used to write in their textbooks that recurrent ulcers never respond to drugs. Now you have to weigh up the balance sheet very carefully.

Side effects

CHAIRMAN: Is there in fact adequate machinery for collecting and measuring side effects of a drug which, like cimetidine, comes into general use very quickly? There have been large numbers of series published on patients followed for 12 months. Are there enough series in hand at the moment of patients who are being followed for a longer period than that?

DR BENNETT: I think there are. As we know the Committee on Safety of Medicines is considering monitored release of new drugs and I'm certain that will be a change that will prove

crucial for the patients' benefit. The companies themselves are going to see such a change in their own interest because the reaction today of any patient who has any suspected adverse effect is to slap a writ on the company. But I think that Smith Kline and French are very actively collecting all the information there is and long-term trials are being done.

CHAIRMAN: So that within a year or two we should be able to say to patients that just as we can measure the long-term risks as well as the immediate risks of vagotomy we can do the same thing with cimetidine.

DR BARON: Data from double-blind trials of cimetidine over one year so far suggest it is reasonably safe. So far I have been happy to provide it for a year. I'm not confident in prescribing it for more than a year—but I am willing to do so because I'm a physician and if I don't prescribe new drugs for periods longer than that for which there are data, who will?

For Debate . . .

Fats and atheroma: an inquest

Sir JOHN McMICHAEL

British Medical Journal, 1979, 1, 173-175

Summary and conclusions

All well-controlled trials of cholesterol-reducing diets and drugs have failed to reduce coronary (CHD) mortality and morbidity. Nevertheless, commercial, professional, and even government-sponsored propaganda continues. Experimentally some vegetable oils and hardened fats can be more damaging to arteries than butter. There are other hazards to heart muscle from vegetable oils.

Israelis consume a high polyunsaturated fat diet equal to that recommended for prevention of CHD in USA but their CHD incidence is very high. Urban Bedouins are also affected. The primary clofibrate prevention trial underlines unacceptable risks which could apply also to diets. Official medical endorsement of these cholesterol reducing measures should be withdrawn.

Introduction

Because cholesterol deposition is an important feature in the anatomy of atheromatous plaques, though in only 50% of them,¹ and since cholesterol can move from the blood in and out of the plaque, it has been assumed that raised concentrations of cholesterol in the blood increase the severity of the lesion and may be a factor in its development. This has been the basis of many reports by national committees and epidemiologists who have correlated the incidence of coronary heart attacks and

deaths from coronary heart disease with a high fat intake in more prosperous populations. Recommendations have been made to lower the cholesterol content of the blood,² and indeed many trials have been organised to test if this might be beneficial. The best-conducted dietary trials under the auspices of the MRC's statistical control have given convincingly negative results. In survivors who have had coronary manifestations, and are thus at special risk, low-fat³ and soy-bean oil diets,⁴ which can lower the blood cholesterol concentration, have been entirely ineffective in slowing the progress of the disease towards recurrences or death. Drugs that reduce the blood cholesterol concentration also failed to influence⁵ outcome when tried on large numbers of similarly affected patients whose disorder was liable to deteriorate.

In addition to the carefully conducted British trials evidence had accumulated to suggest that raised cholesterol concentration had little to do with atheroma. Anitschkow, who first produced patchy fatty lesions in the arteries by feeding large amounts of cholesterol to rabbits, said that the blood cholesterol concentrations were raised to a degree that is never seen in man and he did not believe that this was the cause of atheroma.⁶ Substantial rises in cholesterol concentration after thyroidectomy in the treatment of heart disease before the war equally did not produce an excess of coronary atheroma in man.⁷ Diets with a high and low fat content that were consumed by different monastic orders did not alter the incidence of coronary disease.⁸

Polyunsaturated fats

Nevertheless, many committees who have recommended taking hopeful attitudes to potential benefits from cholesterol reduction continue to make their assertions, and the propaganda is now being endorsed by political and government organisations. Senator McGovern's Committee in the USA⁹ recommended reduction of fat intake by substituting polyunsaturated

