Commentary: Lactose and ischaemic heart disease: a sweet hypothesis...but nothing more!

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In 1964 John Yudkin and colleagues published a report on sucrose intake by patients with vascular disease and control subjects. The mean sugar intake of the patients was nearly twice as high as that of the...
control subjects and much of the additional sugar appeared to have been taken in cups of tea and coffee. This focus on sucrose is strangely inconsistent with the far-reaching conclusion drawn in an earlier paper by Yudkin\(^2\) that it is ‘difficult to support any theory which supposes a single dietary cause of coronary thrombosis... (and) it is suggested that relative over-consumption of food associated with reduced physical exercise, may be one of several causes of the disease’. The mention of sucrose, however, stimulated a number of reports. These either refuted the relevance of sucrose\(^3,4\) or suggested that factors other than sucrose explained the association of heart disease with the drinking of these beverages. Thus, coffee\(^5,7\) or the cigarettes smoked along with the drinks\(^8\) were suggested. Jeffrey Segall however pointed out with surprise that no one seemed to have considered that milk added to the drinks could be the harmful component and he supported this hypothesis with ‘strong’ correlations between national per capita consumption of milk and mortality rates within 43 countries.\(^9\)

In his 1980 paper, Segall refined his hypothesis about milk and asked: ‘Is lactose a dietary risk factor for ischaemic heart disease?’ and he answered this by showing a significant correlation between estimates of the prevalence of lactose malabsorption, used as an inverse surrogate for lactose absorption within 23 ethnic groups and ischaemic heart disease mortality.\(^10\) The validity of this surrogate for lactose ingestion was tested against data for the national per capita milk intake in 19 of the countries. Segall expressed his conclusions with caution, stating that ‘if the correlation reported previously between milk consumption and IHD mortality is causal, lactose could be the responsible dietary factor’. Segall proposed no possible mechanism whereby lactose might affect vascular disease. In 1988, however, Strain pointed out that absorption of copper, a nutrient involved in a number of mechanisms relevant to vascular disease, including defence against free radicals, could be compromised by lactose.\(^11\) Furthermore, experimental evidence that is supportive of the hypothesis comes from a study of the water flea (Daphnia pulex) in which exposure to lactose causes an inhibition of heart rate and severe arrhythmia.\(^12\) While all this fulfils many of the criteria proposed by Bradford Hill for judging the causal nature of an association, yet an adequate evaluation of a complex food such as milk, cannot be based on evidence relating to one possible mechanism.

In a further paper Segall\(^13\) published an extensive review of epidemiological evidence from 22 countries and concluded that ‘international and ethnic variations in experience of ischaemic heart disease show greater consistency for a possible protective effect against IHD from a diet low in lactose... than from a high intake of polyunsaturated or monounsaturated fatty acids, wine, alcohol or dietary fibre’. Yet again, Segall expressed all this with caution, calling for further epidemiological and biochemical investigation of the topic.

The aim in this commentary is to review further evidence from epidemiological and other studies—evidence that was not available to Segall.

Most mammals stop drinking milk soon after weaning and for the majority of people around the world the gene for the enzyme lactase gets switched off and the ability to digest lactose, the sugar in milk, is lost. Most people of European origin, however, have a version of the gene that remains active and around 90% of Europeans can digest lactose throughout life, and consequently have a relatively high intake of milk.

As early as 1965 striking racial differences in the prevalence of lactose malabsorption had been noted.\(^14\) A ‘geographic hypothesis’ was proposed, based on ‘random genetic drift...or some other process of selection independent of dairying’, which led certain communities ‘to take up dairying and the use of milk as food’. The ‘aberrant’ persons ‘would then enjoy a significant selective advantage’.\(^15\) In addition to a survival advantage, it was proposed that lactose absorbers may have also experienced a small breeding advantage.

Support for all this was recently obtained in an archaeological dig. DNA samples were obtained from 55 bone samples belonging to eight Neolithic subjects dated to around 5500 BC. The mutation in the lactose gene was found to be absent, suggesting that the ability to digest lactose and hence to consume virtually unlimited quantities of milk, evidently developed within the past 7000 years.\(^16\) A prevalence of this mutation now of well over 90% within most Northern European communities is consistent with it having conferred a considerable survival advantage. At the same time, even if the mutation in the lactase gene did confer advantages to primitive man, modern man has such a different diet and different environment, such that it could well be that milk consumption no longer carries any survival or breeding advantage.

The relevance of lactose ingestion and milk consumption to health at present, and to cardiovascular health in particular could only be evaluated with confidence with data from overviews of a number of randomized controlled trials. Unfortunately the size, duration and compliance required for adequately powered trials are such that it is highly unlikely that any such studies will ever be attempted. In the absence of evidence from randomized trials, the best evidence therefore comes from cohort studies, though evidence from retrospective case-control studies should also be considered.

There have been three case-control studies of milk or dairy consumption by patients with an acute myocardial infarction (MI). In a study of 287 women with acute MI and 649 control women about the frequency and amount of various foods
consumed prior to infarction. The odds ratio for the risk of MI in one-third of the women with the highest consumption of milk, compared with one-thirds with the lowest consumption, was 0.9.\textsuperscript{17} In another study based on 507 patients with an acute MI, and 478 control patients, an adjusted odds ratios for infarction in patients who had been drinking seven or more cups of milk per week, compared with patients who had drunk no milk, of 0.78 (0.54–1.12).\textsuperscript{18} Most recently, Biong et al.\textsuperscript{19} have reported a study of dairy fat and dairy food consumption by 111 patients with an acute MI and 107 control subjects. No association was found between the intake of dairy fat and the risk of an acute MI.

These case–control studies have many limitations, and in particular, they were dependent upon recollection of past milk consumption. Evidence from cohort studies is also limited in that milk drinking may be confounded with other dietary and behavioural factors relevant to vascular disease. Nevertheless, an overview of seven large, long-term cohort studies yielded relative odds for ischaemic heart disease in one-fifth of the subjects with the highest milk intakes, compared with one-fifths with the lowest intakes, of 0.87 (0.74–1.03), and for either heart disease or stroke the odds were 0.84 (0.78–0.90).\textsuperscript{20} A more recent estimate (unpublished), based on 12 cohorts (see Supplementary data) has given an estimate of relative risk for milk consumption of 0.84 (0.79–0.89) for vascular disease events.

Lactose malabsorption can be a cause of marked morbidity in occasional subjects,\textsuperscript{21} but the likelihood of its involvement in vascular disease would seem to be refuted by the results from case–control and cohort studies, together with evidence derived from the genetic studies cited above. Although the evidence on vascular disease is favourable to milk consumption, the evidence is not conclusive and in the absence of evidence from randomized trials the arguments are likely to continue—perhaps indefinitely.

Conflict of interest: None declared.

Supplementary data

Supplementary data are available at *IJE* online.

References