Association of Differing Dietary, Metabolic, and Clinical Risk Factors with Macrovascular Complications of Diabetes: A Prevalence Study of 503 Mexican Type II Diabetic Subjects. I.

R. B. PAISEY, M.D., G. ARREDONDO, L.N., A. VILLALOBOS, L.N., O. LOZANO, M.D., L. GUEVARA, M.D., AND S. KELLY, B.A.

Macrovascular and microvascular complications of diabetes may be associated with different environmental factors. To investigate this further, a prevalence study of 503 Mexican type II diabetic subjects was carried out while their patterns of nutrition were constrained by government food subsidies. Average daily dietary intakes were 1866 kcal; 46.5% as carbohydrate, 13.7 mmol cholesterol, 8.7 g fiber, and a polyunsaturated/saturated fat ratio of 0.98. With respect to macrovascular disease, 49.3% of patients had evidence of peripheral vascular disease, and 21.6% myocardial ischemia, 6.0% angina, 10.8% EKG evidence of ischemia, 4.8% EKG evidence of myocardial infarction. Only 1.2% (six patients) had a clear history of completed stroke, and all were hypertensive. Six patients had also undergone amputations for diabetic gangrene. Tabulation of the means of clinical characteristics according to presence or absence of myocardial ischemia showed that higher cholesterol, calorie, and fat intake, higher mean blood pressure, higher serum cholesterol, and serum triglyceride levels were found in those with myocardial ischemia. Patients with peripheral vascular disease were more commonly smokers. Stepwise logistic regression revealed significant positive associations between myocardial ischemia and dietary cholesterol, serum cholesterol, and mean blood pressure. In contrast, the presence of peripheral vascular disease was significantly related only to smoking and retinopathy. There were no associations between macrovascular complications and duration of diabetes in the multivariate analysis, and they occurred with equal frequency in men and women. Prospective studies of atherosclerosis in maturity-onset diabetes should assess and seek to modify dietary cholesterol, serum cholesterol, and hypertension. DIABETES CARE 1984; 7:421–27.

For the past 20 yr the Mexican government has pursued a policy of food subsidies to ensure that maize tortillas, beans, eggs, vegetable oil, and wheat bread are freely available. (Fresh fruit and vegetables are plentiful throughout the year.) This policy, together with traditional patterns of nutrition, has resulted in the usual diabetic individual's diet consisting of 46.5% cal from carbohydrate with a high polyunsaturated/saturated fat ratio.[1] It has been suggested by Himsworth[2] and Mann et al.[3] that such a pattern of nutrition should allow reasonable diabetes control, and reduce the incidence of macrovascular complications of diabetes.

The purpose of this study was to assess the prevalence of macrovascular complications in 500 consecutive type II diabetic subjects attending the National Institute of Nutrition for follow-up of diabetes.

PATIENTS

The National Institute of Nutrition, Tlalpan, Mexico City, is a secondary referral hospital in the subsidized Mexican health service. Patients are means tested on arrival and pay accordingly. Approximately 20% of patients attending the general medical clinic at this hospital have diabetes mellitus, though patients with advanced complications will be referred to other specialist clinics.

All type II diabetic patients between the ages of 35 and 60 yr attending the general medical clinic were invited to have a dietary and clinical assessment after their outpatient visit. Seven hundred such patients were expected in the clinic from June 1, 1981 to December 1, 1981, but only 503 were seen, principally because the others did not arrive for their outpatient appointments (see Table 1).

