Table V.9

Relationship between fibre intake tertiles and male CHD mortality expressed as relative risk (RR) males. 17–23 year follow-up.

		CHD mortality		
Fibre intake tertile		Lowest 3rd	Middle 3rd	Highest 3rd
RR	Crude *	1.0	0.73	0.46
	Adjusted **	1.0	0.88	0.57[1]

* Adjusted for cohort and age

** Adjusted additionally for systolic BP, total serum cholesterol, EKG abnormalities, cigarette smoking and alcohol intake

[1] Difference from reference RR significant ($P<0.05$).

Adapted from data published by L H Kushi *et al.*, 'Diet and 20-year mortality from coronary heart disease. The Ireland–Boston diet-heart study', in *New Engl J Med*, 1985, **312:** 811–18, p. 816.

By 1961 the situation had become reversed. The fibre consumption of the highest income groups relative to that of the lowest increased steadily during this period. When compared to the lowest two social classes the highest two with the *higher* overall fibre intake emerged with a *lower* incidence of CHD over the twenty years.[73] Finally, in a prospective secondary prevention study, Daan Kromhout and his colleagues obtained a dietary history with respect to fibre intake in a group of 871 men who were followed for six to twelve months. The twenty-seven men who died from CHD during the period under review had an average daily fibre intake of 27.2 $\pm$ 8.1 g per day, appreciably less than the 30.8 $\pm$ 9.7 g per day of the survivors. When corrected for other factors by multivariate analysis, the difference approached conventional levels of significance, the P value being 0.06.[74]

In conclusion, the fibre intake of the English middle and upper classes declined during the Georgian era. Recent studies have shown that a low fibre intake affects the lipid profile and incidence of coronary heart disease adversely. The decline in oat fibre intake, in particular, during the eighteenth century could therefore be considered a contributory cause for angina pectoris then becoming manifest in England as a disease of the affluent and increasingly common thereafter.

Sugar

Wild cane sugar plants probably grew originally on the island of New Guinea, which was possibly the site of its first cultivation.[75] By the end of the fifteenth century

[73] M G Marmot *et al.*, 'Changing social-class distribution of heart disease', *Br Med J*, 1978, **ii**: 1109–12, p. 1110.

[74] D Kromhout, E B Bosschieter and C de Lezenne Coulander, 'Dietary fibre and 10-year mortality from coronary heart disease, cancer, and all causes. The Zutphen study', *Lancet*, 1982, **ii**: 518–22, p. 519.

[75] N Deerr, *History of sugar*, 2 vols, London, Chapman and Hall, 1949–50, vol. 1, p. 44.

they had become disseminated, although to a very limited extent, throughout the Middle East and the Mediterranean littoral. The sweetness of beets was known from classical times and recognized in medieval Europe, but the sugar they contained made only a small contribution to diet, the mixture of glucose with fructose in honey then being the principal source of sweetening. The large-scale production of sucrose from the sugar cane began only after the European colonization of the Caribbean Islands. From the English standpoint it assumed significance only with the annexation of Jamaica, Barbados and other West Indian islands by England in the mid-seventeenth century.[76] The climate and soil in the Caribbean were ideal for growing sugar cane and large plantations developed, manned mostly by slave labour that was imported from West Africa. In addition to large-scale cultivation, factory style techniques were developed for harvesting and crushing the cane and for extracting and refining the sugar, which was then despatched to Europe in the form of loaves.[77] Mercantilist economic policies ensured that production in the colonies resulted in preferential trade with the mother country and bulk importation was facilitated by improvement in ship design. The West India Docks in London became known as the sugar docks because sugar grown in the Caribbean English colonies was the principal commodity that they handled. Production in Jamaica alone, slightly less than 1,000 tons a year during the 1670s, rose to 3,586 tons by 1684 and 19,641 by 1739, and virtually all of the output was exported to England.[78]