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fats which might lower the blood cholesterol concentration. Important evidence was given to the McGovern Committee against these recommendations by many authorities, including the American Medical Association, which suggested that dietary changes should be promoted only for control of obesity. Many researchers of high standing who previously had a favourable attitude to the lipid hypothesis admit that proof of benefit from cholesterol-reducing measures is lacking.¹⁰⁻¹²

The UN Food and Agriculture Organisation¹³ gave massive prominence to epidemiological evidence and neglected critical scientific analysis. The EEC produced a report¹⁴ that also supported a change in diet, except for an important and highly critical chapter by Professor J R A Mitchell of Nottingham, who recommended no change. The COMA Committee under Sir Frank Young found that the evidence in favour of polyunsaturated fats was unconvincing.¹⁵ This opinion was re-endorsed and the Department of Health added a warning on possible harm from vegetable oils in margarines.¹⁶ An important and critical analysis by a scientific biomedical committee of the Irish Agricultural Council¹⁷ pointed out gross defects in the recommendations of the committee of the Royal College of Physicians and the British Cardiac Society to follow a polyunsaturated fat diet. The British Heart Foundation circularised 35 senior cardiologists in our teaching hospitals and found that only seven were in favour of changing to a polyunsaturated fat diet. The rest (28) were not convinced that this would be of benefit. Most of the supporters of polyunsaturated-fat diets ignore the mass of negative evidence in the above-mentioned important studies. Their reports, which are based mainly on epidemiological surveys, are misleading and grossly biased by their failure to recognise and consider the complete investigative picture.

The recently recorded decline in death rates from coronary heart disease in the USA cannot be ascribed to propaganda about diet, since similar dietary recommendations in Sweden were accompanied by a rise of 30% in the death rate from coronary heart disease in 1969-73.¹⁸ As Armstrong says, the only arterial disease that can be reversed by diet is that which has been induced by diet, and this is a poor model of atheroma in man.¹⁹ The blood cholesterol concentration and the severity of coronary disease are not correlated.²⁰ Many other factors are at work.

Safety of suggested dietary changes

Leaders in a profession have a duty to sift all the relevant evidence and give guidance to general practitioners. In view of the continued controversy about fats and arterial disease some doctors may think that the suggested dietary changes will at least do no harm. This is questionable.

DIETARY FACTORS IN ISRAEL

Israelis consume a diet that is higher in polyunsaturated fats than that of any other Western society.²¹ This has been shown both by analysis of their food balance sheets, in which the ratio of polyunsaturated fat : saturated fat (P:S) was about 1.0, and by sampling storage fat in subcutaneous tissue, which shows a P:S ratio in Israeli Jews of 0.88 to 1.13. In the USA in 1969 the P:S ratio was just under 0.4.²² Thus the Israelis' diet is similar to that recommended for prevention of coronary heart disease (the McGovern Committee recommends equal amounts of polyunsaturated and saturated fats—that is, P:S = 1), yet mortality from coronary heart disease in Israel is high (about three-quarters of that in the USA).

Desert Bedouins are alleged to have singularly little coronary artery disease; they eat frugally—carbohydrates with some animal fats, milk, etc (subcutaneous fat P:S ratio = 0.76)—but when they move to Israeli towns their susceptibility to develop coronary heart disease increases. The depot fat acquires a P:S ratio of 0.95, near to the Jewish ratio, around unity.²³

Thus the polyunsaturated fat diet does not prevent coronary heart disease, but might even be suspected of contributing to its development.