TABLE 1
Demography of 503 type II diabetic subjects attending The General Medical Clinic, National Institute of Nutrition, Mexico City

Age	52.2 yr (38–60) ± 5.8
Sex (F/M)	304/199
Duration	10.7 yr (1–29) ± 6.1
Treatment	
Diet	43
Oral hypoglycemic drugs	399
Insulin	61
Family history of diabetes	65.0%
Family history of ischemic heart disease	16.5%

TABLE 3
Clinical characteristics of 503 type II diabetic subjects attending The General Medical Clinic, National Institute of Nutrition, Mexico City

Mean degree of obesity at diagnosis*	145 ± 21.0%
Mean degree of obesity currently*	119.5 ± 17.3%
Smoking cigarettes >5/day	20.1%
Exercise km walked ≥5 km/day	18.1%
Initial blood pressure	21.9% ≥ 150/100
Mean blood pressure†	16.7% ≥ 150/100

*Mean degree of obesity = percentage of standard value for height.
†Mean blood pressure = average of all clinic blood pressure readings available.

METHODS

Dietary assessment. The typical daily intake of each patient was assessed by direct questioning of each patient, and corroborated in 86 patients by asking them to fill in a questionnaire of a full week's food intake prospectively. All patients were initially advised that no diet in particular had been unequivocally shown to be "good" for diabetic subjects, and that actual, typical food consumption was wanted. All interviews were conducted by one of us (R.B.P.) without prior knowledge of the cardiovascular status of the patient, and the analysis of the dietary data was carried out independently by G.A. and A.V. with no contact with, or knowledge of, the patients. Eight patients provided insufficient or unreliable dietary information and were excluded from the dietary part of the analysis.[4]

The correlation coefficients between the two dietary assessments in 86 patients were cholesterol, r = 0.686; total calories, r = 0.578; % calories as carbohydrate, r = 0.473; fiber, r = 0.2; and polyunsaturated fat ratio, r = 0.410. Some of these correlations may be lower than expected because the interview attempted to assess dietary habits for the previous 10 yr, whereas the questionnaire will have been influenced by more recent changes in diet. Fiber had been underestimated at the interview because of failure to include fruits and vegetables taken as snacks.

Percentages of energy intake as fat and carbohydrate were inversely related ($r = 0.86$, $P < 0.001$).

Ischemic heart disease. This was considered to be absent unless there was a clear history of angina pectoris, myocardial infarction, or if ischemia or infarction or left bundle branch block was present on a resting EKG. Equivocal EKGs were reviewed with a cardiologist, and 50 subjects who had no evidence of myocardial ischemia on the above criteria had exercise EKGs. None of these exercise tests showed any suspicion of ischemia. EKGs were assessed in accordance with the Minnesota code, and adaptations in Spanish of the WHO study questionnaire were used to assess history of macrovascular disease.[5]

Peripheral vascular disease. This was assessed as being present if there was a history of intermittent claudication, or if one or more peripheral pulses (dorsalis pedis or posterior tibial) were absent.

Laboratory investigations. Full blood count was performed by Coulter counter; blood glucose,[6] serum cholesterol,[7] and triglycerides[8] were measured by adaptations of standard laboratory techniques; analysis of lipids employed Boehringer-Mannheim enzymatic kits (Boehringer, Mannheim, West Germany). Urine protein concentration was measured by turbidity, serum electrolytes by flame emission spectrometry, and serum creatinine by the Jaffé reaction.

Other data. In addition to the above, age, sex, means test classification, parity, smoking and drinking habits, exercise, and family history were all noted. Presentation, duration, and treatment of diabetes were elicited from each patient and corroborated from the hospital notes. Percent overweight was determined from the tables of height and weight of the Metropolitan Life Insurance Co., New York. Percent obesity is expressed as percent of ideal weight.

Statistics. Stepwise logistic regression analyses were performed to relate presence of ischemic heart disease to age,

TABLE 2
Mean daily intake of 493 type II diabetic subjects attending The General Medical Clinic, National Institute of Nutrition, Mexico City

Daily dietary intake	
Cholesterol (mmol)	13.7 ± 7.6
Kcal	1866 ± 581
% Cal from carbohydrate	46.5 ± 10.6
% Cal from fat	33.5 ± 9.12
Polyunsaturated/saturated fat ratio	0.97 ± 0.24
Fiber (g, all sources)	8.7 ± 4.9

The means are followed by standard deviation.

