

thought I detected some clustering of cases in some villages north of Oxford, but the statistics are difficult in a disease so rare. There is another suspected cluster to the east of London. Institutional clusters have not been seen.

This conference was recorded and edited by Dr W F Whimster. We regret that the names of the speakers from the audience were not picked up on the tape, so they remain unidentified.

References

- ¹ Nick, J, *et al*, *Revue Neurologique*, 1971, **125**, 15.
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APPOINTMENTS OF SPEAKERS

- (1) Professor W B Matthews, DM, FRCP, professor of clinical neurology, Oxford University
- (2) Dr N M Hyman, MRCP, senior registrar in neurology, Churchill Hospital, Oxford
- (3) Sir R Bannister, DM, FRCP, consultant physician, the National Hospital for Nervous Diseases, London WC1, and St Mary's Hospital, London W2
- (4) Dr J Trevor Hughes, MD, consultant neuropathologist, Radcliffe Infirmary, Oxford OX2 6HE
- (5) Dr D A Pyke, MD, FRCP, consultant physician, King's College Hospital, London SE5
- (6) Professor M D Milne, MD, FRCP, professor of medicine, Westminster Medical School, London SW1

The Other Side

Fats and atheroma: a retrial

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Summary and conclusions

The controversy over medical endorsement of dietary measures to reduce cholesterol intake has been reconsidered. The results of several published reports that apparently do not confirm the association between diet, cholesterol concentrations, and ischaemic heart disease (IHD) were found to be largely inapplicable to the argument. Results of primary prevention trials, however, suggested that lowering the cholesterol concentration had a beneficial effect in reducing morbidity from IHD. The "average Western diet" is particularly associated with accelerated or premature atherosclerotic disease, yet the saturated fatty acid component of the diet may be only one of several factors relevant to IHD. Such diets are usually high in refined carbohydrate and total energy intake.

Disordered nutrition generally, and other environmental and constitutional factors seem to be important in the aetiology of IHD. A prudent diet, incorporating decreased intake of fats, simple sugars, and refined carbohydrate, with polyunsaturated fats comprising less than 25% of total energy intake, may be the best method of reducing the incidence of IHD and other diseases of overnutrition.

Introduction

Sir John McMichael has held another inquest¹ and concluded that medical endorsement of cholesterol-reducing measures should be withdrawn. He considers that polyunsaturated fats

may actually be harmful. I request a retrial, not because I regard a diet high in polyunsaturated fat as the single most important aspect of a diet more prudent than the current Western diet, but because Professor McMichael has suggested that raised concentrations of cholesterol have little to do with atheroma, that atheroma is not a nutritional disorder, and that a reduction of blood cholesterol concentration may be more harmful than beneficial. The practising doctor who has not had the opportunity to evaluate the published reports in detail may therefore conclude that dietary modification should not be recommended. I believe that this conclusion is not valid. The mass of evidence in favour of recommending change has been presented in more detail elsewhere,^{2,3} and I shall principally examine some of the "mass of negative evidence" that McMichael offers to counteract the positive reports based on "epidemiological surveys which are misleading and grossly biased by their failure to recognise and consider the complete investigative picture." I believe that it is more helpful to discuss ischaemic heart disease (IHD) rather than atheroma, since this clinical entity, rather than the pathological process, is one of the principal causes of premature morbidity and mortality in most Westernised countries and factors other than atheroma may be concerned.

Negative evidence

Sir John McMichael cites a number of investigations which do not apparently confirm the association between diet, cholesterol levels, and IHD: "Diets with a high and low fat content that were consumed by different monastic orders did not alter the incidence of coronary disease." This statement is based on an interesting *cross-sectional* investigation by Groen *et al*⁴ of 181 Trappist and 168 Benedictine monks; the former consuming a frugal vegetarian diet and the latter a mixed "Western" diet. There was indeed no difference in the prevalence of IHD between the two groups, but the most striking finding in this study (which can be criticised from several points of view) is the virtual absence of major ischaemic events in either group—only one out of the 349 monks studied had evidence of myocardial infarction (a Trappist with diabetes and appreciable hypercholesterolaemia). The authors' principal conclusion concerned the protective effect of a monastic life against ischaemic heart disease. Professor

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McMichael considers that the data of Blumgart *et al*⁵ provide further negative evidence: "Substantial rises in cholesterol concentrations after thyroidectomy in the treatment of heart disease before the war did not produce an excess of coronary atheroma in man." This study was based on eight cases who survived 1-13 years (average 7.4 years) after surgical total thyroidectomy. Even those who are not epidemiologists might be unimpressed by this evidence.

