Discussion

Enthusiastic claims for the simplicity, reliability, and reproducibility of the biothesiometer^{2,4} have led to its wide use in diagnosing peripheral neuropathy and in studying the epidemiology, natural course, and response to treatment of this condition.^{1,7,9} The extent to which vibration perception threshold varies at different sites in the same person is obviously important when this measurement is used to diagnose peripheral neuropathy but has not, to our knowledge, been systematically examined. Our results show considerable and unpredictable variability at the big toes and medial malleoli, both in randomly selected diabetics and in a group of non-diabetic subjects stratified by age. Such variability may partly be due to the physical characteristics of the tissues at the test sites, which affect damping of the vibratory stimulus.¹⁰ Greater variability in the diabetic than the non-diabetic group may have reflected neuropathic damage, which was presumably patchy and asymmetric in most cases.

In this study vibration perception threshold exceeded the largest published normal range⁴ at one or more sites in a fifth of the diabetic patients, but only a few of these had the symmetric distal pattern suggesting classical diabetic polyneuropathy. Because of variability among sites, which is present in normal subjects but accentuated in diabetic patients, the diagnosis of abnormality may be difficult. Most patients with a generalised abnormality of the vibration perception threshold probably have peripheral neuropathy, but there remains the diagnostic dilemma of deciding whether a subject with abnormal values at some sites but not others has neuropathy or not. The practice followed in many studies of taking measurements only at a single site or on one side of the body may produce unrepresentative or misleading results.

Biothesiometry may be criticised for several other reasons. Firstly, as with all sensory measurements the technique may be unsuitable for the large proportion of cases (11% in this study) in which readings at each site are inconsistent; variability within sites may be due to psychological factors such as lack of motivation, easy distractibility, fatigue, and poor comprehension^{2,3,11} rather than to a genuine defect in the perception of vibration. Secondly, the immense variability of values with time¹¹ must be considered when interpreting longitudinal studies of the evolution of neuropathy or

its response to treatment.^{7,9} Thirdly, the currently available biothesiometer has several drawbacks, including unsatisfactory standards of electrical safety¹² and poor sensitivity at the upper end of the voltage scale (>40 volts).

In conclusion, wide and previously unreported variability in the vibration perception threshold among different anatomical sites must be recognised when using biothesiometry to diagnose neuropathy, especially when interpreting data based on measurements at single or unilateral sites. Bilateral readings should always be taken, and all sites examined should be considered when deciding whether neuropathy is present.

We thank ICI Ltd for providing a biothesiometer and financial support for JSG; Professor S R Bloom, Dr P V Rao, Sister Alison Hetreed, and Miss Joan Welch for their help with the study; and Caroline Williams for typing the manuscript. GW was supported by the British Diabetic Association.

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(Accepted 27 October 1987)

Effective lipid lowering diets including lean meat

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Abstract

The plasma lipid and lipoprotein responses to two modified isoenergetic diets including meat were studied in 15 free living men with hyperlipidaemia (mean plasma cholesterol and triglyceride concentrations 8.1 and 3.4 mmol/l). A reference diet (diet A, 42% energy from fat, ratio of polyunsaturated to saturated fatty acids (P:S ratio) 0.2) was compared with a fat

reduced diet (diet B, 35% energy from fat, P:S ratio 0.5) and with a further fat modified diet supplemented with fibre (diet C, 27% energy from fat, P:S ratio 1.0). Daily intake of meat and meat products (180 g/day) was the same in each dietary period; that in diet A had a fat content typical of the average British diet, whereas that in diets B and C was based on very lean meat and meat products. During consumption of diet B the plasma cholesterol concentration fell by 8.6% and low density lipoprotein cholesterol by 11%. During consumption of diet C plasma cholesterol fell by 18.5% and low density lipoprotein cholesterol by 23.8%. Triglyceride and high density lipoprotein cholesterol concentrations and body weight did not change appreciably during the study.