The developments described resulted in a dramatic increase in cane sugar (specifically sucrose) consumption in England during the eighteenth century. The period from 1713 to 1739 has been selected to illustrate trends, as this was the longest period in the century during which England was not involved in any major wars, with their attendant disruptions of trade. The earlier date is that in which the Treaty of Utrecht was signed, ending the War of the Spanish Succession, and the later year is that which preceded the outbreak of the War of the Austrian Succession. Net imports of sugar rose from 15,771 tons in 1713 to 43,103 tons by 1739. The figures for this have been obtained by subtraction of re-export tonnage from that of imports, both of which were well documented when subjected to customs inspection for taxation purposes. No cane sugar was produced at home. Only about 20 per cent of the sugar brought into the country was re-exported so that minor inaccuracies in the import and re-export figures would not have affected unduly the differences between them, i.e. the net imports.[79] Independent corroboration of the legitimate trade estimates is available for the year 1731 when N Deerr's figure for net imports was 35,063 tons[80] whilst W Reed arrived at the figure of 36,123 tons,[81] a difference of under 3 per cent. There is, however, some probable underestimation because of smuggling which took place on a very large scale, often using remote coastal inlets but also through ports and with either intimidation or the connivance of the revenue

[76] Ibid., p. 150.
[77] Ibid., p. 162.
[78] Ibid., vol. 2, p. 423.
[79] Ibid., p. 423.
[80] Ibid., p. 423.
[81] W Reed, *The history of sugar and sugar yielding plants*, London, Longmans, Green, 1866, p. 188.

officers. With the rise in volume of commerce with foreign lands "the eighteenth century marked the classic epoch of illicit trade".[82] As the population increased by barely one-tenth during 1713 and 1739,[83] the figures indicate a marked increase in English per capita sugar consumption. Despite two intervening wars, imports continued to rise, Reed reporting that they reached 69,146 tons by 1768,[84] the year of Heberden's presentation to the Royal College of Physicians of London. Deerr estimated that the amount consumed per capita rose from about 4 pounds a year during the first decade of the eighteenth century to 13 pounds annually during the last ten years, a greater than threefold increase.[85] Sugar was used in baking, in desserts and above all to sweeten the coffee and tea which were being drunk in ever greater amounts.

When the present project was first considered in the early 1960s, sugar was under suspicion as a CHD risk factor and its rising eighteenth-century usage considered a contributor to the emergence of angina as a recognizable complaint. John Yudkin had published a series of papers showing a relationship between sugar consumption at varying times and in different countries and the incidence of coronary heart disease.[86] However, J N Morris and others reported absence of any such association in a ten-year prospective study[87] and Yudkin's findings were challenged by Ancel Keys. The latter demonstated that the relationship appeared initially to be very similar to that previously established for fat consumption and CHD. When standardized for sugar consumption, the relationship between fat intake and coronary heart disease continued to hold. However, the reverse was not true, because when standardized for fat consumption, the relationship between sugar intake and incidence of ischaemic heart disease ceased to be significant.[88] Keys also pointed out that there was a dramatic rise in the incidence of CHD deaths in Great Britain during the first half of the twentieth century when fat consumption increased dramatically but sugar consumption rose a mere 25 per cent.[89] The importance of sugar as a possible risk factor was subsequently discounted to such an extent that a recent exhaustive epidemiological survey of coronary heart disease risk factors did not even see fit to mention sugar, even if only to question its significance.[90]

However, before dismissing the dramatic rise in eighteenth-century English sugar consumption and the appearance and subsequent increase in frequency of angina pectoris as merely coincidental, several factors need consideration. Carbohydrate

[82] G D Ramsay, 'The smugglers trade, a neglected aspect of English commercial development', *Royal Hist Soc Trans*, 5th series, 1952, **2**: 131–157, p. 132.

[83] Wrigley *et al.*, op. cit., note 17 above p. 614.

[84] Reed, op. cit, note 81 above, p. 190.

[85] Deerr, op. cit. note 75 above, vol. 2, p. 532.

[86] John Yudkin, 'Diet and coronary thrombosis: hypothesis and fact', *Lancet*, 1957, **ii**: 155–62, p. 157; John Yudkin, 'Dietary fat and dietary sugar in relation to ischaemic heart disease and diabetes', *Lancet*, 1964, **ii**: 4–5; John Yudkin and Janet Roddy, 'Levels of dietary sucrose in patients with occlusive atherosclerotic disease', *Lancet*, 1964, **ii**: 6–8.