Perhaps rather less trifling negative evidence is the fact that results of trials which have attempted to lower cholesterol concentrations have not been particularly beneficial. Nevertheless, here too I consider that Professor McMichael may perhaps have misled his readers: "The best conducted dietary trials under the auspices of the MRC's statistical control have given convincingly negative results." The trials^{6, 7} to which he refers are "secondary prevention" studies in which prevention is attempted in individuals who have already experienced an ischaemic episode. The results, while disappointing, are perhaps not surprising. In such subjects atherosclerosis is already well established and the subjects are no longer young, so it might be a case of trying to shut the stable door at rather too late a stage. The negative results of the drug trial to which he refers⁸ concerned similar individuals, and the drugs tried were all hypolipidaemic drugs that were given to patients after infarction, many of whom did not have hyperlipidaemia. It would almost have been surprising if such studies had yielded positive results.

It is rather surprising that Professor McMichael did not mention the three "primary prevention" studies,⁹⁻¹¹ in which prevention was attempted in subjects who had not yet had an ischaemic episode. All suggested that lowering the cholesterol concentration had a beneficial effect in terms of morbidity from IHD, though not always of total mortality. The studies can be criticised on many counts, yet the results of each indicate the same beneficial effect. Not surprisingly, the effects have not been dramatic, since most of the subjects included in the trials thus far have been in their late middle age. The ideal trial would include many relatively young subjects followed for a long period of time. Such a study might cost several hundred million dollars, and the definitive clinical trial may never be undertaken. More indirect evidence that dietary modification is beneficial must therefore be sought.

Professor McMichael disregards the decline in death rate from coronary heart disease in the USA that has paralleled changes in diet because dietary recommendations similar to those made in the USA were also made in Sweden, where a similar decline was not observed.^{12*} Furthermore, the IHD rate in Sweden is less than half that seen in the United States. No one has seriously disputed that factors other than diet are concerned in IHD and these may predominate in a country such as Sweden, where relatively low rates prevail. Under such circumstances modification of diet might not substantially affect the disease rates. In Australia, where the IHD rate is more similar to that of the USA, death rates have similarly declined in parallel to dietary change.¹³

This, then, is some of the negative evidence quoted by McMichael against the influence of nutritional factors in the aetiology of IHD, and it seems to be rather thin in comparison with the bulk of evidence presented in favour of such an aetiology. I think that the evidence presented by McMichael is misleading to the uninitiated reader: the fact that rabbits with severe hypercholesterolaemia do not develop true coronary atheroma is clearly stated, but the fact that individuals homozygous for familial hypercholesterolaemia almost invariably have angina as teenagers and myocardial infarctions soon afterwards is not mentioned. Is the human model not more relevant than the experimental animal?

Polyunsaturated fats and dietary recommendations

Professor McMichael considers at some length the dangers of polyunsaturated fats. No convincing evidence suggests that polyunsaturated fats are clinically harmful. Results of one of the primary prevention trials showed a significant increase in deaths from cancer among subjects consuming cholesterol-lowering diets.⁹ Nevertheless, the excess mortality from cancer in the diet group occurred mostly in those whose compliance was poor,¹⁴ and a combined assessment of five lipid-lowering dietary trials provided no confirmatory evidence of an increased risk of cancer from a high intake of polyunsaturated fat.¹⁵ Many thousands of subjects receiving such diets have now been observed over long periods and no further untoward effects have emerged. Clofibrate is certainly associated with an increased risk of

*I am not aware of the published data that show that the dietary recommendations made in Sweden were actually implemented to the extent that they were in the United States.

gall stones,¹⁶ but so far as I am aware the clinical evidence does not support the statement that "*dietary interference* may be suspect for similar reasons" (my italics).

