CONDENSED REPORT

Nutrient intake, adiposity, and diabetes

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Summary and conclusions

To study the role of nutritional factors in the genesis of diabetes, estimations of blood sugar concentration, food intake, and adiposity (as body mass index; BMI) were carried out on three normal population samples—namely, 961 employees of Beecham Ltd, 1005 employees of the Greater London Council, and 1488 middle-aged male civil servants (Whitehall study). Blood sugar concentrations and indices of glucose tolerance correlated positively with the degree of adiposity but tended to be negatively correlated with total food energy intake and its component nutrients (total carbohydrate, sucrose, and fat). This inverse trend was largely accounted for by highly significant inverse correlations between food energy intake and adiposity, a relation found in both sexes and in all three population samples and which extended across the whole range of nutrient intake and BMI. These findings suggest that greater degrees of adiposity are associated with lower than average food energy intakes and hence lower total energy expenditures.

The association of increased adiposity with low food energy consumption may indicate an underlying "low energy throughput" state, and it may be the mechanisms of this, as well as the obesity, that are responsible for disease.

Introduction

Two major hypotheses have been formulated linking diet with diabetes mellitus: the "fat hypothesis," of which Himsworth[1] was the main protagonist, and the "sugar hypothesis," championed mainly by Yudkin[2] and Cohen *et al.*[3] Each suggests that a high intake of the particular nutrient increases the risk of diabetes. The evidence for both is largely circumstantial. Two other nutritional factors—namely, dietary fibre depletion[4] and trivalent chromium deficiency[5]—have been considered as having an aetiological role in diabetes, and there may be other specific factors responsible for regional variants of the diabetic syndrome.[6] Obesity has a well-established role in diabetogenesis[7] and must clearly be included in any consideration of food intake in relation to the aetiology of diabetes.

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Over the past decade we have collected dietary information from three large British population groups. This report relates nutrient intake both to blood sugar behaviour and to adiposity, taking the effects of age into consideration. The findings run counter to expectation but may cast new light on certain metabolic variations within the population.

Population samples studied

Beecham sample—From the office staff of Beecham Ltd in Greenford, Middlesex, 961 employees were recruited, representing 93% of those approached. The capillary blood sugar concentration was measured in each subject two hours after standard dietary preparation and a carbohydrate load, as described.[8] Each completed a standard dietary intake form for two weekdays about two weeks before the survey visit. A subgroup of 220 subjects (Beecham subsample) drawn at random and stratified for even representation of the sexes, decades of age, and tertiles of adiposity were subjected to full standard 50 g oral glucose tolerance tests with half-hourly measurement of venous blood sugar and plasma insulin concentrations.[9]

GLC sample—A population stratified for age and sex was drawn at random from employees of the Greater London Council and Inner London Education Authority from a centrally held computerised staff list.[10] Out of 1103 approached, 1005 participated, each providing a single capillary blood sample after an overnight fast. One dietary intake form was completed two weeks before the survey visit.

Whitehall sample—A total of 1488 male civil servants aged 40 years or more from central London were drawn at random as a one-in-10 subsample of subjects included in a screening survey for cardiovascular and respiratory diseases.[11] Each made a three-day record of dietary intake and had their capillary blood sugar concentrations measured in the morning two hours after a 50 g oral glucose load following an overnight fast.

Methods

All subjects were weighed and measured standing without shoes. Blood sugar was estimated in all by the same standard autoanalyser ferricyanide reduction micromethod (Technicon N24a). The standard dietary records, listing unweighed but semiquantitative descriptions of all food and drink consumed, were coded and submitted to computerised analysis with use of a comprehensive food table devised by J W Marr and modified and expanded to suit our requirements. The computerised Statistical Package for the Social Sciences[12] was used for all statistical tests.

Results

BLOOD SUGAR AND NUTRIENT INTAKE

Beecham sample—In the total Beecham sample all the simple correlation coefficients relating total food energy (or nutrient) intake with two-hour blood sugar estimation were negative in direction (table A*), although none achieved statistical significance. These inverse trends were supported by analysis of the more standardised glucose tolerance data from the subsample of 220. When the area under the curve of glycaemia and insulinaemia was calculated for each subject the lowest areas of glycaemia and insulinaemia tended to occur in the highest quintiles of food energy intake (fig A*).