[87] Morris, Marr and Clayton, op. cit., note 23 above, p. 1311.

[88] Ancel Keys, 'Sucrose in the diet and coronary heart disease', *Atherosclerosis*, 1971, **14**: 193–202, pp. 194–5.

[89] Ibid., p. 196.

[90] M Lawrence *et al.* (eds), *Prevention of cardiovascular disease: an evidence-based approach*, Oxford General Practice series No. 33, Oxford University Press, 1996.

Table V.10
Comparative effects of starch and sugar intake on lipid profile. Mean and SD (mg/dl)

		Males		Females	
Serum lipid (mg/dl)	Week	Starch	Sugar	Starch	Sugar
Total	0	798 ± 85	782 ± 81	711 ± 42	716 ± 52
	6	766 ± 67	883 ± 113	744 ± 46	802 ± 34
Triglycerides	0	113 ± 11	136 ± 30	94 ± 7	94 ± 8
	6	126 ± 23	165 ± 31	87 ± 6	109 ± 9
Total cholesterol Pooled male and female results	0	178 ± 12	176 ± 8		
	6	191 ± 12	217 ± 19		

Source: S Reiser *et al.*, 'Isocaloric exchange of dietary starch and sucrose in humans. Effects on levels of fasting blood lipids', *Am J Clin Nutr*, 1979, **32**: 1659–68, pp. 1663–4. (With permission © American Society for Clinical Nutrition.)

taken in excess of energy requirements is converted in the body into saturated fats in which form it is stored in adipose tissues. Sucrose, possibly because of its speed of absorption from the gut, has a propensity to elevate serum cholesterol. Thus, Sheldon Reiser and his colleagues compared the effects of sucrose with those of wheat starch when one or the other constituted the principal source of carbohydrate during a six-week dietary trial. It was conducted in volunteers with a normal lipid profile and for whom 43 per cent of the energy requirements was supplied as carbohydrate, of which 30 per cent was either sucrose or wheat starch. No significant weight gains were recorded during the period of observation. When compared with starch administration, sucrose intake was associated with significantly higher serum total cholesterol levels (Table V.10).[91] M A Antar and colleagues had comparable results when fourteen patients with various lipoprotein abnormalities consumed experimental diets during two four-week periods and a cross-over sequence was used. Either sucrose or starch constituted 40 per cent of the energy intake. In other respects the diets "simulated a typical North American diet". During both the starch and sugar phases 35 per cent of the energy intake was in the form of fat, predominantly saturated. The serum cholesterol levels, initially about the same, fell during the period of starch intake but rose with sucrose with final means of 285 and 328 mg/dl respectively. The differences were highly significant.[92]

High sugar consumption results in elevation of serum triglycerides as well as

[91] S Reiser *et al.*, 'Isocaloric exchange of dietary starch and sucrose in humans. Effects on levels of fasting blood lipids', *Am J Clin Nutr*, 1979, **32**: 1659–69, pp. 1663–4.

[92] M A Antar *et al.*, 'Interrelationship between the kinds of dietary carbohydrate and fat in hyperlipoproteinemic patients, Part 3: Synergistic effect of sucrose and animal fat on serum lipids', *Atherosclerosis*, 1970, **11**: 191–201, p. 199.

cholesterol, as has been shown by Reiser and his colleagues.[93] In a prospective study, Meir Stampfer and his colleagues have recently shown that serum triglyceride levels *are* related directly to risk of coronary heart disease. In a seven-year follow-up of 14,916 men aged forty to eighty-four years who were enrolled in a physicians' health study they found a positive linear association between non-fasting serum triglyceride levels and myocardial infarction rates. Men in the highest quintile had a relative risk about two and a half times greater than males in the lowest one.[94] Michael Miller and his colleagues showed that particularly when above 100 mg/dl, fasting serum triglyceride levels are significantly predictive of CHD events.[95] Finally, Melissa Austin, in an extensive meta-analysis, has shown that among men serum triglyceride elevation is a significant risk factor for coronary heart disease, even when adjusted for the serum HDL levels with which triglyceride concentrations have an inverse relationship.[96] The one time benign perception of elevated serum triglycerides would therefore seem to need revision. The interaction between cane sugar consumption and elevation of serum triglyceride levels provides a further possible basis for linking sucrose intake with predisposition to development of coronary heart disease.