TABLE 4
Laboratory analyses of type II diabetic subjects attending The General Medical Clinic, National Institute of Nutrition, Mexico City

Serum cholesterol (491 patients)	5.97 ± 2.5 mmol/L
Serum triglycerides (257 patients)	2.41 ± 1.46 mmol/L
Mean fasting blood glucose (360 patients)	9.7 ± 2.7 mmol/L
Hemoglobin concentrations (502 patients)	15.4 ± 1.7 g%

These measurements accepted only if available in the time of absence of renal disease, parasitosis, or gastrointestinal hemorrhage.

duration of diabetes, dietary cholesterol, total calories, percent calories from carbohydrate, polyunsaturated/saturated fat ratio, obesity at diagnosis and current degree of obesity, cigarette smoking, initial and mean blood pressures, serum cholesterol and hemoglobin concentration, and presence or absence of diabetic retinopathy.

The analysis was repeated with respect to peripheral vascular disease. Because of the smaller numbers of patients with mean fasting blood glucose levels and serum triglyceride levels, these factors were not included in the logistic regressions. However, to assess the relationship between micro- and macrovascular complications, retinopathy was also entered as a predictor variable. For each complication, a computer program[9] was selected from the set of predictor variables (i.e., the patient characteristics) that best explained the presence of the complication using the logistic model. The complications were represented by response variables taking the value "0" for presence of each complication and "1" for absence. The predictor variables were entered into the logistic model in order of ability to improve success of the model in predicting the complications. (The stepwise computations were based on the maximum likelihood ratio.) The program stopped when the variables that significantly improved the model were entered, and none of the remaining predictor variables improved the success of the model.

RESULTS

Table 2 shows the mean energy, cholesterol, and fiber intake of the study group, as well as the percentage of total calories derived from fat and carbohydrate, and the polyunsaturated/saturated fat ratio.

Table 3 gives the means of clinical characteristics of the patients. The percent obesity at diagnosis was invariably near or just below the maximum body weight of patients. Duration of diabetes was taken from the time of first appearance of unequivocal symptoms of diabetes or the finding of a fasting blood glucose level of >7 mmol/L in the very few asymptomatic cases.

Table 4 shows the mean values for blood analyses. Tables 5 and 6 show the clinical data from Tables 1–4 expressed as means in columns relating to presence or absence of my-

TABLE 5

Myocardial ischemia: relationships between myocardial ischemia and clinical characteristics of 503 Mexican type II diabetic subjects

	No	Angina	Ischemia	Infarction	P-value
Age	52.1	52.1	52.6	52.7	NS
Sex					
Female	234 (59.9%)	21 (70%)	35 (64.8%)	11 (45.8%)	NS
Male	157 (40.2%)	9 (30%)	19 (35.2%)	13 (54.2%)	NS
Duration	10.4	11.8	11.0	13.7	P < 0.05
Treatment					
Diet	30 (7.7%)	2 (6.7%)	8 (14.8%)	3 (12.5%)	NS
Hypoglycemic drugs	317 (81.1%)	23 (76.7%)	36 (66.7%)	19 (79.2%)	NS
Insulin	44 (11.3%)	5 (16.7%)	10 (18.5%)	2 (8.3%)	NS
Cholesterol	12.7	15.7	18.1	18.6	P < 0.001
Kcal	1829	2100	2001	1886	P < 0.001
% Cal from carbohydrates	47.3	44.1	43.2	42.9	P < 0.001
% Cal from fat	32.9	35.9	35.6	35.2	P < 0.01
Fat ratio	0.98	0.94	0.97	0.96	NS
Fiber	8.6	10.3	8.8	8.0	NS
Obesity at diagnosis*	144.7	151.4	141.4	153.3	NS
Obesity currently*	119.2	121.6	119.7	124.8	NS
Smoking >5/day	74 (18.9%)	9 (30%)	10 (18.5%)	8 (33.3%)	NS
Exercise >5 km/day	77 (19.7%)	2 (6.7%)	10 (18.5%)	2 (8.3%)	NS
Initial blood pressure ⩾150/100 (mm Hg)	85 (21.7%)	6 (20%)	12 (22.2%)	7 (29.2%)	NS
Mean blood pressure ⩾150/100 (mm Hg)	61 (15.6%)	5 (16.7%)	13 (24.1%)	8 (33.3%)	P < 0.01
Serum cholesterol (U)	5.9	6.4	6.8	6.4	P < 0.001
Serum triglycerides (U)	191.1	213.1	231.0	291.5	P < 0.01
Mean fasting blood glucose (U)	9.9	10.1	9.5	9.3	NS
Hemoglobin concentration (U)	15.4	14.5	15.7	16.3	NS
Number of patients (used for percentages)	391	30	54	24	
Total	499	4 missing			