A modified diet including a moderate amount of lean meat and meat products is compatible with a reduced lipoprotein mediated risk of atherosclerotic heart disease.

Introduction

Atherosclerotic coronary heart disease is the main cause of death in most industrial communities.¹ There is compelling evidence that

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raised plasma concentrations of cholesterol and of low density lipoprotein cholesterol are causally related to coronary heart disease.^{2,4} Nutritional patterns are a major determinant of plasma low density lipoprotein cholesterol values and of the incidence of coronary heart disease.^{5,6} Changes in the diet of communities prone to coronary heart disease have been advocated, in particular reduction in the intake of saturated fatty acids and substitution by complex carbohydrate.⁷⁻¹⁰

To maximise acceptance of such a modified diet by the public habitual food selection should be changed as little as possible. Conventional lipid lowering diets often proscribe red meats or permit only very small amounts, which many people find uncongenial. Traditionally prepared meats are a main source of fatty acids in the diet¹¹; but meat is also an important source of protein, vitamins, and minerals. Newer techniques of animal husbandry and food processing have made available meat and meat products of substantially reduced fat content,^{12,13} and this study was designed to examine the lipoprotein effects of lipid lowering diets including these foods; the diets were in other ways similar to those routinely recommended.^{7-10,14}

Patients and methods

Fifteen ambulant hyperlipidaemic men referred to the St Thomas's Hospital lipid clinic were recruited (mean age 49.9 (SD 3.1) years, mean body mass index (weight (kg)/height (m)²) 27.2 (SD 1.57)). Five had hypercholesterolaemia alone (mean plasma cholesterol concentration 7.7 (SD 0.7) mmol/l and 10 increased concentrations of cholesterol (8.3 (1.0) mmol/l) and triglyceride (4.2 (0.8) mmol/l). No patient had xanthomas. Five gave a family history of coronary heart disease in a first degree relative presenting before the age of 60. Renal, hepatic, and thyroid biochemical values were normal. No acute medical illnesses were reported during the study. Four patients had clinical evidence of coronary heart disease and were taking a calcium channel blocker or long acting nitrate preparation, or both, for angina pectoris; one hypertensive patient was treated with atenolol. Treatment remained unaltered throughout and no lipid lowering drugs were prescribed. Participants gave informed consent and the study was approved by the ethical committee.

DIETS AND EXPERIMENTAL DESIGN

The study comprised a four week baseline period followed by two four week experimental dietary periods in random sequence. Table I shows the nutrient composition of the diets. The composition of the baseline diet (A)

TABLE I—Nutritional characteristics of diets studied

	Diet A	Diet B	Diet C
Protein (% energy)	13	15	17
Carbohydrate (% energy)	43	50	56
Dietary fibre (g/1000 kcal*)	8	10	20
Pectin (g/1000 kcal*)	1.0	1.3	3.25
Fat (% energy)	42	35	27
Saturated fatty acids (% energy)	21	14	8
Monosaturated fatty acids (% energy)	15	8	7
Polyunsaturated fatty acids (% energy)	4	7	8
Polyunsaturated to saturated fat ratio	0.27	0.5	1.0
Cholesterol (mg/1000 kcal*)	207	180	110

*1000 kcal≈4.18 MJ.

was that described as the average British diet in the report of the Committee on Medical Aspects of Food Policy.¹⁰ Diet B conformed with the general recommendations of that report and diet C was a previously described lipid lowering diet with a relatively high content of pectin and other gel forming fibres derived from fruit and vegetables.^{14,15} Patients and their spouses were provided with frozen boneless meat and meat products approximating in quantity to that consumed by the average British couple at home.¹⁶ An experienced butcher prepared meat for diet A using a conventional level of trim and for diets B and C using a very close trim; these two batches of meat were also used in the meat products (see table II). To provide variety and thus aid compliance a mixture of meat and meat products was included in

each meat pack. Total daily intake of meat and meat products (180 g/day) was constant throughout the three dietary periods. The fat content of two batches of meat was estimated after extraction with hot solvent at the start and near the end of the study; fat made up 16% of bone free weight of meat plus meat products prepared for diet A and 8.5% of that for diets B and C.

