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THE MANAGEMENT OF ISCHAEMIC (CORONARY) HEART DISEASE*

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Without belittling in any way the valuable contribution which can be made in the management of ischaemic heart disease through therapeutics, it is still true that the most important aspect of management is what is said to the patient and his relatives by the doctor in charge. There is a great deal of iatrogenic heart disease resulting from errors of commission and omission on the part of the medical practitioner in the verbal management of ischaemic heart disease. These errors arise in part from uncertainty as to the prognosis in the individual case, either in terms of natural history or in terms of the modification of natural history which can be achieved by medical management or therapy. It will probably always be difficult to assess individual prognosis, as in many other diseases; the best that can be done is to form a judgment on group prognosis and assume that the patient may well do better than the average. This optimism is better for the patient than the reverse pessimism.

Few doctors now make the mistake of attributing the pain of myocardial ischaemia to indigestion, but many patients make this mistake and do not report to their doctors. Furthermore, there is more and more evidence for infarction without pain. For these reasons unexplained breathlessness or arrythmia among the classes of people defined later as being 'at risk' of ischaemic heart disease justifies careful examination and electrocardiography.

This commendable consciousness of the wide prevalence and potential severity of the disease leads some doctors to give the patient an exaggerated impression of the potential severity during the period of diagnostic uncertainty which is often unavoidable. Patients are often unnecessarily frightened by the opinion given by the doctor at the first consultation. In doubtful cases some such words as 'I believe' or 'I hope that this is not a coronary heart attack but I can't afford to take the risk of not confining you to bed until electrocardiography and two or three days of observation have excluded the condition' will save patients much unnecessary worry. When the diagnosis is established it is much easier to correct the preliminary opinion in a direction of greater gravity than to dispel unnecessary and unjustified fears which have been raised in the patient's mind.

For practical purposes, ischaemic heart disease is the result of atheroma or atherosclerosis of the coronary arterial trunks. Other rare causes will be ignored in this discussion. Atherosclerosis may be very local and may in some cases be precipitated into occlusion by subintimal haemorrhage or other mechanisms which are at present obscure. In general, however, both coronary trunks are considerably occluded before infarction occurs. The cause of the infarction is often obscure, but in the majority of cases it is due to thrombosis of blood in a small segment of one trunk (coronary thrombosis from occlusive thrombogenesis). Myocardial infarction without coronary thrombosis is still a little mysterious; in some cases it is undoubtedly due to effort of sufficient intensity to render the blood flow through narrowed arteries inadequate for the oxygen requirement of the very active myocardium. This variety of causation will be facilitated by myocardial hypertrophy as in hypertension, or by failure of the oxygen-carrying capacity of the blood resulting from anaemia or methaemoglobinaemia. In other cases it is not unreasonable to assume that the coronary system, or a small segment of one of these trunks, undergoes functional narrowing of the lumen through vasoconstriction. Such precipitating events as exposure to a cold wind, excitement and anger, or effort on a full stomach, are suspected to operate in this way. In the last resort, however, we must recognize that a certain proportion of cases of infarction are not explainable in terms of coronary occlusion by thrombosis or of any other mechanism which is at present understood.

Any pathologist will confirm that severe coronary atherosclerosis is often seen at autopsy in the absence of any clear evidence of infarction. Indeed, Morris has deduced from the evidence of the Bernard Baron Institute of Pathology that the extent and severity of coronary atherosclerosis has not increased in the London population over the last 3 decades although there has been a great increase in myocardial infarction in the same population over the same period of time. Unless Morris's deduction is refuted we must conclude that the modern epidemic of myocardial infarction is determined by an increase in those factors which precipitate infarction as opposed to those factors which cause atherosclerosis; in other words, the study of occlusive thrombogenesis may be more rewarding than the study of atherogenesis in explaining the increasing prevalence of myocardial infarction. It is admitted that the mechanisms through which blood is caused to coagulate within a segment of a narrowed coronary artery (occlusive thrombogenesis) are not at present understood and may not represent all the mechanisms whereby myocardial infarction is precipitated; nevertheless, they must be very important for study. By the same token, therapy through anticoagulant drugs may have a sound basis in theory.

The encouraging feature in the outlook of the last decade is the epidemiological demonstration that myocardial infarction, as diagnosed, is increasing in prevalence among the privileged groups of the more developed races. If it be accepted that this is not due to better diagnosis, then we must conclude that it is due to recently operating and, therefore, remediable aspects of the environment of these privileged groups. This view is supported by the Norwegian statistics for mortality from myocardial infarction during and shortly after the Second World War. It also gives reason-

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able hope for an improvement in the next decade in what has been a deteriorating trend in the last decade.