P-values from Mann-Whitney U-test. Units and number of observations for each variable as shown in Tables 1–4.

*Definition of obesity = percentage of ideal weight.

TABLE 6
Peripheral vascular disease: relationships between peripheral vascular disease and clinical characteristics of 503 Mexican type II diabetic subjects

	No	Yes	P-value
Age	52.0	52.3	NS
Sex			
Female	159 (62.4%)	145 (58.5%)	NS
Male	96 (37.6%)	103 (41.5%)	NS
Duration	10.0	11.4	P < 0.01
Treatment			
Diet	20 (7.8%)	23 (9.3%)	NS
Hypoglycemic drugs	211 (82.7%)	188 (75.8%)	NS
Insulin	24 (9.4%)	37 (14.9%)	NS
Cholesterol	13.4	14.1	NS
Kcal	1836.2	1898.1	NS
% Cal from carbohydrates	47.2	45.7	P < 0.05
% Cal from fat	33.0	34.0	NS
Fat ratio	0.97	0.97	NS
Fiber	9.1	8.3	P < 0.01
Obesity at diagnosis*	144.5	145.7	NS
Obesity currently*	119.8	119.2	NS
Smoking >5/day	39 (15.3%)	62 (25%)	P < 0.01
Exercise >5 km/day	45 (17.6%)	46 (18.5%)	NS
Initial blood pressure ≥150/100	52 (20.4%)	58 (23.4%)	NS
Mean blood pressure ≥150/100	41 (16.1%)	46 (18.5%)	NS
Serum cholesterol	6.0	6.1	NS
Serum triglycerides	202.2	203.6	NS
Mean fasting blood glucose	9.8	9.8	NS
Hemoglobin concentration	15.6	15.3	P < 0.01
Number of patients (used for percentages)	255	248	

P-values from Mann-Whitney U-test. Units and number of observations for each variable as shown in Tables 1–4.
*Definition of obesity = percentage of standard value for height.

ocardial ischemia and peripheral vascular disease, respectively.

A stepwise logistic regression was performed to measure the association between dietary and other factors and macrovascular complications of diabetes. Results for the group as a whole are shown in Table 7. This shows patient characteristics in the order in which they enter the logistic model for each complication and the associated P values, which indicate that the characteristics significantly improve the model. Note that the significance levels quoted relate to the improvement in the explanatory power of the logistic model as each variable is entered rather than to the straight associations between the complications and patient characteristics. Also shown are the coefficients of the model. A negative coefficient for a continuous variable such as duration indicates that larger values of that variable are associated with a greater likelihood of the complication. For categoric variables such as mean blood pressure, which was grouped into four ranges, there is one coefficient associated with each category. Again, a negative value would indicate that a category was associated with presence of the complication. The standardized coefficients given for the continuous predictor variables can be read roughly as t-statistics and should not be <2.0 for variables in the model.

Figure 1 shows a graphic representation of the prevalence rates of ischemic heart disease in increasing groups of cholesterol ingestion, serum cholesterol, and mean blood pressure.

