Special Article

CORONARY HEART DISEASE

ITS MEDICAL MANAGEMENT AND TREATMENT IN 1965

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One purpose of this article is to give practical guidance to medical practitioners who have to give advice about management and treatment to patients who are at risk of coronary thrombosis or other complications of coronary atherosclerosis. If it is to achieve its object it must necessarily simplify a mass of complex and conflicting evidence in which knowledge is still rapidly advancing. Medical practitioners, both general and specialist, are repeatedly asked by their patients what advice can be given and what steps the patient himself can take to improve his prognosis if he is 'at risk'. Recommendations are therefore made, but they must be recognized as tentative and almost certainly subject to change as knowledge advances.

My simplification of conclusions from recent research may, doubtless, give offence to those who have pet theories and may well be regarded by people actively engaged in research in the field as 'misleading oversimplifications'. To these people I offer my apologies with the statement that this article is not intended for them; it is intended for the practising doctor who has to answer the questions of his patients.

For similar reasons my list of references is quite brief. It is selected from a very large bibliography maintained by the coronary research project in our department. The references cited are mostly quite recent and serve to illustrate, for those who care to look them up, a conclusion of mine which, as emphasized above, must be regarded as tentative in a controversial field.

At the East London Medical Congress in 1959[6] I went so far as to state, in discussion, that in view of the rapid accumulation of knowledge on preventable environmental factors, which contribute to the final occlusion of moderately atheromatous coronary arteries, it was not unreasonable to hope that the steadily rising curve of mortality and morbidity might be slowed or even reversed within the next ten years. I am now forced to the conclusion that this was too optimistic a prognosis, and it seems wise and timely to inform doctors who are not closely concerned with research in this field how far we have got and what they can reasonably recommend.

Definitions

These again must of necessity be tentative, but they are necessary to ensure that my readers are at one with me in their understanding of what it is that I am advising them to manage or treat. The terms in common usage, 'coronary heart disease' (CHD) and ischaemic heart disease (IHD), as adopted by the World Health Organization, may be regarded as synonymous. They include all the pathological and clinical manifestations and results of degenerative and other diseases of the coronary arteries which interfere with the luminal capacity of the coronary arteries to supply sufficient blood to the myocardium at any given moment. Although there are many pathological processes which so affect the coronary arteries, the major problems of the present and the last few decades are atheroma and atherosclerosis, and the following discussion will confine itself to the effects of these two related processes on the coronary arteries of human beings.

PATHOLOGY AND PATHOGENESIS

The nature and definition of what I have called 'atheroma and atherosclerosis' is itself a very controversial subject. Fortunately I can avoid its discussion by referring the reader to a very recent authoritative monograph by Mitchell and Schwartz.[25] The consideration of 'atheroma and atherosclerosis' of the coronary arteries, as distinct from the rest of the vasculature, introduces further controversy, since the long-term process of atherogenesis affects different parts of the vasculature to varying degrees in different individuals, classes, and races of mankind.

The effects of coronary atheroma are usually unrecognizable until it is well or even severely advanced, presumably because the coronary system has a very large reserve intended for vigorous physical exertion. By the time the arterial lumina are becoming seriously narrowed most people have restricted their physical exertion significantly, as is common in middle age. Moreover, like all parts of the vasculature, the coronary arteries develop collateral channels as the lumina become narrowed. It happens, therefore, very frequently that, at autopsy on people who have died of other causes, never having had any symptoms of IHD during life, the coronary vasculature is found to be extensively atherosclerotic. This state of affairs is probably responsible for the progressive increase in ectopic rhythms as age advances. It is possibly the explanation of many cases of atrial extrasystole in middle age, and very probably of the majority of cases of ventricular extrasystole and unexplained atrial fibrillation and flutter.

The encroachment on the coronary lumina can be detected presumptively by certain 'age' changes in the resting electrocardiogram and more certainly by certain changes of pattern in the ST-segment after a properly conducted effort-tolerance test.