TABLE II—Average meat supplied (g) per person per week

Meat pack	Diet A	Diets B and C
Carcass meat	612	705
Offal	34	34
Bacon	165	180
Cooked meats	34	49
Canned meats	100	100
Sausages	120	120
Meat pies and convenience products	206	60

Diets were prescribed in isoenergetic form after baseline dietary assessment by a metabolic dietitian (PJ) using food frequency data; mean energy intake was 2100 kcal (8.8 MJ)/day (range 1600-3200 kcal; 6.7-13.4 MJ). Habitual alcohol intake (which was not excessive in any patient) and exercise patterns were unrestricted but patients were encouraged to keep these constant throughout.

Dietary advice was reinforced at regular intervals, and each participant completed a four day food diary at the midpoint of each dietary period.¹⁷ Diaries were assessed by a nutritional analysis program designed by the Nuffield Laboratories (Institute of Zoology, Regents Park, London NW1 4RY), which confirmed that compliance with dietary advice was satisfactory. The mean percentage of dietary energy derived from fat was 42% for diet A, 35% for diet B, and 27% for diet C; the ratio of polyunsaturated fatty acids to saturated fatty acids was 0.27 for diet A, 0.5 for diet B, and 1.0 for diet C.

Blood samples were obtained from every patient at the end of weeks 3 and 4 of each dietary period.

Laboratory measurements—Venous blood was collected for plasma lipid and lipoprotein measurements into tubes containing disodium edetic acid (final concentration 2.7 mmol/l) after an overnight fast of 12-14 hours and with patients semirecumbent and without venous stasis. Cholesterol and triglyceride were assayed enzymatically in plasma and in lipoprotein subfractions (Boehringer-Mannheim reagents, numbers 237674 and 16448). Very low density lipoprotein was isolated by preparative ultracentrifugation.¹⁸ High density lipoprotein was isolated by selective precipitation of very low density lipoprotein and low density lipoprotein,¹⁹ excess manganese being chelated by disodium edetic acid before cholesterol assay. Low density lipoprotein cholesterol was calculated by difference. Quality control was based on the use of Precilip and Precilip EL (Boehringer-Mannheim). Mean interassay coefficients of variation were cholesterol 3.6 at 8.9 mmol/l and 2.8% at 2.5 mmol/l, and triglyceride 2.8% at 3.2 mmol/l and 3.0% at 1.8 mmol/l.

Statistical methods—As lipid and lipoprotein concentrations were not significantly different in the two blood samples taken at baseline and in each dietary period it was admissible to use mean concentrations in assessing responses to the diets. The paired *t* test was used to assess the significance of differences in the mean concentrations of total and lipoprotein subfraction lipids in addition to the low density lipoprotein to high density lipoprotein cholesterol ratio among patients consuming the three diets. The percentage changes in plasma lipid and lipoprotein concentrations from baseline at the end of diet A were also calculated for the two experimental dietary periods.

Results

The figure shows the plasma lipid and lipoprotein concentrations during the three dietary periods. Compared with baseline the mean plasma total cholesterol concentration decreased during consumption of both experimental diets; the reduction from baseline during consumption of the fibre rich diet (C; -18.5%, mean difference 1.5 mmol/l, 95% confidence limits 1.2 and 1.8 mmol/l; *p*<0.001) was greater than during the fat modified diet (B; -8.6%, mean difference 0.7 mmol/l, 95% confidence limits 0.3 and 1.1 mmol/l; *p*=0.002). The reduction in plasma cholesterol attributable to diet C was significantly greater than that due to diet B (*p*=0.0012). All participants showed qualitatively similar responses, though these varied in magnitude. There was, however, no significant change in the concentration of plasma triglyceride. Mean body weight did not differ significantly at the end of each dietary period.