DISCUSSION

The considerable prevalences of ischemic heart disease and peripheral vascular disease encountered in this study (Tables 5 and 6) may not be representative of all Mexican type II diabetic subjects, as symptoms of cardiac or peripheral ischemia may have prompted the referral of some patients to the hospital. In order to minimize this effect, only patients from the general medical clinic, not those from specialist cardiology or vascular clinics, were recruited into the study.

Recent epidemiologic surveys have shown striking interpopulation differences in prevalence rates of macrovascular but not microvascular disease between diabetic groups living in different environments.[5,10] The diabetic descendants of Japanese migrants from Hiroshima, now living in Hawaii, have been shown to have a higher prevalence of macrovascular complications than genetically similar Japanese diabetic individuals who have remained in Hiroshima.[10] This suggests that some of this variation in prevalence of ischemia is due to environmental factors.

An important environmental difference between these populations is nutrition, and Himsworth in the 1930s first recommended that diabetic individuals should be prescribed high-complex carbohydrate diets to reduce vascular disease.[2] More recent work from Mann and colleagues has shown that such diets can be well accepted, and may result in improved diabetes control.[3,11]

The diet-heart controversy has raged for many years,[12] though the results of two recent prospective studies support the view that ingestion of greater quantities of animal fat[13] and cholesterol[14] are associated with an increased death rate from ischemic heart disease. The subject has been extensively reviewed.[15] It has been suggested that different factors may be associated with peripheral vascular disease, though it is clear that both peripheral vascular and cardiac ischemia are more common in diabetic individuals and are the most common causes of morbidity and mortality among persons with type II diabetes.[16,17]

It is therefore of considerable interest to find substantial prevalences of both ischemic heart disease and peripheral vascular disease among this group of Mexican type II diabetic subjects. The diets contained on average 46.5% of energy from carbohydrate and 34% from fat and, before diagnosis, virtually all the patients admitted ingesting large quantities of refined sugars in addition to their current diet. Because of government subsidies, vegetable oils have been cheaper than animal fats for cooking, and this is reflected in the polyunsaturated/saturated fat ratio of 0.98. However, eggs have also been subsidized, and are one of the cheapest concentrated forms of protein. Consequently, the mean cholesterol intake of 13.7 mmol daily is quite high, and the range of 3.4–42 mmol daily is very large. This has afforded the opportunity to analyze the relationships between risk factors for ischemic disease including the cholesterol and carbohydrate intake, and presence of ischemia. The stepwise logistic regressions (Table 7) show that cholesterol intake, serum cholesterol, and hypertension are all associated with ischemic heart disease, though only retinopathy and smoking were associated with the presence of peripheral vascular disease.

The weakly significant association between duration of diabetes and ischemic heart disease in the raw data disappears on multivariate analysis, possibly because of interdependence with other variables such as blood pressure. Furthermore, dietary variables are clearly interdependent, particularly the proportions of energy intake from fat and carbohydrate, which were inversely related. Therefore, although dietary cholesterol was the only dietary factor with predictive value in the multivariate analysis for ischemic heart disease, this may be a "marker" for a combination of other dietary factors.

The Western Electric study demonstrated a strong positive correlation between saturated fat and cholesterol intake (as Keys or Hegsted score) and serum cholesterol. This was not found in the present study, perhaps because diets and weight loss,[18] treatment of diabetes,[19] and control of diabetes[20] all independently alter lipid metabolism. However, a recent study[21] has shown a direct relationship between cholesterol intake and serum cholesterol, which is blunted but not abolished by a high polyunsaturated fat intake. Such an effect could be operating in the population of Mexican diabetic subjects studied, and could contribute to the substantial prevalence of ischemic heart disease in the presence of a high polyunsaturated fat intake.