The clinically recognizable effects include angina pectoris and myocardial infarction and various intermediate stages between these two extremes of myocardial ischaemia. Because of the dramatic frequency, serious mortality (15% sudden, 20 - 30% immediate),[32] and resultant morbidity of myocardial infarction in privileged westernized communities, coronary thrombosis must be given special attention. By 'coronary thrombosis' I mean sudden, massive occlusion of the lumen of a main coronary trunk or branch by blood clot. Such 'coronary thrombosis' usually occurs in the lumen of an artery already narrowed, roughened, and rendered inelastic by atheroma or atherosclerosis. One of the perplexing problems in this whole field can be put in proper perspective by asking, not the question why the thrombosis occurs without warning, but the more obvious question why it does not occur in large numbers of people of similar age and type with the same distribution and severity of coronary atherosclerosis. Morris[26] has indeed stated that whereas among the autopsy records of the London Hospital in the East End of London there has been a great increase in the last few decades in the frequency of coronary thrombosis with resultant myocardial infarction, there has been little increase in the severity and distribution of coronary atherosclerosis. This statement is based on a most careful study of one of the biggest and most accurately recorded long-term autopsy studies. It needs to be confirmed, but it is relevant to state that up to the present it has not been denied nor even seriously questioned. If it is correct, it must leave the inevitable conclusions that the 'epidemic' of

myocardial infarction of the last two or three decades is due to short-term and presumably modifiable factors which determine unexpected coagulation of blood in coronary arteries already narrowed, roughened, and rendered inelastic by atherosclerosis.

THE CORONARY-PRONE PERSON

For brevity these patients will be referred to as 'coronary-prone persons' (CPPs). Many such persons can be identified on the following criteria: (1) They may have a family history of IHD; (2) they may have had any of the symptoms or have any of the signs (including electrocardiographic) of IHD, e.g. angina pectoris, myocardial infarction; (3) they or members of their families may suffer from any of the diseases which, being statistically associated with IHD, appear to increase the risk of suffering from its effects, e.g. hypertension, diabetes mellitus, essential xanthomatosis, etc.; or (4) they may persistently show certain abnormal trends in certain fractions of their serum lipids. Of these the best established is a level of serum total cholesterol (STC) in or above the range 233 - 266 mg. per 100 ml. Others are referred to later.

Readers may be surprised that nothing has been said in the identification of CPPs on the question of physical habitus and temperamental qualities. There is no doubt that certain characters under these headings would be found in greater prevalence than in unselected males of the same age and sex.

I refer to mesoendomorphy in bodily habitus and to the 'driving' temperament so well described by Friedman *et al.*[17] The same is true of certain blood groups.[19] But in all these respects the overlap in distribution between CPPs and normal controls is so wide that the characteristics are of little value in the selection of the individual CPP. It must be frankly admitted, however, that not all CPPs can be recognized.

In the case of CPPs the major problem facing the medical practitioner is what to advise or how to treat prophylactically.

Acute Management and Treatment

Before tackling the difficult subject of long-term management and therapy let us deal with some acute, urgent and often unexpected manifestations of IHD.

The Management of Impending Myocardial Infarction

In a CPP any symptoms of distress on effort or excitement must be taken seriously, whether they consist of pain of anginal type, unaccustomed dyspepsia, tightness in the chest, dyspnoea or palpitation. The patient's ideas about the symptoms vary greatly. Sometimes those who are anxious about their hearts are crying 'wolf', but the doctor who too readily comes to this conclusion ignores the potential seriousness at peril of the patient's life and of his own reputation.

A great many patients minimize the symptoms and particularly pass them off as indigestion. Olin and Hackett[27] have recently examined the psychology of this type of person and the 'it couldn't happen to me' philosophy. I have even known a doctor go for a stiff walk on the mountain slopes to 'walk off my indigestion'. The result was disastrous!

Crescendo angina should always be suspected of being a possible forerunner to myocardial infarction. The degree of probability and urgency will depend upon many circumstances surrounding the onset of the crescendo angina. If there is any doubt about the matter, the patient should be transferred to a hospital where he is under close observation, if not under electrocardiographic monitoring. This is, in my opinion, one of the circumstances in which anticoagulant therapy is strongly indicated. Being an emergency, the therapy should be with heparin in the absence of contraindications, since anticoagulant control with oral preparations of the coumarin type takes upwards of 48 hours to establish.

