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SYMPOSIUM ON 'NUTRITION AND THROMBOSIS'

Diet and arterial disease—the myths and the realities

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'What passes for knowledge is often no more than well-organised ignorance' ANON

What matters to patients is death and disability, rather than mechanisms or theories. The studies which have linked diet and arterial disease have concentrated on coronary heart disease (CHD) and have virtually ignored stroke and limb artery disease despite the major contribution which these diseases make to the burden of suffering. Even in the field of CHD, we know less than many people think, so let us first examine the myths which have evolved; then let us try to answer the questions our patients pose to us about the benefits which they can expect, in terms of prolongation of life and freedom from disability, if they follow the dietary advice which is now being so freely dispensed.

The myths

The chain of beliefs about diet and CHD runs as follows: CHD is caused by atherosclerosis; atherosclerotic plaques are cholesterol deposits in artery walls; a high-serum cholesterol is a risk marker for CHD: dietary lipids determine serum cholesterol. If one accepts that these statements are true and that they belong to the same logic-chain, then two further statements arise: dietary lipids cause CHD; dietary modifications will prevent CHD. As we shall see, most of the statements set out here are either untrue or irrelevant.

CHD is caused by atherosclerosis. While the presence of underlying coronary artery-wall disease provides a necessary infrastructure for CHD, myocardial infarction and sudden death are rapid events. There is abundant evidence that the critical process in transmural myocardial infarction is thrombotic occlusion of a

coronary artery (Mitchell, 1978*a*) and that in sudden death, thrombosis, often in association with plaque disruption, is also the crucial underlying event (Davies & Thomas, 1984).

Atherosclerosis is synonymous with lipid deposition. When Virchow (1858) looked at clinically-relevant artery-wall plaques he thought that they represented chronic inflammation. He recognized that lipid deposits could be found in many other necrotic and reparative foci (such as tuberculous lesions in the lungs) but he would never have assumed that such foci were caused by lipid deposition. His observations showed him that all the layers of the artery wall were involved. The presence of lymphocytes, plasma cells, giant cells, fibroblasts and calcium deposits would not have permitted him to lend his name to any description of atherosclerosis that regarded it merely as lipid deposition in the intima.

Atherosclerosis can be imitated in animals. Ever since Anitschkow showed that lipid feeding produces fatty lesions in the walls of vessels (Cowdry, 1933), billions of animals have been sacrificed on the altar of the 'animal model' concept. The vascular lesions produced reflect the erroneous concept of human disease which we have already discarded since they merely show intimal foam-cell/modified smooth-muscle-cell lesions which resemble clinically-irrelevant fatty streaks rather than multi-layer, multi-process, stenosing and thrombosing human lesions (Mitchell & Schwartz, 1965).

Serum cholesterol predicts the risk of CHD. Since the earliest days of cholesterol measurement, it has been clear that for groups of individuals, it is a risk predictor for coronary events. Until the role of the lipid subclasses (high-density, intermediate-density, low-density and very-low density lipoproteins or their carrier apo-proteins) becomes clarified, I propose to use cholesterol to develop my arguments, because it is cholesterol itself which has caught the layman's imagination and has been labelled as the 'cause' of coronary disease by the media. Within groups, the link between serum cholesterol concentration and coronary risk is not a strong one. It is perfectly possible to have a heart attack with normal serum lipids and not to have a heart attack with elevated lipids, so cholesterol cannot stand in the same relation to CHD as was demanded of the acid-fast bacillus by Koch when he put forward his postulates about the proof required of a supposed cause for disease.

Association does not imply causality, but cholesterol has been assumed to play a prime causal role because of the 'articles of faith' set out previously. Moreover, one can blame the victim's life-style and can set about tidying it up, whereas for other equally-powerful risk markers one has to blame his parents and his genes. For example, short stature and high blood pressure have both emerged from major studies (Logan *et al.* 1978; Mitchell, 1978*b*) as risk predictors and yet both of them owe almost everything to inheritance and very little to environment. Social class is an extremely powerful mortality risk-marker (in the UK, the death-rates for men and women aged 15–64 years in the unskilled social class V are 2·5 times higher than in the professional social class I; Black *et al.* 1982). These are, however, not social classes but educational classes; in the USA, Hinkle *et al.* (1966) found that

asking healthy people about the duration and type of their education was just as powerful a predictor of CHD risk as cholesterol, smoking and hypertension. On these findings it would be as logical to assert that compulsory college education for all would halve the death toll from CHD as to make the more conventional claim that cholesterol-reduction would be similarly beneficial.

Serum cholesterol is determined by diet. Cholesterol, like urate, is an endogenous material which in a free-range society is genetically determined and is minimally related to diet (Neufeld & Goldbourt, 1983). It is true that dietary change will modify serum cholesterol and that between-population comparisons show that total fat intake and saturation-level of that fat are correlated with serum cholesterol (Keys, 1980), but if one makes within-population comparisons, the influence of diet on cholesterol levels is minimal. Cholesterol is a marker of who you are rather than what you do.