The high prevalence of peripheral vascular disease based on palpation of foot pulses is interesting, and could be associated with the high mean hemoglobin concentrations of the population studied. In Mexico City, at 7000 feet above

TABLE 7
Characteristics associated with cardiac ischemia and peripheral vascular disease in 503 Mexican type II diabetic subjects by stepwise logistic regression

Response variable	Predictors entering the model (in order of entry)	Logistic regression coefficients	Standardized coefficients	P-values
	Dietary cholesterol	−0.002	−5.7	< 0.001
Cardiac	Serum cholesterol	−0.008	−3.9	< 0.001
ischemia	Mean blood pressure			
	1	+0.11		
	2	−0.58		
	3	−0.97		
	4	1.44		
	Constant	5.07		
Peripheral	Smoking	−0.04	−3.6	0.003
vascular	Retinopathy			< 0.001
disease	1	0.46		
	2	0.33		
	3	0.02		
	4	−0.78		

Number of patients: 485 in each analysis.

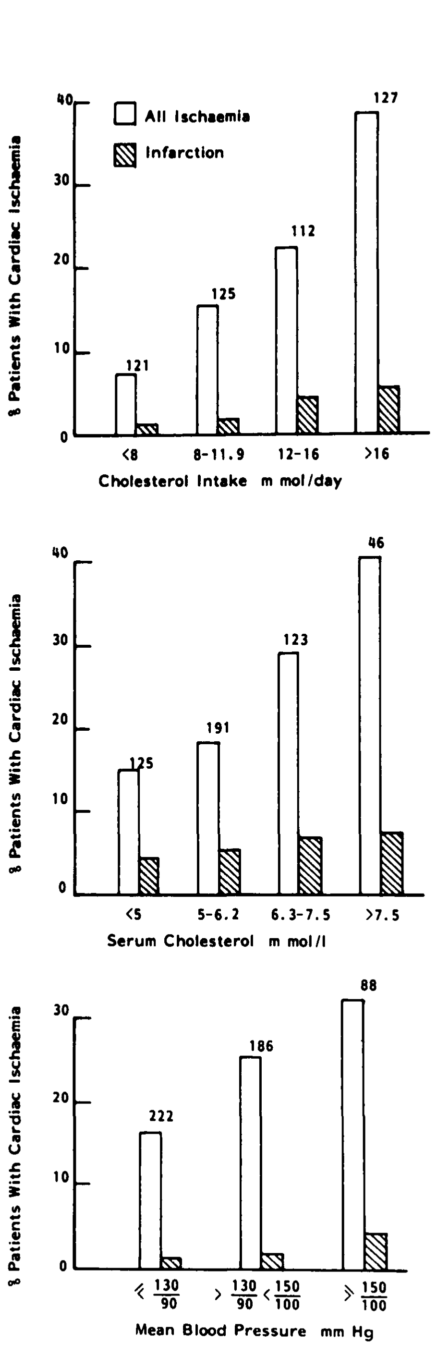

FIG. 1. Prevalence rates of cardiac ischemia and infarction with increasing dietary cholesterol, serum cholesterol, and mean blood pressure. (Numbers at head of columns = number of patients in each group.)

sea level, normal human hemoglobin levels range from 13 to 20 g%. However, neither the raw data nor the multivariate analysis show a convincing link between hemoglobin concentration and peripheral vascular disease. In spite of this apparent high prevalence of peripheral vascular disease, only six patients had required amputations. Severe neuropathy was rare, and the vast majority of patients wore wide, deep footwear likely to cause a minimum of pressure ulcers. However, only 10 patients had an unequivocal history of intermittent claudication, which implies that in this population diminution in foot pulses is only rarely related to clinically important peripheral vascular disease.

Peripheral vascular disease is well known to be strongly related to smoking, but the association with retinopathy suggests the possibility that diminution in dorsalis pedis and posterior tibial pulses may partly be related to widespread microvascular disease. Other alternatives are that the association results from an effect of atherosclerosis on retinopathy, or that both are related through a third causative factor. To throw more light on this association, the logistic regression analysis was repeated without retinopathy as a predictive variable, but with mean blood glucose levels included. The only new factor associated with peripheral vascular disease was duration of diabetes.

