. Pioneering epidemiological work by Ansel Keys in Minnesota (the Seven Countries Study) was the first to show this clearly.¹ Over the succeeding quarter century others went on to show that what was true of populations was also true of individuals,^{2,3} that it was the cholesterol in low density lipoprotein that was deleterious,⁴ and that high concentrations of high density lipoprotein were protective.⁵ Low density lipoprotein appears to be the major source of cholesterol in atheromatous lesions, and high density lipoprotein is important in removing cholesterol from the arterial wall and returning it to the liver. Recent investigations have shown that lowering the low density lipoprotein and raising the high density lipoprotein cholesterol concentrations in the blood of high risk individuals reduces their risk of heart disease (the Helsinki Heart Study).⁵

There is now good evidence that atherosclerosis begins early in life.⁶⁻⁸ Not only are atheromatous plaques found in young adults killed accidentally or in war,⁹ but fatty streaks can be found in the aortas of 3 year olds and in the coronary arteries in the second decade of life. Newman *et al*, in a carefully conducted community study in Bogalusa County, Louisiana, showed that of those young people (age 5-24) dying of accidents or non-vascular disease in early life, the vast majority had aortic fatty streaks or atheromatous coronary plaques.⁶ These streaks or plaques correlated closely with previously measured cholesterol, low density lipoprotein, and very low density lipoprotein concentrations and also with blood pressure; there was an inverse correlation with cholesterol in high density lipoprotein. Blood lipids, therefore, are important even in children as risk factors for the development of atherosclerosis. The concentrations of blood lipids vary between populations and diet is a major (although by no means the sole) factor in determining the blood lipid concentrations.

As paediatricians we have two separate problems to consider:

- (1) What advice do we give to improve the health of the community as a whole?
- (2) What do we do about high risk individuals?

(1) Community advice

PRESCHOOL CHILDREN

Considerable disquiet exists among paediatricians and nutritionists over the advisability of altering the fat intake over the first few years of life. Fat is an important energy source to the infant and young child. Infants fed low fat milks grow less well,¹⁰ and the larger quantities of protein and solutes these infants consequently take in carry the potential hazard of azotaemia and renal damage.¹¹ In addition there is a possible risk of deficiency of fat soluble vitamins.

Over the age of 1 year there is little evidence that a low fat intake per se does any harm as long as basal requirements of fat soluble vitamins and of essential fatty acids are maintained.¹¹ A reduction in fat content implies a less energy dense diet, however, and, often, one that is less palatable. When this is combined with the frequently recommended increase in dietary fibre, a diet is produced that is relatively unattractive to the toddler or young child, and poor growth^{12,13} or actual failure to thrive may result.¹⁴

Nevertheless a reasonable middle course can be found. The fat intake of many British children currently exceeds 50% of total energy. This can be reduced to 35% without prejudicing their energy intake or producing an unpalatable or vitamin deficient diet. In addition, much of the saturated fat can be replaced by monounsaturates or polyunsaturates, which will themselves lower the blood cholesterol concentration. As a 1% reduction in total plasma cholesterol is associated with an approximately 2% fall in mortality from coronary heart disease in a population,¹⁵ even this modest recommendation is likely to have a significant effect on the long term health of our population.

THE ROLE OF DIETARY CHOLESTEROL

It has been traditional to recommend restriction of dietary cholesterol as well as limiting total and saturated fat intake both in normal people and in those with hypercholesterolaemia. Most cholesterol, however, is endogenously synthesised and recent research suggests that a low cholesterol intake may be less important than previously supposed. A group of adult volunteers including both normal subjects and those with hypercholesterolaemia,

while eating an otherwise 'healthy' high fibre, low fat diet, did not alter their blood lipid concentrations when they increased their dietary intake of eggs (which are very rich in cholesterol) from two to seven per week for an eight week period.¹⁶ More work needs to be done in this area but for most people total and saturated fat intake is likely to be more important than intake of dietary cholesterol. (There may, however, be a small group of people who are unduly sensitive to dietary cholesterol changes.)

(2) High risk individuals

One in 500 children has familial hypercholesterolaemia, a dominantly inherited defect of the low density lipoprotein receptor gene that is associated with raised plasma cholesterol concentrated almost entirely within the low density lipoprotein fraction and a family history of premature vascular disease. In many cases heart disease will occur in early to middle adult life. One in a million will inherit homozygous hypercholesterolaemia, receiving a defective gene from each parent. These children have very high cholesterol concentrations (even exceeding 20 mmol/l), skin and tendon xanthomas, and develop vascular disease in late childhood or adolescence. Very few live through their 20s. They need heroic measures to treat their disease (combined heart and liver transplantation has been tried) and diet alone will have little effect. Most families with familial hypercholesterolaemia in our population still remain undetected. As there is every likelihood that the prognosis in children with this genetic disorder can be improved by improving their diet and lifestyle,^{4 5 15} all children from families with a history of premature vascular disease should be screened and appropriate advice offered to those from affected families.