Professor McMichael claims that Wissler's group in Chicago have shown that certain vegetable oils (for example, peanut oil and coconut oil) fed as 25% of the diet to rhesus monkeys caused considerable intimal-cell proliferation and scarring.¹⁷ This leads to a most important practical point. While the earliest recommendations for the dietary prevention of IHD chiefly concerned increasing intake of polyunsaturated fats, I would not necessarily regard this as the cornerstone of prudent dietary advice. At present it seems to be the "average Western diet" that is particularly associated with accelerated or premature atherosclerotic disease. Although results of studies have suggested that the saturated fatty acid component of the diet is particularly relevant in IHD, it is difficult to be confident, since diets rich in saturated fat are invariably also high in refined carbohydrate and total energy intake.¹⁸ Furthermore, advice on prudent diet should also consider possible prevention of other diseases of overnutrition, and might include the following recommendations.

(1) Ideal body weight must be maintained.

(2) Complex carbohydrate intake, especially whole-grain cereals and unprocessed fruits and vegetables, should be increased at the expense of fats, simple sugars, and refined carbohydrate.

(3) Fat intake should be reduced to constitute around 30-35% of total energy intake, rather than 40% as at present, and the ratio of polyunsaturated : saturated fatty acids should be approximately 1:1. Such a diet would not be high in polyunsaturated fat, which would constitute substantially less than 25% of the diet, a level which seems to concern Professor McMichael because of the rhesus-monkey experiments mentioned earlier. (Other aspects might include recommendations on salt intake, breast-feeding, fluoridation and alcohol, food additives, and measures to reduce the incidence of iron-deficiency anaemia, rickets, and osteomalacia, but these aspects are beyond the scope of this report and are not directly relevant to IHD.)

Under the heading "safety of suggested dietary changes," Professor McMichael describes the Israeli diet, which is high in polyunsaturated fats, yet the IHD rate in Israel is roughly three-quarters of that in the USA. This seems to have little bearing on the safety of dietary change, nor to provide strong evidence against dietary change, for factors other than diet are concerned in the aetiology of IHD. I cannot comment on the experience of bedouin migrating from the desert to Israeli towns, since the reference quoted is that of an MD thesis from the Hadassah Hebrew University. The suggestion that fatty acids with "trans" double bonds may be harmful is based on slender laboratory evidence and other work (not quoted in his paper) has not confirmed this suggestion.^{19, 20}

Comment

I have chosen to comment chiefly on Professor McMichael's "mass of negative evidence," which presumably caused the 28 "senior cardiologists" circulated by the British Heart Foundation to advise against a change to a polyunsaturated-fat diet, rather than discuss in detail the positive evidence, which has been extensively reviewed elsewhere.² If the same cardiologists were asked to comment about a change to a generally more prudent diet (which is the advice most nutritionists would now offer) they might cast their vote rather differently. While quoting surveys, McMichael did not mention that conducted by Professor Norum,²¹ who asked 200 internationally based investigators in atherosclerosis research for their opinions on several key questions. Most (98%) considered that cholesterol concentrations and IHD were associated. I think that the evidence for a nutritional aetiology of ischaemic heart disease is overwhelming. As suggested above, the negative evidence is flimsy. Certainly, other extremely important environmental (for instance, cigarette smoking) and constitutional factors are concerned, some of which are probably still to be identified, but this does not invalidate the association between disordered nutrition and IHD. The evidence in favour of a beneficial effect from dietary change is less conclusive, and the definitive clinical trial may now be impossible to conduct. Nevertheless, considerable circumstantial evidence suggests that a prudent diet may be beneficial, not only in reducing the incidence of premature ischaemic heart disease, but possibly that of maturity-

onset diabetes, diverticular disease, and other gastrointestinal diseases.¹⁸

Nutritional factors are clearly implicated in the aetiology of IHD and the trends in incidence in at least two countries where dietary modification has taken place are most encouraging. Such dietary change has not been shown to be harmful and the recommendations could easily become acceptable and palatable to most people who were prepared to try them.

I am grateful to Professor Sir Richard Doll, Professor M P Vessey, Dr D Skegg, Mrs M Thorogood, and Mrs A Reeve for their help.

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STRANGE ENCOUNTERS

Coma

Last year—and I wish that it might not be possible this year, or any year—a pathologist, not in practice, was called urgently by a neighbour to see her daughter, whom she had found unconscious in bed. The girl was hot, dry, and unrouseable. There was an almost empty box, labelled “the sleeping capsules,” by her bed. Her breath smelt of alcohol. She had a little bruising about one eye, with a small sub-conjunctival haemorrhage.