If the factors responsible for the recent increase are concerned with the mechanisms of occlusive thrombogenesis, we might expect a distinct difference between White and Bantu blood in South Africa in respect of coagulation mechanisms and fibrinolysis. The disappointing results reported by Merskey *et al.* do not necessarily negative the theory of increased thrombogenesis. It may be that we have not yet developed techniques of *in vitro* study adequate for the recognition of disturbed coagulation mechanisms *in vivo*. This possibility is a challenge to haematologists who are interested in this field. There is considerable evidence that postprandial lipaemia from fatty meals may be connected with some form of increased *in vivo* tendency to coagulation.

Turning to the consideration of atherogenesis, although Morris's figures do not support the idea of increasing severity of atherosclerosis in the London populations affected by the great increase in myocardial infarction, we can nevertheless point to the considerable difference between South African Whites and Bantu in respect of atherosclerosis of the aorta and coronary trunks. There can be no doubt that there is a very considerable difference between the two races in the extent and severity of atherosclerosis in these two regions, although the Bantu is by no means in such a favoured position in respect of cerebral atherosclerosis. This dissociation in the extent and severity of atherosclerosis between the aorta and coronary trunks on the one hand and the cerebral arteries on the other hand has also been observed in Japan. It is extremely puzzling but does not concern us in the present discussion.

Disturbed Lipid Metabolism

The most hopeful aspect of the study of the epidemiology of ischaemic heart disease is the link between disturbed lipid metabolism and myocardial infarction.

In general those diseases which are associated with hypercholesterolaemia (e.g., diabetes and familial xanthomatosis) show a high prevalence of ischaemic heart disease.

Apart from such diseases, the privileged groups who suffer from the increasing prevalence of myocardial infarction are the groups who have high levels of total serum cholesterol in their blood, and who consume large quantities of fat, especially saturated fat, in their diets. The evidence for this association has been fully reviewed elsewhere. The link between dietary fat and serum-cholesterol levels is now clear. The link between high serum cholesterol and myocardial infarction might be through either or both of the mechanisms described above as thrombogenesis and atherogenesis. If the link is through thrombogenesis there is great hope for immediate reduction of mortality from myocardial infarction. If it is also through the mechanisms of atherogenesis, there is reasonable hope that this pathological process, for so long regarded as an inevitable result of aging, may be in part preventable.

Applying these principles to the management of coronary heart disease we have felt that a diet which reduced serum cholesterol is likely to favour prognosis in general in those who are at risk of coronary heart disease. This term 'at risk' will include those who have already had symptoms, those who have a strong family history, and those whose serum cholesterol is consistently high. We do not yet know the normal range for men of 40-50 years, but in general 275 mg.% may be taken as too high and figures between 275 and 225 as worth trying to reduce. We have shown that the majority of men with serum cholesterol figures above 225 will drop their level towards or to below 225 mg.% for as long a time as they consume 50-75 g. daily of an unsaturated oil such as sunflower-seed oil. The same result can probably be obtained by reducing dietary fat calories to 30% and substituting unsaturated oils for at least half of the total. This dietary adjustment can be made without undue discomfort to the patient and his household. Jolliffe *et al.*[4] have confirmed these findings in New York with his 'prudent diet'. In the present uncertain state of our knowledge we have not felt justified in making recommendations for populations in general or for people not at risk. There are many other ways in which the diets of populations with high prevalence of myocardial infarction differ from those of populations with low prevalence. These differences have been reviewed and in the present state of our knowledge the quantity and quality of dietary fat appears to be of greatest relevance. Advancing knowledge, however, may bring other factors to light.

The application of these dietary principles can be combined with any other method of therapy, including the short-term or long-term use of anticoagulants which will be reviewed by Dr. Suzman.* This appears to be the most promising line of drug therapy at present. Its value for periods up to 2 years after the last infarction has been supported by a careful study by the Medical Research Council of Britain, although there are still many dissenting voices.

Oestrogen therapy has given conflicting results in the hands of Oliver and of Katz. In full dosage the discomforts and disadvantages are such that a stronger case is required to support their use. A recent report with doses much smaller than conventional is encouraging, but will require critical examination and confirmation. In my opinion, oestrogen therapy cannot at present be recommended.

Treatment

In practical management coronary heart disease can be divided into 4 grades of severity. The management will be discussed in relation to these 4 grades.

1. *Angina pectoris on effort without infarction and with normal electrocardiograph.* If the ECG can be decisively altered by effort, then the patient is at risk. If the ECG is not altered by effort, the patient is nevertheless at risk if the symptomatology is clear cut. The explanation given to the patient is of paramount importance. It must be adapted to the patient's personality and circumstances. It is preferable to err on the side of optimism because angina pectoris can so easily be complicated by anxiety neuroses. On the other hand, the diagnosis must not be taken lightly. Physical effort should be maintained to the limit of capacity without pain, but the limit must definitely not be exceeded and nitroglycerine should not be used to achieve greater physical-effort performance. The use of that drug for the relief or prevention of angina resulting from emotional strain and causes other than effort is however entirely legitimate and often constitutes the only effective therapy. Rest should immediately be enforced and anticoagulants used if the angina

* Dr. M. M. Suzman contributed a paper at the Congress on the use of anticoagulants.

should develop crescendo qualities not related to effort; this sequence suggests impending infarction. The patient should avoid heavy meals and particularly exertion soon after meals. If he is over-weight, his calories should be reduced. His serum cholesterol should be determined by a reliable laboratory with reasonable agreement between at least two readings. If the mean is above 275 mg.% restriction of total fat and a swing towards unsaturated fats should be recommended as discussed above. The same recommendation is reasonable at mean levels between 275 and 225. At lower figures, the diet has less rationale but a case may still be made on the assumption that the individual may have a postprandial lipaemic tide which encourages thrombosis.