GLC sample—Although observations on the GLC sample were

*Tables A-E and fig A may be obtained from the authors.

restricted to fasting blood sugar concentrations, the inverse trend of blood sugar with nutrient intake was again found in men, with significantly lower blood sugar values in the highest than lowest quintile of energy (table I), fat, carbohydrate, and sucrose intake (table B*). Among the GLC women, however, quintile-to-quintile trends in fasting blood sugar values were not apparent.

Whitehall sample—In this male population all nutrient intakes were inversely correlated with the two-hour blood sugar concentration (table A), significantly so in the case of total carbohydrate ($r = -0.06$; $P < 0.05$) and sucrose ($r = -0.07$; $P < 0.01$) intakes.

TABLE I—*Mean fasting blood sugar concentrations ± SD by quintiles of nutrient intake in GLC men and women (numbers studied given in parentheses)*

Quintile of energy intake		Blood sugar concentration (mmol/l)	
		Men (n = 502)	Women (n = 503)
Lowest	1	4·58 ± 0·51 (90)	4·31 ± 0·42 (87)
	2	4·56 ± 0·60 (97)	4·36 ± 0·45 (119)
	3	4·59 ± 0·60 (98)	4·50 ± 0·53 (76)
	4	4·48 ± 0·44 (111)	4·31 ± 0·42 (105)
Highest	5	4·43 ± 0·39*(104	4·31 ± 0·38†(115)

Significance of difference from value in lowest quintile of energy intake: *$P < 0.05$; †not significant.
Conversion: SI to traditional units—Blood glucose: 1 mmol/l ≈ 18 mg/100 ml.

BLOOD SUGAR AND BODY MASS INDEX

Beecham sample—The total population sample was divided into quintiles of the distribution of body mass index (BMI). In both sexes the highest mean blood sugar concentration was found in the highest BMI quintile with, in men, the lowest in the least adipose, although these differences were not significant (table C*). In the Beecham subsample the area under the curve of glycaemia rose steadily with increasing adiposity in men, though this was less apparent in women. Nevertheless, women in the quintile of largest BMI had the highest mean area of glycaemia (fig 1). Increasing areas of glycaemia were associated with increasing areas of insulinaemia. In the top BMI quintile the ratio of insulin area to glucose area was highest, particularly in women, suggesting increased insulin resistance.

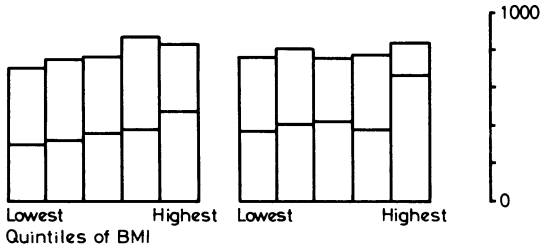

FIG 1—Mean areas of glycaemia (represented by total height of bar) and insulinaemia (lower part of bar) for each quintile of BMI in age-sex-adiposity-stratified subsample of 220 Beecham employees. Area under glucose tolerance curve increases with adiposity.

GLC sample—In both sexes in the GLC sample there was a clear trend to rising blood sugar concentrations with increasing adiposity (table C), and simple correlation coefficients between the two variables were highly significant (men: $r = 0.30$, $P < 0.001$; women: $r = 0.18$, $P < 0.01$).

Whitehall sample—Analysis of the Civil Service sample (table C) also indicated a trend of rising blood sugar values with increasing adiposity ($r = 0.07$; $P < 0.01$).

NUTRIENT INTAKE AND BMI

Mean blood sugar concentrations falling with increasing nutrient intake and rising with increasing BMI led us to examine further the apparently anomalous implication of an inverse relation between food intake and adiposity.

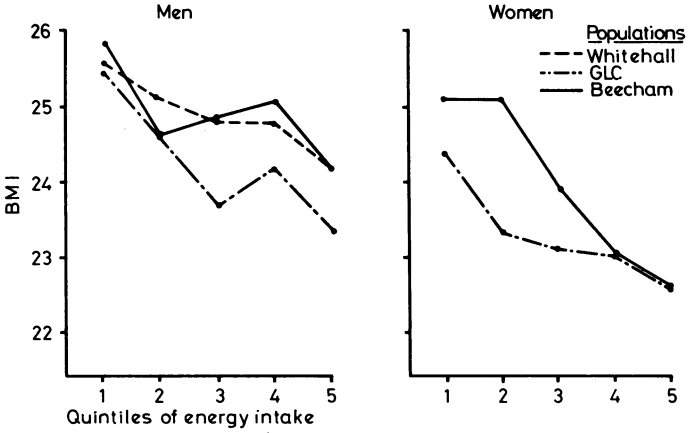

FIG 2—Mean BMI of subjects in each quintile of energy intake in three populations studied. In each group, and in both sexes, relation is inverse—that is, mean BMI falls with increasing quintile of energy intake.