It is also of interest that the diet was low in total fiber content, principally because of the low level of consumption of wholemeal flour, and the processing of maize before preparation of tortillas. This may have had a bearing on the overall prevalence of vascular disease,[22] though there was no association within the group of patients studied of fiber intake with any of the microvascular or macrovascular complications of diabetes.

The recently reported WHO study analysis of "risk factors" for arterial disease in diabetic individuals[23] also demonstrated positive associations between serum cholesterol and triglyceride levels and ischemic heart disease, though in that study there were weaker but significant associations between duration of diabetes and a single plasma glucose estimation with peripheral vascular disease, though this complication was defined as "those with intermittent claudication and or amputation attributable to ischemia," and occurred in only 2.8% of patients as in our population. In the same study smoking was not related to peripheral vascular disease defined in this way, either by Chi-square analysis or Mann-Whitney U-test of the raw data or multivariate analysis.

In 3450 subjects of the WHO study, serum cholesterol, age, and adiposity were all strongly associated with the finding of major Q-wave abnormalities on EKG, and systolic blood pressure only approached significance as a "risk factor." Some of the differences between the studies may result from the inclusion of both type I and type II diabetic subjects in the WHO analysis.

Insulin-dependent diabetes is associated with a very different metabolic derangement, in that the treated patients are often relatively hyperinsulinized, and therefore have higher HDL cholesterol levels, lower triglyceride levels with increased triglyceride removal rate,[19] but often much more variation in blood glucose and free fatty acid levels.[24] These factors,[25] coupled with changes in platelets and coagulation factors,[26] may all contribute to ischemic heart disease in ketosis-prone diabetic individuals as well as the previously favored advice to restrict dietary carbohydrate with the inevitable consequence of a high-fat diet. In view of these differences, it would seem wise to analyze atherosclerosis rates separately for individuals with type I and type II diabetes.

In conclusion, this study is consistent with the hypothesis that atherosclerosis may develop with maturity-onset diabetes rather than as a direct result of it, and that future prospective studies should assess and seek to modify dietary fat and cholesterol, blood pressure, and serum lipids in this group of diabetic individuals.

ACKNOWLEDGMENTS: We thank Raimundo Pali of the Department of Computation, the Archives Department, and the medical outpatient staff at the National Institute of Nutrition, Mexico City, for their help. We are also indebted to Dr. M. Hartog and Dr. J. Arreaga for helpful advice, to Z. Fear for typing the manuscript, and the Department of Medical Illustration, Southmead Hospital, Bristol.

This work was supported by the University of Bristol in collaboration with the National Institute of Nutrition, Mexico City. A travel grant was made available by the Bristol Health District.

All of the data on which these analyses have been performed are available from R.B.P.

From the University of Bristol, United Kingdom, and Departamento de Diabetes, Instituto Nacional de la Nutricion, Tlalpan, Mexico City, Mexico.

Address reprint requests to R. B. Paisey, M.D., University of Bristol, Department of Medicine, Bristol Royal Infirmary, Bristol, BS2 8HW, England.

REFERENCES

[1] Paisey, R., Arredondo, G., Villalobos, A., Guevara, L., and Lozano, O.: Diet and complications in Mexican type II diabetics. In press. Diabetologia.

[2] Himsworth, H. P.: Diet in the aetiology of human diabetes. Proc. R. Soc. Lond. 1949; 42:323–24.

[3] Simpson, R. W., Mann, J. I., Eaton, J., Carter, R. D., and Hockaday, T. D. R.: High carbohydrate diets and insulin dependent diabetics. Br. Med. J. 1979; 11:523–25.

[4] Instituto de Nutricion de Centro America y Panama (INCAP): Tabla de composicion de alimentos para uso en America Latina. Interamericano, Mexico, 1978.

[5] Keen, H., and Jarrett, R. J.: The WHO multinational study of vascular disease in diabetes: 2 macrovascular disease prevalence. Diabetes Care 1979; 2:187–95.

[6] Trinder, P.: Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. Ann. Clin. Biochem. 1969; 6:24–27.