Hazards of polyunsaturated fat diet

Reducing the cholesterol concentration in the blood diverts lipid into the liver, with increasing hazards of gall stones, whether it is achieved by drugs or polyunsaturated fat diets. The recent scrupulous report on the massive long-term primary prevention trial of clofibrate emphasised the risk of developing gall stones, with some suspicion of a possible increase of bowel cancer as well.²⁴ Clofibrate did not affect the death rate from coronary heart disease. Although the reduced score of myocardial infarctions reached a marginal level of significance the difference in the incidence of milder manifestations such as angina was not significant. The drug is not recommended for prevention. Dietary interference may be suspect for similar reasons.

But there are other fears. Wissler's group in Chicago²⁵ showed that certain vegetable oils (for example, peanut oil and coconut oil) that were fed as 25% of the diet to rhesus monkeys caused considerable intimal cell proliferation and scarring. Butter fat in similar amounts produced little intimal fibrous reaction but extensive superficial foam-cell deposition that resembles the "early lesions in man"—namely, fatty streaks that most consider to be harmless.²⁶ Natural fatty acids usually have "cis" double bonds, but when vegetable oils are hardened to make margarine the natural cis forms may be converted into "trans" forms. The cholesterol esters of trans forms are intensely sclerogenic on implantation into tissues, while those of the cis forms are only slightly sclerogenic.²⁷ Trans fatty acids might contribute to altered characteristics of cell membranes,²⁸ and these occur in considerable amounts in some margarines.

Another possible adverse influence of vegetable oils, first shown for erucic acid in rape-seed oil, is unsuitability to myocardial cells.²⁹ The heart metabolises fatty acids preferentially, but in certain experimental animals, including cynomolgous monkeys,³⁰ vegetable fats may accumulate and cause degeneration of cardiac muscle cells. Not only rape-seed oil but other vegetable oils may produce similar lesions in the sensitive young male Sprague-Dawley rat.³⁰

Comment

I do not subscribe to the view that atheroma is a nutritional disorder caused by faulty dietary habits. It is a complex process influenced by heredity, infection, and other factors, but basically it is a wear-and-tear disease, in which mechanical stresses and injury at special points of turbulence in the blood stream break the vascular endothelium. The resulting insudation of plasma into the vessel walls leads to complex biochemical sequences of deposition of fibrin and later cholesterol in the plaque.^{26 32} At some stages in the development of the lesion the presence in the circulation of damaging agents such as products of some of the vegetable oils might increase the severity of this reaction to injury.

Conclusion

Reducing blood cholesterol by diet or drugs may have injurious effects on the liver and gut. Naturally occurring animal fats can be less damaging to the heart or the blood vessels than some vegetable oils which, when hydrogenated, constitute an important part of many margarines. Massive exposure of the public to hardened oils should be avoided until we know more about the oils in the margarines. In hydrogenating vegetable oils more unnatural trans fatty acids are formed, and these, or possibly other injurious factors associated with vegetable oils,

may be more damaging than natural animal and dairy fats, which in excess produce only innocent lesions in the blood vessels. The time has come to reject advice to substitute polyunsaturated fats for animal and dairy fats in the nation's diet.

I am deeply indebted to Sir Frank Young and Dr Elspeth Smith for valuable discussions.

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(Accepted 26 October 1978)

MATERIA NON MEDICA

Expedition in Borneo

The luxuries of base camp being as they are it was something of a shock to be asked to accompany a rescue party deep into the alluvial forest of Sarawak. I was serving as Medical Officer to the Royal Geographical Society Expedition to the rain forests of Gunong Mulu National Park, East Malaysia, and my wife and I were the only doctors within a day's journey of here.

We set off in a long boat with an outboard motor (there are no roads of any sort) and had travelled for about 45 minutes when it became obvious why there were six men accompanying me. The Melinau river soon runs into the Tutoh river, which is a mighty river of almost South American proportions, with fierce and treacherous rapids. Every now and again the boat had to be unloaded and our packs and spare fuel carried upstream while the boat was manipulated through the more difficult rapids. We had three Punans with us—the nomadic people of the Borneo jungles, who know their way around vast expanses of jungle like nobody else; the broken stick or twig means everything to them. They carry enormous loads through the most rugged country and densest jungle for many miles.