These patients deserve early and intensive management starting in childhood. Their prognosis for leading a healthy adult life is poor, and they may well be struck down prematurely at a time when their whole family is financially and emotionally dependent on them. They should be managed initially by diet alone, but if this is inadequate (as it may well be) there should be little hesitation in using effective modern lipid active drugs to reduce the plasma cholesterol fraction present in low density lipoprotein, and to raise that in high density lipoprotein.

Few would attempt to restrict dietary fat in infants and toddlers, even from high risk families, but sensible eating habits with a restriction of total fat to approximately 30–35% of total energy can be effectively managed by the age of 5 or even earlier

with no evidence of deleterious effects on nutrition, growth, or social development, and with good long term compliance.^{17 18}

References

- 1 Keys A. *Seven countries: a multivariate analysis of death and coronary heart disease*. Cambridge: Harvard University Press, 1980.
- 2 Dawber TR. *The Framingham study: the epidemiology of atherosclerotic disease*. Cambridge: Harvard University Press, 1980.
- 3 Hjermann I, Velve Byre K, Holme I, Leren P. Effect of diet and smoking intervention on the incidence of coronary heart disease. *Lancet* 1981;iii:1303–10.
- 4 Lipid Research Clinics Program. The lipid research clinics coronary primary prevention trial results. I and II. *JAMA* 1984;251:351–74.
- 5 Frick MH, Elso O, Haapa K, *et al*. Helsinki heart study: primary prevention trial with gemfibrozil in middle-aged men with dyslipidemia. *N Engl J Med* 1987;317:1237–45.
- 6 Newman WP, Freedman DS, Voors AW, *et al*. Relation of serum lipoprotein levels and systolic blood pressure to early atherosclerosis: the Bogalusa heart study. *N Engl J Med* 1986;314:138–44.
- 7 Holman RL, McGill HC, Strong JP, Geer JC. The natural history of atherosclerosis: the early aortic lesions as seen in New Orleans in the middle of the 20th Century. *Am J Pathol* 1958;34:209–35.
- 8 Strong JP, McGill HC. The natural history of coronary atherosclerosis. *Am J Pathol* 1962;40:37–49.
- 9 McNamara JJ, Molot MA, Strempel JF, Cutting RT. Coronary artery disease in combat casualties in Vietnam. *JAMA* 1971;216:1185–7.
- 10 Foman SJ, Filer LJ, Ziegler EE, Bergmann KE, Bergmann RL. Skim milk in infant feeding. *Acta Paediatr Scand* 1979;65:17–30.
- 11 Yeung DL. Infant nutrition update. *Journal of the Canadian Dietetic Association* 1984;45:20–5.
- 12 Rutishauser I, Frood JDL. The effect of a traditional low-fat diet on energy and protein intake, serum albumin concentration and body weight in Ugandan pre-school children. *Br J Nutr* 1973;29:261–8.
- 13 Burkitt D, Morley D, Walker A. Dietary fibre in under and over nutrition in childhood. *Arch Dis Child* 1980;55:803–7.
- 14 Shull MW, Reed RB, Valadian I, Palombo R, Thorne H, Dwyer JT. Velocities of growth in vegetarian pre-school children. *Pediatrics* 1977;60:410–7.
- 15 Kwiterovich PO. Biochemical, clinical, epidemiological, genetic and pathological data in the pediatric age group relevant to the cholesterol hypothesis. *Pediatrics* 1986;78:349–62.
- 16 Edington J, Geekie M, Carter R, *et al*. Effect of dietary cholesterol on plasma cholesterol concentration in subjects following reduced fat, high fibre diet. *Br Med J* 1987;294:333–6.
- 17 Tarlow M, Green A, Worthington D, Buchanan E. The paediatric lipid clinic in Birmingham. *J Inherited Metab Dis* 1988;11(suppl 1):91–3.
- 18 Glueck CJ, Mellies MJ, Dine M, Perry T, Laskarszewski P. Safety and efficiency of longterm diet and diet plus bile acid binding resin cholesterol lowering therapy in 73 children heterozygous for familial hypercholesterolemia. *Pediatrics* 1986;78:338–48.

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