The Immediate Resuscitation and Management of Myocardial Infarction

With the best will in the world and with all due care by doctors the majority of cases of myocardial infarction will occur suddenly and unexpectedly.

Until recently, estimates of prognosis and principles of management in myocardial infarction were based upon hospital statistics. These statistics ignored the very considerable proportion of patients who died outside hospital or were never admitted. More representative statistics have been published in the last few years. These indicate that 15% of patients who have a myocardial infarction die suddenly.[32] Many of these are never admitted to hospital. A study of all coronary deaths under the age of 50 in the city of Seattle[4] showed in men 63% deaths within one hour and 85% deaths within 24 hours; 41% of the latter had had no symptoms or signs of disease before the attack. Only 23% lived long enough to be medically attended. Many patients die unexpectedly after admission to hospital. There are good grounds for believing that many of the early and unexpected deaths are due to alterations in cardiac rhythm, particularly asystole and ventricular fibrillation, which are the result of temporary disturbances of rhythmicity and conductivity resulting from the acute ischaemia. Many of these when followed to autopsy are found to have only mild degrees of apparently recoverable infarction. These have been aptly called 'unnecessary deaths'. If the full facilities of an intensive care ward in a hospital had been available, they might have been saved and have gone on to many years of reasonable life. Continuous electrocardiographic monitoring of patients admitted to hospital shortly after myocardial infarction shows a high incidence of temporary disturbances of rhythm and conductivity. Most of these pass unnoticed and are not important. Others are responsible for unnecessary deaths. In view of the importance to the individual, the family and the community of these 'unnecessary deaths', it seems to me inevitable that modern hospitals must develop intensive care wards with continuous electrocardiographic monitoring to cover the first 24 - 72 hours of myocardial infarction.[29]

In emergency situations outside of hospital a doctor or someone trained in first-aid methods can save life in some cases of myocardial infarction. If the circumstances are such that a pulseless patient may have had a myocardial infarction during the last five minutes, one or more blows to the precordium followed by external cardiac massage are procedures which can do no harm. Attention should of course be given to the breathing and in certain circum-

stances it may be necessary to alternate cardiac massage and mouth-to-mouth pulmonary resuscitation.[5]

The detail of resuscitation and monitoring within the hospital precincts will not be dealt with here.[36,37]

Silent Infarction

It is becoming increasingly apparent that silent or undetected myocardial infarction occurs not infrequently, especially during anaesthesia and operation and in the postoperative phase. Arkins *et al.*[2] have stressed the seriousness of postoperative myocardial infarction. They had a 69% mortality among 55 cases. Routine ECGs should certainly be done on CPPs, and might well be extended to all people of appropriate age and sex who are to undergo operation. If the ECG is, in any way, abnormal, non-urgent operations should be postponed for up to 3 months in order to ensure, by clinical observation and serial ECGs, that an operation is not done in the dangerous postinfarctive period in cases of silent infarction.

Long-term Prophylaxis

In reviewing, at the East London Congress in 1959, the management of ischaemic (coronary) heart disease, I said:[6]

> '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.'

In reviewing the situation in 1965 one is faced with a welter of basic and applied research which has added greatly to our understanding in many fields of the medical sciences. Reviews prepared in the early 1960s[7,9] indicated that, apart from the uncontrollable factors of inheritance and sex, there were four groups of environmental factors which might possibly be controlled with resultant improvement in the morbidity and mortality statistics for IHD. These factors were listed as tension and strain, lack of exercise, cigarette smoking, and diet. Under the heading of diet, considerable emphasis was placed upon the adverse effect of increasing quantities of total fat and proportion of saturated to unsaturated fats in privileged, western-type diets with resultant increase in serum total cholesterol. It is not necessary in 1965 to withdraw any of these tentative conclusions, but the mechanisms through which they operate have proved to be very much more complex than was imagined at the time. I have just received from the US Department of Health a review of research grants supported by the National Heart Institute between 1958 and 1964 under the heading, *Diet, Lipid Metabolism, and Atherosclerosis*.[28] The review runs to 370 pages. The summary alone occupies 10 pages and gives the impression of fascinating advances in the medical sciences which have reached a stage of bewildering complexity. During 1964 I had the privilege of visiting many of the centres at which work is in active progress in Australasia, the United States and Great Britain. None of the men whom I met was any more prepared than I am to gather together the sorts of evidence reviewed in *Diet, Lipid Metabolism, and Atherosclerosis* and apply them with any confidence to the pressing problems of prophylaxis.