The calculated mean BMI was plotted for quintiles of total energy intake in all three populations (fig 2). In both sexes there was a clear trend to a fall in mean BMI with increasing quintiles of food consumption; in women the mean BMI fell progressively with each increasing quintile of intake. Table II gives the calculated correlation coefficients between BMI and total energy and nutrient intakes. In all groups there were highly significant negative correlations throughout for women; in men the negative correlations were of a lower order but highly significant for BMI versus total energy, carbohydrate, and sucrose intake.

INTERACTIONS OF BLOOD SUGAR, NUTRIENT INTAKE, AND ADIPOSITY AND EFFECTS OF AGE

Since the blood sugar concentration appeared to be related inversely to nutrient intake and directly to adiposity and these second two were inversely related to each other, further analysis was necessary to try to disentangle the interrelations. Age affects all three variables and so was also included in the forward stepwise multiple regression analysis undertaken.

Blood sugar and nutrient intake—In all population groups most of the variance in both fasting and two-hour blood sugar concentrations could be explained by the effects of age (in both sexes) and BMI (particularly in men, though, to a less but significant extent, also in women) (table D*). Nutrient intake maintained a consistently negative relation with blood sugar but achieved significance only in men in the Beecham subsample, in whom energy, fat, and protein intakes were each negatively correlated with two-hour blood sugar values, and in the Whitehall population, in which sucrose intake showed a significant negative relation.

Adiposity and nutrient intake—In the Beecham sample age accounted for a large part of variability in BMI; in both sexes, particularly women, the relations were positive and highly significant (table E*). But even after allowing for the effects of age (and blood sugar value) a clear inverse relation between nutrient intake (total energy, carbohydrate, sucrose, protein, and fat) and adiposity persisted. In women these trends were all highly significant ($P < 0.001$). In men the negative correlations between nutrient intake and BMI just failed to achieve significance for fat, protein, and total energy but were significant for carbohydrate and sucrose ($P < 0.01$). Analysis repeated after excluding all those known to be on a weight-reducing diet affected neither the direction nor the level of significance of these relations. In the Whitehall sample age influenced BMI less (probably because of the limited age band). Total energy, carbohydrate, and sucrose showed highly significantly negative correlations with BMI ($P < 0.001$); protein and fat showed the same trends but did not achieve significance.

Discussion

We failed to find diminished glucose tolerance in subjects at the higher end of the nutrient intake range; indeed, especially

*Tables A-E and fig A may be obtained from the authors.

in respect of carbohydrate and sucrose intake, we found trends towards lower blood sugar values (both fasting and after an oral glucose load). Most of the inverse relation between blood sugar concentration and nutrient intake was explained by adiposity, leaving the unexpected finding of a highly significant but inverse relation between food intake and BMI—that is, those who ate most had on average the least degree of adiposity. This trend was found in both sexes in each population studied and was independent of age. These inverse relations were greatest between BMI and total food energy, total carbohydrate, and sucrose intakes.

One obvious explanation for this finding is that obese people were deliberately restricting their food intake in an attempt to lose weight. All subjects were routinely questioned about this, and when those known to be dieting were excluded from the analysis the results were not affected.

Another possibility is that those who were most obese were systematically (consciously or unconsciously) under-recording their food intakes. Such deceptions may be found among groups of "clinically obese" patients but the populations studied here were "normal" and so less likely to have developed secondary behavioural responses to severe adiposity. Further, the inverse relation applied across the *whole of the range* of BMI and was not restricted to the manifestly obese versus the rest (fig 3). It seems highly unlikely that self-restriction or a "deception artefact" would be distributed across the whole of the body weight range in this way.