Changes in low density lipoprotein cholesterol values reflected those in total cholesterol, decreasing by 11.1% when diet B was followed (mean

Plasma lipid and lipoprotein concentrations and low density lipoprotein to high density lipoprotein cholesterol ratios (means and SEM) during consumption of baseline diet (A), fat reduced diet (B), and high fibre fat modified diet (C). Percentages refer to changes in values from reference diet.

difference 0.7 mmol/l, 95% confidence limits 0.2 and 1.2 mmol/l; $p=0.007$) and 23.8% when diet C was consumed (mean difference 1.5 mmol/l, 95% confidence limits 1.1 and 1.9 mmol/l; $p<0.001$); the reduction in low density lipoprotein cholesterol with diet C was significantly greater than that with diet B ($p<0.001$). Very low density lipoprotein triglyceride and high density lipoprotein cholesterol concentrations did not differ significantly among the three dietary periods. The low density lipoprotein to high density lipoprotein cholesterol ratio decreased by 11.4% (mean difference 0.8, 95% confidence limits 0.3 and 1.3; $p=0.04$) during use of diet B and by 31.4% (mean difference 2.2, 95% confidence limits 0.1 and 4.3; $p=0.004$) during use of diet C.

Changes in plasma lipid values were similar in patients with and without hypertriglyceridaemia. The percentage reduction in total cholesterol concentration was significantly related to the baseline concentration for both diet B ($r=0.65$; $p=0.005$) and diet C ($r=0.73$; $p<0.001$).

All diets were well tolerated by patients with no untoward effects reported.

Discussion

The main finding was that a substantial reduction of plasma cholesterol, and of the atherogenic lipoprotein class low density lipoprotein, occurred during consumption of diet C. The study subjects were ambulant, moderately hypercholesterolaemic men who continued with normal day to day activities. Our findings underline the view that a main component of lipid lowering diets is to reduce the fat content of carcase meat. We have shown that, provided that care is taken to reduce the fat content substantially, a moderate quantity of meat and meat products may be included in a cholesterol lowering diet. To enhance the acceptability of a lipid lowering diet changes in traditional food selection should be minimised; our findings imply that newer techniques in meat preparation allow greater freedom in prescribing a cholesterol lowering diet, both in recommendations to the public for reducing the risk of coronary heart disease and in treatment of individual patients with hypercholesterolaemia. That the moderate use of

specified very low fat meat and meat products is compatible with effective cholesterol reduction may improve dietary compliance by permitting greater variety in the choice of foods.

The greater reduction in cholesterol during consumption of diet C compared with diet B was related to its lower content of saturated fatty acids and cholesterol, its supplement of n-6 polyunsaturated fatty acids, and its greater content of vegetables and fruit containing fibre. The equation developed by Keys *et al*, based on extensive feeding experiments in normal men,²⁰ predicts that reduction in serum cholesterol is directly related to the reduction in intake of saturated fatty acids; and it indicates that supplementation with polyunsaturated fatty acids has a smaller but additive influence on serum cholesterol. In other studies we have shown an additive effect in reducing serum cholesterol concentration of dietary fibre supplements and dietary fat modification¹⁵ and have predicted the greater efficacy of nutritional recommendations based on diet C than on diet B.²¹

Neither modified diet led to any reduction in concentrations of high density lipoprotein cholesterol, which were non-significantly higher during consumption of diet C than during intake of the baseline diet. This is interesting, as more extreme changes in dietary fatty acids have been shown to reduce high density lipoprotein cholesterol.²² There was no significant reduction in plasma triglyceride concentration; the diets were necessarily designed to be isoenergetic, and body weight did not change appreciably between dietary periods. Energy balance is an important determinant of plasma triglyceride concentrations, and weight reduction of overweight people is an essential component of the treatment of hypertriglyceridaemia.²³

We are grateful to the Meat and Livestock Commission (Queensway House, Bletchley MK2 2EF) for supplying the meat for this study.

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(Accepted 13 November 1987)