Ingestion of sugar is also followed by surges in pancreatic production of insulin which is associated with sympathetic nervous system activation and a rise in blood pressure.[97] Although high serum insulin levels were not found to be significant a risk factor for atherosclerotic cardiovascular disease in Edinburgh and Swedish men,[98] prospective long-term studies in Finland, France, and among Australian men tended to show a positive association, as have investigations involving immigrant South Asians in England.[99] The divergent results of these studies arise in large measure from difficulties in isolating the effects of raised serum insulin levels when it is associated, as is frequently the case, with other factors, notably excessive consumption of animal fats, obesity, elevation of serum triglycerides, Type II diabetes mellitus (the form which usually arises in middle life and is associated with insulin resistance rather than insulin deficiency) and hypertension.

[93] Reiser *et al.*, op. cit., note 91 above, pp. 1663–4.

[94] Meir J Stampfer *et al.*, 'A prospective study of triglyceride level, low-density lipoprotein particle diameter, and risk of myocardial infarction', *JAMA*, 1996, **276**: 882–8, p. 882.

[95] Michael Miller *et al.*, 'Normal triglyceride levels and coronary heart disease events: the Baltimore coronary observational long-term study', *J Am Coll Cardiol*, 1998, **31**: 1252–7, p. 1253.

[96] Melissa A Austin, 'Plasma triglyceride and coronary heart disease', *Arterioscler Thromb*, 1991, **11**: 2–14, p. 9.

[97] Gerald M Reaven, Hans Lithell and Lewis Landsberg, 'Hypertension and associated metabolic abnormalities—the role of insulin resistance and the sympathoadrenal system', *N Engl J Med*, 1996, **334**: 374–81, p. 376.

[98] A D Hargreaves *et al.*, 'Glucose tolerance, plasma insulin, HDL cholesterol and obesity: 12-year follow-up and development of coronary heart disease in Edinburgh men', *Atherosclerosis*, 1992, **94**: 61–9, p. 66; L Welin *et al.*, 'Hyperinsulinemia is not a major coronary risk factor in elderly men. The study of men born in 1913', *Diabetologia*, 1992, **35**: 766–70, p. 768.

[99] Kalevi Pyörälä, 'Relationship of glucose tolerance and plasma insulin to the incidence of coronary heart disease: results from two population studies in Finland', *Diabetes Care*, 1979, **2**: 131–41, p. 136; P Ducimetiere *et al.*, 'Relationship of plasma insulin levels to the incidence of myocardial infarction and coronary heart disease mortality in a middle-aged population', *Diabetologia*, 1980, **19**: 205–10, p. 206; T A Welborn and K Wearne, 'Coronary heart disease incidence and cardiovascular mortality in Busselton with reference to glucose and insulin concentrations', *Diabetes Care*, 1979, **2**: 154–60, p. 156; Jatinder Dhawan *et al.*, 'Insulin resistance, high prevalence of diabetes, and cardiovascular risk in immigrant Asians. Genetic or environmental effect?', *Br Heart J*, 1994, **72**: 413–21, p. 418.

To a large extent these difficulties were overcome by J P Després, who measured the fasting plasma insulin of 2,103 men aged thirty-five to sixty-four years who were free of ischaemic heart disease at entry into a five-year follow-up study. At the start of the follow-up the plasma insulin was 92.1 ± 27.5 μU/mL in the group of 114 men who subsequently developed at least one manifestation of CHD, significantly higher than the 78.2 ± 20.8 μU/mL in the group who remained free of coronary heart disease. The association of insulin with CHD was independent of differences in lipid profile, systolic blood pressure, body mass index and smoking.[100] Kalevi Pyörälä and colleagues obtained similar results in a nine and a half year follow-up of 982 men aged thirty-five to sixty-four years and free of coronary heart disease at entry. The initial fasting plasma insulin levels, and the ones at one and two hours after a standard glucose drink all correlated positively with the subsequent incidence of both coronary heart disease death and non-fatal myocardial infarction.[101] Finally, high insulin levels in the blood are frequently associated with insulin resistance. Evidence reviewed by Peter Savage and Mohammed Saad suggests that the latter may be an important link between abnormalities in carbohydrate metabolism and arteriosclerotic changes.[102] There does therefore appear to be a series of linkages whereby high sucrose intake produces surges in insulin production and eventual insulin resistance with its adverse cardiovascular consequences.