It also seems improbable that the inverse relations found in each of the three quite distinct populations were attributable to our method of assessing dietary intake (unweighed and made over a relatively short period). The method lacks precision but there is no reason to suppose it to be biased. The emergence of the relations we observed in the face of randomly distributed inaccuracies strengthens rather than weakens the conclusions

TABLE II—*Simple correlations between nutrient intake and BMI in three population samples*

	Correlation between BMI and:									
	Total energy		Protein		Fat		Carbohydrate		Sucrose	
	r	P	r	P	r	P	r	P	r	P
Beecham sample										
Men (n = 385)	−0·12	**	−0·04	NS	−0·08	NS	−0·19	***	−0·15	***
Women (n = 519)	−0·27	***	−0·17	***	−0·18	***	−0·31	***	−0·31	***
GLC sample										
Men (n = 500)	−0·19	***	−0·09	*	−0·14	***	−0·24	***	−0·18	***
Women (n = 502)	−0·18	***	−0·01	NS	−0·13	***	−0·21	***	−0·17	***
Whitehall sample										
Men (n = 1488)	−0·14	***	−0·01	NS	−0·05	*	−0·23	***	−0·24	***

*P < 0·05. **P < 0·01. ***P < 0·001. NS = Not significant.

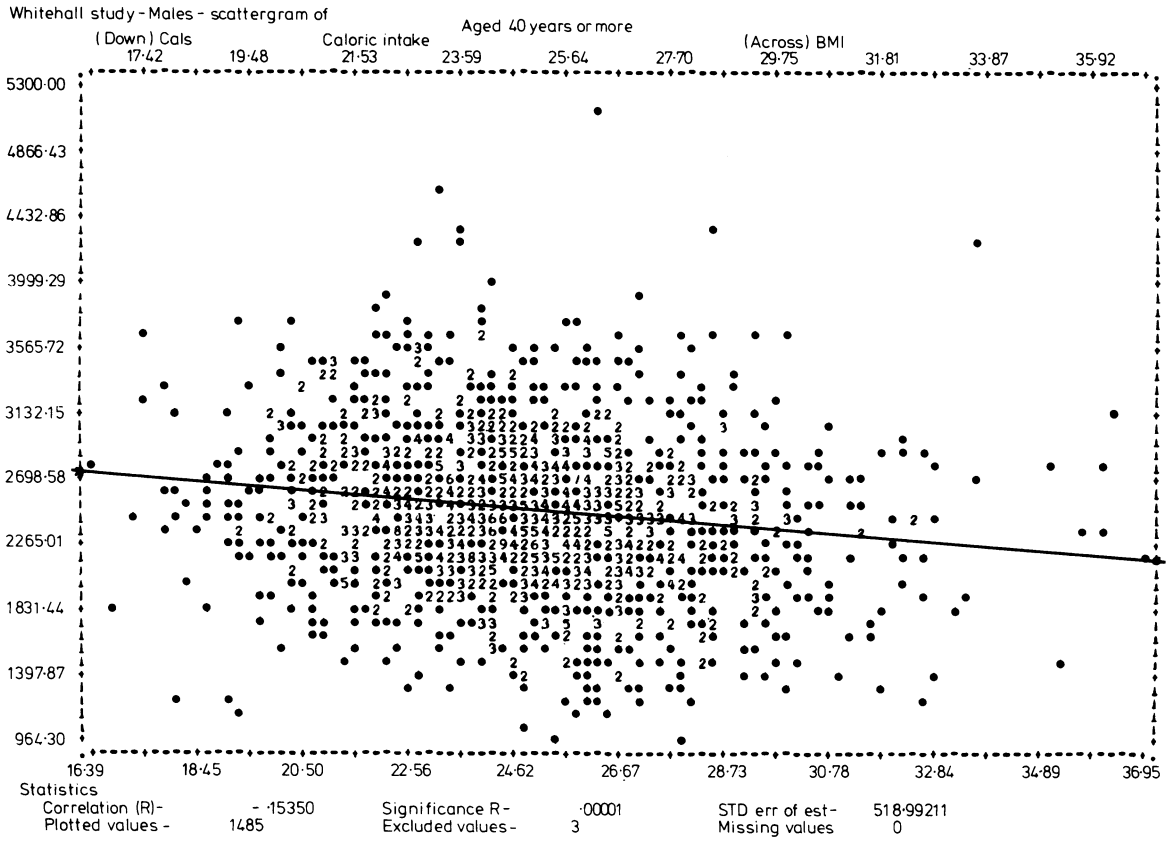

FIG 3—Computer-generated scattergram of individual energy intakes plotted against BMI in men from Whitehall population. ● indicate single observations and numerals number of coinciding points. Line is calculated linear regression of energy intake on BMI. Highly significant inverse correlation (r = −0·15) extends across entire range of adiposity and is not an artefact attributable to dietary restriction in obese subjects.

we draw. The order of magnitude of the correlations, though not their direction, may also have been influenced by the BMI, which cannot distinguish between muscularity and adiposity. Keys *et al*,[13] however, concluded that the BMI was the best available field measurement of adiposity and unlikely to cause serious errors of interpretation.