Her profession, at which she was reputed to be good, was travel. She had just come back from southern Africa, her return delayed (as had been the outward flight three weeks earlier) by an unscheduled overnight stay in West Africa. The consequences of the earlier delay showed her to be a less competent traveller than her professional standing and responsibilities should have guaranteed.

At the local general hospital, which is well spoken of, and whither the pathologist and the patient's mother had thought it best to transport her themselves, to save time, the following conversation took place. To set the scene it is necessary to note that the pathologist had first telephoned the hospital, a few minutes' drive from the girl's home, to ask that the staff be ready to look after a young woman with cerebral malaria. I omit his obvious lines in the exchange between him and the staff when the patient arrived in the casualty department.

Resident medical officer (four years since qualification in a British medical school; MRCP recently acquired at the first attempt), to *pathologist*: You say you are a pathologist? Are you a doctor?

RMO: Why didn't you wash out her stomach before bringing her here? I don't suppose you tested her pee either.

RMO: Malaria? Of course I'm not going to treat her for malaria. You don't get malaria in this country. A pathologist would know that.

RMO: I've said, I will not telephone the consultant.

RMO (to night porter): This man is not to use the telephone.

Porter (to "this man"): Sorry, sir. But there's a coin-box down the corridor, to the left. The consultant on call is Dr So-and-So.

Dr So-and-So, who lived some eight miles away, arrived within minutes, jacket and flannels over his pyjamas. He had already ordered treatment, over the telephone, and this had been given by the now shaken RMO. Dr So-and-So said, later, that he had never before treated anybody for any form of malaria. He had been asked about cerebral malaria in the oral examination when he sat for the MRCP, and the examiner had remarked that he ought to know a lot more than he did: although he had passed the examination, he had taken some trouble then to find out about the disease.

The diagnosis of malaria was confirmed when the girl's blood was examined by the hospital's pathologist, who came as quickly and as willingly as his colleague, the consultant physician on call. The other possible causes of coma were also considered, but there was no evidence from laboratory tests and x-ray examination that any other condition had contributed to the illness.

The girl got better. She is said to be as well as ever. I hope so. The only person I know personally who has survived cerebral malaria

is not—to those of us who know him well—the same person, though professionally as competent, as he was before he could not be bothered to take his antimalarial.

Cover-up

The picture on the front of an issue of *The Listener* that showed Dr Jonathan Miller in the anatomical theatre in Padua reminded me of an incident in the history of a textbook, published in the 1960s and now out of print. The book was jacketed with a photograph of a model of that theatre that, if I recall correctly, used to be in the Wellcome Historical Medical Museum on the Euston Road in London. On the table in the well of the model theatre was the supine naked cadaver of a man. The jacketeers at the book-bindery, dignified Cockney matrons every one, walked out, refusing to handle an obscene picture. Publication of the book was delayed by three months while negotiations took their delicate course. It was as well that the good ladies did not page through parts of the book itself, else there might have been further delays.

Perhaps it was their sisters who, likewise manually occupied in inserting long-playing gramophone records in their decorative card sleeves, went on strike, affronted by the nakedness of the cherubs on a baroque altar chosen to illustrate the cover for a new interpretation of—let me think—was it Cherubini?

How strange to be able to date such prudery to only a dozen years ago. . . .

What's in your name, author?

At last the prepublication copy of my first book reached me, with the publisher's compliments. It looked magnificent, I thought, until someone pointed out that my name was misspelt on the dustjacket. I telephoned the publisher. He listened patiently, making soothing but equivocal sounds. He said he would look into the matter and let me know what was to be done about it.

Next day he telephoned to ask if I should mind very much if he did not correct the mistake. It would cost a lot to have the artwork “done” all over again; have new blocks made; buy the special grade of art paper; print, laminate, and fold the new jackets; recall the existing stock from the warehouse; unwrap each parcel of six copies; remove the faulty jackets; put on the new ones (all hand work, and expensive); repack the books in packs of six; and return them to the warehouse.

All this was practicable, the publisher pointed out, only if the price of the book could be marked up substantially, with consequent prejudice to sales. So, would I, in the circumstances, and particularly as it was my name that was responsible, at least share the cost by accepting half the royalty that had been agreed? Alternatively, he added, why not let the misspelling stand? Few purchasers would be aware of the mistake, and, in any case, my name was spelt correctly on the spine of the book itself and on the title page.

After all, the publisher said, not many medical books are bought because of the author's name.—WILL MACREDIE.