The theoretical claims. The case which is being put to the public, rests on this series of statements, out of which emerges a rallying cry that poor diet causes coronary disease, so that by dietary manipulations we could prevent the epidemic of CHD. Before we examine the only way to test these claims, we need to be aware of information which is being used to lend support and credibility to them.

During the last 10 years, the USA coronary mortality has fallen by 25% (Harper, 1983) and there is an unseemly rush to claim the credit for this (prudent eating, better blood-pressure control, anti-smoking campaigns, coronary care units, jogging and weight reduction). The problem is that all sections of the USA community have been equally benefited and at the same time (old and young, rich and poor, black and white, men and women). I remain unconvinced that a poor black elderly woman living in Washington is likely to have changed her life style or been offered the advances in blood-pressure control and coronary care to the same extent as a young, affluent white man from Scarsdale. Those who believe that they can 'explain' the decline in CHD in the USA by better health care would do well to ponder why, in a highly-developed, health conscious and disciplined country like Sweden, CHD incidence and mortality seem to be increasing (Alfredsson & Ahlbom, 1983).

The facts

To those who keep saying that 'better eating prevents coronary disease' we must reply that every evangelist is entitled to his beliefs but every scientist is entitled to ask for the evidence. We should regard advisory committees with a degree of scepticism: 'the alternative to scientific experiment—both in medicine and in politics—is the expert committee. Unfortunately, just as we cannot be sure of the relationship between risk factors and disease, we cannot be sure of the relationship between the opinion of the committee and the truth: the opinion of the committee will depend on who is selected for it' (Anon., 1983). If coronary disease is common and kills, then a reduction in coronary disease will be reflected in a fall in total mortality. Valid trials are few in number and can be divided into those which dealt only with lipids and those which aimed at changing multiple risk factors.

Lipid-orientated studies

The Los Angeles Veterans Administration study (*Dayton* et al. 1969). Men aged 55–89 years residing in a Veterans Administration Centre (*n* 846) were randomly allocated to receive a low cholesterol, low saturated fat, high polyunsaturated fat diet, or to continue on the ordinary North American diet. The experimental diet reduced serum cholesterol by 13% during the 8-year follow-up period but the total deaths were 177 in the control group and 174 in the cholesterol-lowered group. The prevalence of gall stones was significantly increased in the experimental group (34 *v.* 12% in the controls). The total mortality concealed a suggestion of a reduction in CHD deaths and an increase of 12% in non-cardiovascular deaths.

The Finnish mental hospitals study (*Turpeinen* et al. 1979). Two mental hospitals were used; one continued its normal diet for 6 years while the other adopted a diet similar to that used in the Los Angeles Veterans Administration study. After 6 years, the hospitals switched their dietary styles, but of course a constant stream of patients had been moving through them during the trial period for reasons which were nothing to do with the purposes of the trial. The calculations needed to relate the end-points to the exposure period of the trial were therefore very complex. Cholesterol was reduced by 15% in the experimental-diet periods but there was no significant effect on total mortality (34·8/1000 person-years in the cholesterol-reduced periods *v.* 39·5/1000 person-years in the control). Within the unchanged total mortality there was a reduction in cardiovascular-attributed events which was balanced by an increase of 15% in non-cardiovascular deaths.

Multiple risk-factor trials

The North Karelia project (*Puska* et al. 1983). Because Finland had the highest CHD mortality in the world, one of its provinces approached central government and asked for help. It was decided to adopt a community-based multiple-risk-factor-reduction strategy in this province (North Karelia) and to keep the adjacent province of Kuopio as a non-intervention control. In North Karelia there was an aggregated reduction of the main risk factors by 17% and the outcome is set out in Table 1. On the original trial design, the comparison between the designated test and control areas is not significant; to get a difference which is

Table 1. *Average annual regression-based decline in age-standardized coronary heart disease mortality in* 1974–1979

	Men		Women	
Area	%	95% confidence limits	%	95% confidence limits
North Karelia	3·7	1·5	2·2	3·4
Control area: Kuopio	1·9	2·3	1·8	1·4
Finland except North Karelia	1·7	2·2	1·2	2·4

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significant, one has to go beyond the original design (and this is special pleading or 'data-dredging') to show that men in Karelia fared better in respect of CHD than in the rest of the country, minus Karelia. Women were no different on any analysis. In respect of total mortality as opposed to attributed CHD, no demonstrable benefit emerged for any group, even after special pleading.

The Oslo study (*Hjermann* et al. 1981). From 16 202 men aged 40–49 years, 1232 healthy men with normal blood pressure and elevated lipid levels were randomized into a 5-year study in which the intervention men were asked to stop smoking and to reduce their lipids by dietary means. During the trial, mean tobacco consumption per man fell 45% more in the intervention than in the control group while the fall in cholesterol was only 13% greater in the intervention group. Had significant differences in outcome emerged, it would thus have been difficult to disentangle the well-accepted benefit of stopping smoking from any effect of lipid reduction. However, the trial results were not conclusive (total mortality: control 38/1000, intervention 26/1000, which was not significant; fatal and non-fatal infarction plus sudden death were 47% lower in the intervention group (P=0·03)).