Glycosylated haemoglobin is a compound formed by glucose combining with haemoglobin, the carrier of oxygen in the blood. It reflects a tendency for glucose to combine with proteins generally, and in excess the combination is associated with a propensity to development of pathological changes in arteries. The percentage of haemoglobin that is glycosylated constitutes an integrated measure of the fluctuant blood glucose levels over the preceding six to twelve weeks. It is therefore to some extent an indicator of the long-term effects of sugar and complex carbohydrate intake and of the surges in blood glucose that they induce. Gerald Reaven has found that these surges are greater when carbohydrate is taken as cane sugar, i.e. as sucrose, than when a complex form is ingested, on average 137 as against 104 mg/100 mL respectively.[103] In another investigation involving a male cohort of the European Prospective Investigation into Cancer and Nutrition, it was found that among men aged forty-five to seventy-nine, 95 per cent of whom were free of diabetes, glycosylated haemoglobin levels were positively correlated with the subsequent four-year risk of death from ischaemic heart disease. This correlation held even though the levels ranged below the 7 per cent upper limit of normal. Thus the age adjusted relative risk for men with a glycosylated haemoglobin level in the range of 5.0 to 5.4 per cent was 2.74 times that of men in whom it was below 5 per cent. A further

[100] J P Després *et al.*, 'Hyperinsulinemia as an independent risk factor for ischemic heart disease', *N Engl J Med*, 1996, **334**: 952–7, pp. 954–5.

[101] Pyörälä, op. cit., note 99 above, p. 36.

[102] Peter J Savage and Mohammed F Saad, 'Insulin and atherosclerosis: villain, accomplice, or innocent bystander?', *Br Heart J*, 1993, **69**: 473–5, p. 474.

[103] Gerald M Reaven, 'Effects of differences in amount and kind of dietary carbohydrate on plasma glucose and insulin responses in man', *Am J Clin Nutr*, 1979, **32**: 2568–78, p. 2572.

connection between intake of sugar and liability to ischaemic heart disease with its clinical manifestations is thereby established.[104]

Of greater importance in connection with a possible link between sugar and CHD are the effects of its consumption when considered in association with other dietary risk factors. Kevin Grant and his co-workers gave volunteers a single meal of either whipping cream, sucrose or both together. They found that addition of sucrose to a meal with cream amplified both the extent and the duration of the post-prandial elevation of serum triglycerides. There was no short-term deviation of serum cholesterol levels from baseline with either sugar or cream alone, but when taken together an initial mean fasting serum cholesterol of 4.36 rose to 4.52 mmol/L after two hours. This difference, although slight, was significant ($P<0.01$) and persisted for eight hours.[105] These results could explain the absence of a relationship between elevation of blood insulin and incidence of coronary heart disease in populations such as Pima Indians and West Indians who enjoy a diet high in sugar but very low in animal fat. Conversely, they could implicate sugar as a risk factor for CHD in subjects on fat rich "western" diets with attendant serum cholesterol elevation.

The interactions between sugar and fats do not depend exclusively on complex biochemical relationships. Sugar has a direct positive effect on the palatability of many fat rich foods, notably as a result of the successes of the pastry-cook. When sucrose is added to the ingredients, including fats, used in the baking of cakes, pies and pastries, it raises the temperature at which white of egg solidifies and delays conversion of starch into a gel, thereby allowing cake to rise more effectively. The hydroscopic effect of sugar prevents undue drying during the course of baking and slows the chemical changes that predispose to later staleness. The overall consequence of these actions is to give baked goods that incorporate eggs or butter a longer shelf life and to make them lighter, more attractive and more palatable, qualities that make for increased consumption with an accompanying unavoidable higher animal fat and energy intake with all their undesirable consequences. Observations made by P M Emmett and K W Heaton showed that this is indeed the case. They surveyed 739 men aged forty to sixty-nine years and 976 women aged twenty-five to sixty-nine years. It was found that high sugar consumption with cakes and biscuits was associated with a correspondingly high fat intake. When the highest quartile of consumption was compared with the lowest, baked products provided men and women with an extra daily 12.0 and 13.8 grams of fat respectively.[106] In the late eighteenth century a corresponding increase in consumption would have consisted almost exclusively of animal fats.