WHAT CAN BE DONE IN 1965?

In the face of so much uncertainty, complexity and conflicting evidence, what advice or treatment is a practitioner to give to coronary-prone persons when his advice is sought? Firstly, it is clear that if he is intellectually honest he cannot be dogmatic. Secondly, however, it is not helpful to the patient to tell him that the evidence is complex and conflicting. The patient usually wants definite advice on what he can do even if the advice is based only on reasonable probability. Under certain circumstances the doctor may have responsibility to withhold medicinal treatment which is highly thought of and recommended by other responsible colleagues.

Thirdly, it has always been clear to those who have been able to look objectively at a complex problem, that IHD is a disease of multiple causation with roots jointly in the inherited genes and in the controllable environment. It is clear that the atherosclerosis which is at the root of most IHD is a pathological process of slow evolution and doubtful reversibility. Any action to prevent or retard its development (atherogenesis) must start much earlier in life than the fourth or fifth decade when myocardial infarction is most commonly and severely present. However, the many fine studies in geographical pathology and geographical medicine since the publication by Strom and Jensen[31] present a *prima facie* case for the existence of some short-term process, or processes, which determine the occurrence of massive intraluminal thrombosis (thrombogenesis) in atherosclerotic coronary arteries (coronary thrombosis), and which may be capable of environmental control. In all probability the environmental factors which control even these short-term processes of blood coagulation are multiple and complex.

A. Inherited Factors

There can be no doubt at all that certain families are predisposed to myocardial infarction. Although family environmental factors, such as dietary habits, may contribute to familial incidence, there can be very little doubt that genetic factors operate. We are ignorant, however, of the mechanisms through which they operate. It is not unreasonable to conclude, from evidence which has been reviewed elsewhere,[7,9] that genetic operation (1) is associated with blood-group distribution, and (2) might operate through blood-coagulation factors or through enzymatic factors controlling ability to digest, assimilate and metabolize various components of the diet. The genetic predisposition cannot at present be controlled.

Genetically determined sex apparently operates strongly through the sex endocrine secretions, so that the male sex is more heavily predisposed to myocardial infarction during the reproductive era. Female morbidity and mortality from myocardial infarction catches up the curve for males some 10 - 15 years after the female menopause. Oophorectomy in the female raises STC. Conversely STC in the male can be reduced by the administration of oestrogens. There is nevertheless no evidence that the prognosis for the patient is thereby improved in respect of IHD. There is no present evidence to justify the discomfort of oestrogen therapy in this context.

B. **Environmental Factors**

Of the many factors characterizing the environment of privileged Western cultures, only a few are under serious suspicion.

In terms of what has been said above on 'atherogenesis' and '(massive) thrombogenesis' we should attempt to discuss suspicious environmental factors in relation to these long- and short-term processes quite separately. Unfortunately, it is sometimes difficult to do this, since the suggestive statistical associations relate to myocardial infarction as an end-result and do not differentiate between the long- and short-term processes which lead to that result. Moreover, when discussing pathogenetic mechanisms there is undoubtedly some overlap. The overlap is best illustrated through the effects of quantity and quality of dietary fat. There is very little doubt that the quantity and quality of dietary fat may be aetiologically related to the long-term processes of atherogenesis. But there is also a good deal of evidence to suggest that the quantity and quality of fat consumed at a single meal may, through the post-prandial lipid tide, affect the short-term processes which lead to massive intraluminal thrombosis in narrowed and roughened coronary arteries (massive thrombogenesis) so as to produce myocardial infarction after a rich and heavy dinner.