On the second day we set out after dawn through dense jungle and climbed steeply through the fabulous and fantastic diversity of plant and animal life. There are an estimated 100 different species of tree and over 300 species of plant per acre. We saw the expected large numbers of butterflies, including the famous Rajah Brooke's Birdwing, and many other insects. The ants particularly made their presence felt; it is easy to inadvertently put your hand on a tree covered in fire ants, which have a piercing sting. One species of ant stridulates loudly, rubbing its back legs together to ward off danger. Another species makes its home in the fascinating ant plant, a tuber containing a maze of passages within and providing an ideal home for the ants.

Perhaps the most difficult aspect of jungle life to get used to are the leeches. Special leech socks provide some protection but the leeches can penetrate almost any aperture. Men with buttons, not zips, are especially vulnerable.

To begin with the path was well trodden but soon we were traversing nearly vertical slopes made slippery by sandstone and wet leaves. On our second night it rained heavily and by morning all our belongings were saturated. We left very early, passing several old Punan camp sites, and by 9 am we had arrived at the refuge of the unfortunate explorers. The party had been on their way from Long Seridan to the Mulu Expedition base camp when one of the three Europeans had dislocated his shoulder in a fall and was unable to move through the difficult country.

Their Punan guide, Sigang, had left them to summon help and had covered the distance involved, on foot, in an incredible two days. He had now guided us back to their position. With the aid of a chain saw, which we had carried with us, a sizable clearing soon appeared

in the jungle, and within half an hour a Royal Malaysian Airforce helicopter arrived, at a prearranged time. Guided by an enormous smoking bonfire the helicopter pilot, with infinite skill, hovered just above the tree tops and the injured man was winched to safety. I had barely had time to examine him.—ALAN LLOYD-SMITH (Brisbane, Australia).

Lady of the canyon

The first mistake was ordering a medium-sized pizza in Fresno, California. It was 18 inches in diameter and 2 inches thick. I ate my way stoically through three cardinal points of the compass but had to carry out the last 90° segment in a doggy bag. The second mistake was trying to find my own way up Placerita Canyon. The signposts were ambiguous, and my young lady and I disagreed on the best route. Both of us being pig-headed individualists, we agreed to plough our own furrows.

One hour later, scratched and sweaty, I was crashing through dense undergrowth. The vegetation was semi-arid chaparral (from the Spanish word for "stunted growth"): it was way above my head, and I'm 5 feet 8½ inches. I cursed the dryness and heat (24 hours before, I was cursing the thick snow blocking the roads in Sequoia Park—there's no pleasing some folk). I wondered what unpleasant fauna might lurk amid the shrubs. Rattlesnakes were a definite risk and scorpions a possibility. A humming-bird flickered through the branches ahead of me. Eventually I broke through into a dried-up water course. The scour of boulders when in flood had cleared a trail, and with relief I turned downhill towards the car park. There were a couple of waterfalls to negotiate but otherwise it was easy going. I thought, "Won't she be unbearably smug when she hears how I got lost?" Then I heard a faint wailing, high above me. Imagination, surely? No, there it is again. "Help . . . Graham! . . . Oh, help me . . . (sob). . ."

There she was, perched in a tree half-way up the canyon wall. It was dozens rather than hundreds of feet up, but still a nasty climb. The rock was crumbly sandstone: plenty of handholds, but few reliable. She poured out her tale as we nestled in the branches. She had got lost and blundered through the bushes. She had slipped over the canyon edge, and luckily fetched up against the tree. But she could climb neither up nor down.

However, I found a route sideways, which took us to a scree where we could descend. We were flushed and dust-caked as we reached the car. Time for a bite before heading for LA—but the pizza was no longer in my pocket. The branches had snatched it out en route. It would probably feed a Placerita ants' nest for the next six months.—GRAHAM SUTTON (postgraduate student, Edinburgh).