The USA trial (*Multiple Risk Factor Intervention Trial Research Group,* 1982). This trial took 12 886 high-risk men and randomly allocated half to a special intervention (SI) group who had a very extensive programme of advice aimed to reduce blood pressure, smoking and plasma lipids, to conquer obesity and to increase physical activity. The comparative group, who knew of course that they were 'high risk', were simply sent back to their doctors for 'usual care' (UC). As in Karelia, the flaw in this trial design was that the trial organizers assumed that these men would go away and quietly wait for death without attempting to change their own life-style in any way. Because of their refusal to act as true controls, the UC group changed their behaviour markedly, so both groups showed a fall in plasma lipids. Table 2 shows the unpalatable end-result, in that the 'got-at' (SI) men did slightly worse in terms of overall mortality than the 'laissez-faire' (UC) men, which is not much of an advertisement for mass prevention. In his commentary on the trial, Oliver (1983*a*) observes: 'No amount of dredging of the data will turn it into a conclusive one. It is more honest to accept that multiple-risk-factor intervention, under the circumstances of this trial, did not work, than to say it might have worked'.

Table 2. *Multiple Risk Factor Intervention Trial Research Group* (1982) *findings after 7 years*

	Special intervention group*	'Usual care' group†
Total mortality/1000	41·2	40·4
CHD mortality/1000	17·9	19·3

CHD, coronary heart disease.
*Underwent an extensive programme of advice.
†Returned to doctors (comparative group).

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Table 3. *Effect on coronary heart disease risk factors (%) in WHO factory study (WHO European Collaborative Group, 1983)*

	UK	Belgium	Italy
Cholesterol	−0·4	−0·9	−4·8
Cigarettes/d	−15·6	−3·7	−5·5
Wt	−0·4	+0·2	−1·9
Systolic blood pressure	−1·6	−2·3	−4·1

Table 4. *Net percentage difference in outcome between groups in WHO factory study (WHO European Collaborative Group, 1983)*

	UK	Belgium	Italy
Fatal CHD	+8	−21	−30
Total CHD	+5	−24	−14
Total mortality	+14	−17	−6

CHD, coronary heart disease.

WHO European Collaborative Group (1983) study. A group of 49 781 men aged 40–59 years working in sixty-six factories was recruited. The factories were paired and one of each pair was randomly allocated to receive special intervention. Within an intervention factory the intention was to lower cholesterol by diet, to reduce smoking and weight, to increase physical activity and to control high blood pressure. Table 3 shows how the risk factors fared and Table 4 shows the effect on the predetermined end-points. Special intervention is clearly bad news for Britons in that they fared worse in all end-points than their fellows who were left alone. In the light of these findings it is astonishing that Rose *et al.* (1983) 'reach the remarkable conclusion from the entirely negative UK section of the WHO study that effective multiple-risk-factor control probably works and that the problem now is how to get the message through to the public' (Oliver 1983*b*).

The 'bottom line'

What interests patients is staying alive and free from disability. They are not interested in risk markers such as blood lipids and blood pressure but only in their effect and in the benefit which modification of these risk factors will confer on them.

Once we have told our patients to stop smoking, then as scientists and men of commonsense, we have a duty to keep our mouths shut in terms of CHD prevention. If we do not do so, and our patients challenge us to produce evidence that by following the advice given by the Multiple Risk Factor Intervention Trial Research Group (1982) and the factories study (WHO European Collaborative Group, 1983) about diet, weight, activity and blood pressure control they will live longer or stay free from clinical CHD, then we cannot do so. When one pushes the evangelists into a corner they will admit that there is indeed no evidence but they

then turn on to another tack by saying: 'Even if it does no good it can do no harm'. I do not think that they have taken a broad enough view of what constitutes harm.

First, there will be harm to our credibility as scientists and as health advisers. If we go public on diet and CHD on the basis of poor evidence we are weakening our position in respect of measures for which there is clear evidence: that everyone should be a non-smoker and that blood pressure control prevents strokes and heart failure.

Second, harm to individual patients has already been observed in some studies of cholesterol reduction (an increase in gall stones (Dayton *et al.* 1969), an increase in the frequency of cholecystectomy (Committee of Principal Investigators, 1978)).

Third, there has been inadequate discussion of the economic harm that could result from replacing fats which are indigenous to our temperate climate with polyunsaturated fats which mainly derive from warmer countries and so must be expensively imported. There is an interesting parallel with fuel energy, where we have to balance the problems and advantages of our indigenous coal resources against the political and financial problems created by becoming dependent on imported fuels such as oil. As we cannot work out an acceptable agricultural policy for Europe on purely economic grounds, I can foresee that the 1984 miner's strike, which related to the social rather than the economic consequences of pit closures, would fade into insignificance in comparison with the storm that would break if increasing dependence on imported edible oils led to farm closures. Are we prepared to ride out such a storm on the basis of health claims which rest entirely on belief and for which there is at present no hard evidence?

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