[7] Siedel, J. H., Schlumberger, S., Klose, J., and Wahlefield, A. N.: J. Clin. Chem. Clin. Biochem. 1981; 19:838–45.

[8] Wahlefield, A. W.: Triglycerides: determination after enzymatic hydrolysis. *In* Methods of Enzymatic Analysis, 2d edit. Bergmeyer, H. U., Ed. Verlag Chemie, New York and London, Weinheim and Academic Press Inc., 1974:325–30.

[9] Engelman, L.: Stepwise logistic regression. *In* BMDP Statistical Software. Dixon, W. J., Ed. University of California Press, 1981:330–42.

[10] Kawate, R., Yamakido, M., Nishimoto, Y., Bennett, P. H., Hamman, R. F., and Knowler, W. C.: Diabetes mellitus and its vascular complications in Japanese migrants on the island of Hawaii. Diabetes Care 1979; 2:161–70.

[11] Simpson, R. W., Mann, J. I., Eaton, J., Moore, R. A., Carter, R., and Hockaday, T. D. R.: Improved glucose control in maturity onset diabetes treated with high carbohydrate modified fat diet. Br. Med. J. 1979; 1:1753–56.

[12] Mann, G. V.: Diet-heart: end of an era. N. Engl. J. Med. 1977; 297:644–49.

[13] Keys, A.: The diet and all causes of death rate in the seven countries study. Lancet 1981; 2:58–61.

[14] Shekelle, R. B., Shryock, A. M., Oglesby, P., Lepper, M., Stammler, J., Shuguey-Liu, M. S., and Raynor, W. J.: Diet, serum cholesterol and death from coronary heart disease. N. Engl. J. Med. 1981; 304:65–70.

[15] Lewis, B.: Dietary prevention of ischaemic heart disease—a policy for the '80s. Br. Med. J. 1980; 11:177–80.

[16] Eaton, R. P.: Lipids and diabetes: the case for treatment of macrovascular disease. Diabetes Care 1979; 2:46–50.

[17] Goodkin, G.: Mortality factors in diabetes: a 20 year mortality study. J. Occup. Med. 1975; 17:716–21.

[18] Stone, D. B., and Connor, W. E.: The prolonged effects of a low-cholesterol, high-carbohydrate diet on serum lipids in diabetic patients. Diabetes 1963; 12:127–32.

[19] Paisey, R. B., Elkeles, R. S., Hambley, J., and Magill, P.: The effects of chlorpropamide and insulin on serum lipids, lipoproteins and fractional triglyceride removal. Diabetologia 1978; 15:81–85.

[20] Streja, D., Boyko, E., and Rabkin, S.: Nutrition therapy in non-insulin-dependent diabetes mellitus. Diabetes Care 1981; 4:81–85.

[21] Schonfeld, G., Patsch, W., Rudel, L. L., Nelson, C., Epstein, M., and Olson, R. E.: Effects of dietary cholesterol and fatty acids on plasma lipoproteins. J. Clin. Invest. 1982; 69:1072–80.

[22] Burkitt, D. P., and Painter, N. S.: Dietary fiber and disease. JAMA 1974; 229:1068–74.

[23] West, K. M., et al.: The role of circulating glucose and triglyceride concentrations and their interactions with other "risk factors" as determinants of arterial disease in nine diabetic population samples from the WHO multinational study. Diabetes Care 1983; 6:361–69.

[24] Sheppard, M. C., Burrin, J., Alberti, K. G. M. M., and Nattrans, M.: The effect of diet on intermediary metabolic concentrations in type 2 (non insulin dependent) diabetes mellitus. Diabetologia 1983; 24:333–35.

[25] Stout, R. W.: Diabetes and atherosclerosis—the role of insulin. Diabetologia 1979; 16:141–50.

[26] Colwell, J. A., Lopes-Virella, M., and Halushka, P. V.: Pathogenesis of atherosclerosis in diabetes mellitus. Diabetes Care 1981; 4:121–33.