Animal fats have for the most part been eaten with meat and poultry, in food cooked with dripping or lard, and in eggs and dairy products. The fat consumed in

[104] Kay-Tee Khaw *et al.*, 'Glycated haemoglobin, diabetes, and mortality in men in Norfolk cohort of European Prospective Investigation of Cancer and Nutrition (EPIC-Norfolk)', *Br Med J*, 2001, **322**: 15–18, pp. 16, 17.

[105] Kevin I Grant, Marielle P Marais and Muhammad A Dhansay, 'Sucrose in a lipid-rich meal amplifies the postprandial excursion of serum and lipoprotein triglyceride and cholesterol concentrations by decreasing triglyceride clearance', *Am J Clin Nutr*, 1994, **59**: 853–60, pp. 855–6.

[106] P M Emmett and K W Heaton, 'Is extrinsic sugar a vehicle for dietary fat?', *Lancet*, 1995, **345**: 1537–40, p. 1539.

baked goods and therefore with sugar has constituted but a small proportion of its total intake, most fat being eaten independently of any sweetening. In contrast, the association of sugar with cream on fruit desserts and with fat in cakes, pies and similar foods results in an overwhelming proportion of the sugar that is consumed being eaten together with fat. Even when sugar is used to sweeten tea or coffee, the addition of milk or cream results in some association. It is consequently possible to dissociate the effects of fat consumption from those of sugar, but virtually impossible to dissociate the effects of sugar consumption from those of fat. This would readily help to explain the negative findings of the Keys multivariate analysis. Keys drew attention to the rising incidence of coronary heart disease in both the United Kingdom and the United States during the first half of the twentieth century when fat consumption in both countries rose considerably but sugar consumption changed very little. This does not exonerate sugar as a risk factor. Theoretically, if both sugar and animal fats were risk factors and sugar consumption held constant while fat consumption increased, the incidence of CHD would rise. Longitudinal studies of food consumption would only exonerate sugar if a society could be found in which fat intake was constant, sugar consumption rose but coronary heart disease incidence did not change. Such a society is unlikely ever to exist. The observations of Keys therefore, while not implicating sugar as a risk factor, certainly do not exclude it.[107]

In conclusion, excessive sugar intake is conducive to obesity and results in surges in serum insulin levels with an eventual increase in insulin resistance. The results of experimental dietary studies suggest that, particularly in the context of a coincidental liberal saturated fat intake, high sugar consumption is followed by elevation of serum cholesterol as well as triglyceride levels. The relation of high cholesterol levels to increasing incidence of coronary heart disease is well established and recent studies have implicated liberal sugar consumption with serum triglyceride elevation, insulin resistance and rising glycosylated levels as well. All of these are established risk factors for CHD. The great increase in English sugar consumption during the Georgian era has been shown to coincide with a sharp increase in consumption of animal fats and reasons for a direct linkage between the effects of these two dietary changes have been demonstrated. The evidence therefore suggests that the dramatic rise in sugar usage in eighteenth-century England could be implicated as an ancillary factor contributing to the initial emergence of angina pectoris and its increasing prevalence thereafter.

Coffee

The original home of coffee bushes growing in the wild was probably Ethiopia and it was there that they were first cultivated. The necessary knowledge spread initially through Persia and the medieval Arab world. The stimulating properties of the bean were recognized in antiquity and were the subject of many legends. One that originated in Arabia concerned herdsmen who observed that goats grazing on the berries of certain bushes became exceedingly frisky and gambolled the night

[107] Keys, op. cit., note 88 above, pp. 194–5.