The assumption that obese people eat more than lean people is unquestioned by many, but studies other than ours also report obese people eating less than controls.[14 15] Richardson[16] found a striking inverse relation between sugar consumption and the degree of obesity in a group of businessmen, equally evident in those deliberately restricting sugar intake and those not doing so. No information on other nutrient intake was given, but in our three populations we found that total energy intake correlated closely with the consumption of sucrose. Dietary data from the Framingham study[17] also suggest very strongly that in a normal population sample "overweight" subjects ate less than those who were "underweight." A similar conclusion emerged from "within-country" analyses of food intake and adiposity in the "seven countries" study.[18]

"ENERGY THROUGHPUT" AND OBESITY

If we assume that the subjects in our three population samples were neither systematically gaining nor losing weight, it follows that the inverse relation observed between BMI and food energy *consumption* mirrors a similar inverse relation between BMI and energy *expenditure*. Thus in the obese average energy intake and output—that is, "energy throughput"—is lower. While some of the lowered energy expenditure of the obese may be attributable to less physical exercise, this is unlikely to be the sole contributing factor, since overt physical activity constitutes only about 15% of total energy expenditure.

We cannot say from the demonstrated association whether a low energy throughput state is the cause of adiposity or a consequence of it. Indeed, both may be associated manifestations of a person's "setting" in a range of levels of energy utilisation. This setting may be determined for each person by inherited and environmental factors.[19] Obese subjects may also be better at conserving energy (and their adiposity) by reducing metabolic expenditure more when underfed and by augmenting it less when overfed.[20] The regulation of food energy consumption and control of its partitioning among heat production, tissue maintenance, and fat synthesis are poorly understood. Disturbance of these mechanisms may be important, not only for obesity and diabetes. Morris *et al*[21] showed that high energy throughput may be beneficial (and a low throughput harmful) with respect to coronary heart disease.

The inverse relation between food energy intake and adiposity in a population does not, of course, mean that it applies within an individual—that is, that if he eats more he will become less adipose. Nor does it apply to differences between populations; starving people will clearly be less adipose than those with plenty to eat. In some clinically obese people hyperphagia may well contribute to inordinate weight gain (although it is more likely to do so in some than in others[22]), but gluttony is not the cause of obesity in the majority.

FOOD INTAKE AND GLYCAEMIA

The relation between food intake, adiposity, and diabetes mellitus is thus likely to be complex. We found no evidence that higher levels of fat, carbohydrate, or sucrose consumption were directly associated with fasting glycaemia or glucose intolerance; if anything, the reverse was true. Similar negative conclusions regarding the role of total energy intake and sucrose intake in diabetogenesis were arrived at by Kahn *et al*[23] in a prospective study of the development of diabetes in 10 000 Israeli civil servants and, in respect of sucrose intake, by Baird.[24] Our findings support West's conclusions[25] that adiposity is a major environmental determinant of glucose intolerance but suggest that the relation between food consumption and adiposity in Western societies is complex and inverse.

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Reprints and tables A-E and fig A may be obtained from Professor Harry Keen.

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ONE HUNDRED YEARS AGO Dr C Heitzman (*Archives of Medicine*, New York, January 1879) tells us that "marriages should be allowed in doubtful cases only upon the permit of a reliable microscopist. Last season," he says, "a young physician asked me whether I believed in the marriage among kindred. He had fallen in love with his cousin, and his cousin with him. I examined his blood, and told him that he was a nervous man, passing sleepless nights and having a moderately good constitution. The similar condition being suspected in the lady, marriage was not advised, for fear of degenerate offspring. So great was his faith in my assertions, that he gave up the idea of marrying his cousin, offering her the last chance, viz., the examination of her blood. This beautiful girl came to my laboratory, and, very much to my surprise, I found, on examination, her blood of first-class constitution. The next day, I told the gentleman, 'You had better marry her.'" (*British Medical Journal*, 1879.)