2. *Patients who have survived mild infarction without arrythmia, angina decubitus or myocardial failure* may be treated in exactly the same way as the group I.

3. *Patients with persistent angina decubitus or those in whom the angina is more related to tension and excitement than to effort* constitute a most difficult group. The treatments recommended for groups I and II should be applied but in addition special measures may have to be taken for intractable pain. The psychic and emotional aspects of this pain are well appreciated but not easily handled. The most important consideration is to prevent a vicious circle by adequate explanation and reassurance, with reasonable optimism and conviction. Once the vicious circle is established, psychic handling is, in my experience, not of great value. There are certainly unexplained aspects of angina pectoris and it is unfair to attribute all of these to psychic mechanisms. Nitroglycerine and related vasodilators are the stand-by of treatment. If they fail, and life becomes intolerable, after a long enough period of trial and adjustment it may be desirable to render the patient hypothyroid as the lesser of two evils. Many other treatments have been used, but none have stood the test of time and we have to confess that in this group medical treatment is far from satisfactory.

4. *Patients whose infarction has been followed by permanent arrythmia and/or congestive cardiac failure.* The treatments appropriate to these two complications will be of primary importance. At this stage, angina decubitus will seldom be a problem. Caloric restriction for weight reduction when indicated, or salt-restriction for the relief of congestive heart failure, will be the most important parts of dietary treatment. Exercise should not be unnecessarily restricted, although it is usually necessary to put a considerable brake on physical activity and on strenuous and tiring days.

The place of surgical treatment is not ignored but space does not allow the necessary critical consideration. In my opinion, the case has still to be made for most forms of surgical correction. I do not decry carefully controlled surgical experiments with adequate and prolonged follow-up, preferably by someone other than the operating surgeon. On the other hand, no surgical operation has yet fulfilled the criteria for general application. Surgical techniques will include (1) interruption of pain fibres for intractable angina and (2) various operations for the promotion of collateral blood flow. Thyroidectomy for the reduction of basal metabolism tends to be replaced by thiouracil and related drugs or by radio-active iodine.

ADDENDUM

Since preparing this paper for Congress I have personally visited most of the groups in the USA and Britain from which important contributions have been made, and have attended the Gordon Lipid Conference (July 1959). It is possible therefore to bring recent views and trends right up to date.

There is intense activity in many fields, most of it represented at the Lipid Conference. A whole session was devoted to the lipid components of *in vitro* coagulation mechanisms. The study of lipids and their metabolism will rapidly advance under the influence of the new technique of gas chromatography. A promising start has been made in the study of *in vivo* thrombosis in isolated vein segments.

There is further evidence for genetic variability in lipid metabolism, and particularly in the response of total cholesterol and other lipid fractions of the serum, and in the duration of the postprandial lipid tide, when groups of people are fed with different quantities and qualities of fat.

It is evident that total-serum-cholesterol levels in man can, when they are too high, be reduced effectively by a great variety of methods. These include diet, oestrogen therapy, large doses of nicotinic acid, hydralazine, and neomycin. There is still no evidence that effective reduction can be achieved by any small-dose fraction of lipids or vitamins at present commercially available in South Africa. Dr. G. E. Burch has referred to certain new therapeutic preparations for the reduction of serum cholesterol. They sound promising but are still under clinical trial in the USA.

However there is still no direct evidence that mortality and morbidity from ischaemic heart disease is favourably influenced by these manœuvres even though they reduce total serum cholesterol. Nevertheless there must be few who would not give their patients the benefit of the doubt and advise reduction of immoderately high serum-cholesterol levels (see main text for figures) in people at risk of ischaemic heart disease. The statistical association of these high levels with ischaemic heart disease is too close to be ignored when there are so many possible mechanisms of causal association.

The American Council on Foods and Nutrition[2] finds itself at present unable to give advice on how reduction of serum cholesterol should be achieved, but publishes 5 articles to illustrate current trends of thought. I have no doubt that sensible dietary principles should always be recommended to people at risk whether or not other methods of reducing serum cholesterol are added to the dietary regime. On the other hand I think some people are pressing dietary restriction too severely. Our regime has been published as a guide.[3] Jolliffe *et al.*[4] have demonstrated effective reduction of serum cholesterol by a similar type of diet, which they call 'prudent'.

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