Stress and Strain

The lay public are much impressed by the importance of this factor in the causation of myocardial infarction. Their view is presumably reflected from the attitudes of medical practitioners. There must be few medical practitioners who have not at times been impressed by an apparent sequential relationship between periods of acute or chronic stress and strain and the occurrence of myocardial infarction. Stress and strain, however, vary so much that there are no effective standards for measuring their quality or intensity and, from the scientific point of view, no convincing evidence can be adduced. Much consideration has been given to mechanisms through which stress and strain might operate. There is some indirect evidence that they might operate through mechanisms which affect tendency to intravascular thrombosis.

Meyer Friedman and his group[17] have pioneered in this difficult field by studying intensively two groups of patients with contrasting behaviour patterns. Pattern A patients 'occupied a position demanding extreme competitive activity or deadline preoccupations'. Pattern B patients were free from these stresses. Patients with behaviour pattern A had a high incidence of clinical coronary heart disease. Moreover, they showed elevation of both pre- and post-prandial serum triglycerides and increased turbidity of post-prandial sera. The abnormalities in serum lipids could be corrected by administration of corticotrophin, suggesting that they are subject to environmental control. Friedman *et al.* comment on their observations in relation only to the long-term processes of atherogenesis. In my opinion they might be even more relevant to the short-term processes which lead to post-prandial coronary thrombosis.

Lack of Exercise

The widespread belief in the minds of doctors and the public that reasonable exercise, preferably distributed through the week rather than concentrated in the weekend, may have a prophylactic value is perfectly reasonable, but no scientific evidence can be adduced in its support. The matter has recently been the subject of a symposium.[33] The general conclusions are well summarized by Dill.[13] Perusal of this symposium leaves me in very little doubt that reasonable physical activity maintained into middle life is a valuable prophylactic. I have no hesitation in recommending 'reasonable physical exercise up to the limits of tolerance' for all CPPs who have not been in congestive cardiac failure. The same symposium gives powerful reasons for weight reduction among obese CPPs and, for that matter, for all obese persons.[1]

It is conceivable that exercise may affect the tendency to intravascular thrombosis directly or indirectly through its tension-relaxing or recreational effect on stress and strain. There is evidence in animals that exercise encourages the formation of coronary collaterals when a trunk is partially occluded.

Cigarette Smoking

The statistical relationship between heavy cigarette smoking and myocardial infarction is well established; there is strong presumptive evidence for the prophylactic value of cessation of smoking.[34] Functional narrowing of peripheral limb arteries has been convincingly demonstrated in relation to cigarette smoking, but transposition of this observation to coronary arteries has no supporting evidence yet. The widespread effects of smoking on physiological function through the hypothalamus allow of many speculative mechanisms.

Diet

This is a most difficult subject to deal with in a short section in 1965. We in South Africa have a special interest in the role of diet in that the comparison of our White and Bantu populations has given a not inconsiderable part of the evidence upon which current dietary fat manipulation has been based.[21] There are many differences between the diet of South African Whites and of Bantu which need to be reckoned with.[34] It may well be asked why, with so many dietary differences, the quality and quantity of fat have been singled out for special attention. The answer is quite clear. There is no doubt that the level of STC can be reduced by dietary fat manipulation of the type discussed in many communications.[8,15]

The STC remains the best, among serum lipid indicators, of the metabolic changes which can be altered by diet and which have statistical association with coronary-proneness. Its predictive value for myocardial infarction has been firmly established by the Framingham Project.[12] Unfortunately, there is still no satisfactory published evidence that lowering of the STC by long-term dietary modification improves the patient's ultimate prognosis. Jolliffe and his colleagues,[19] of the New York City Health Department, believe that their evidence is convincing, but its full import remains to be published. After some initial hesitation the American Heart Association lent the weight of its authority to the general thesis of the importance of dietary fat manipulation for CPPs. In 1963 the pilot stages of a long-term, nation-wide trial of these dietary principles were undertaken under the combined weighty authority of the National Institutes of Health and the Heart Association of

the USA.[3] I had the opportunity in 1964 to review, with some of the workers in this project, its principles and its application. It was evident that it would be some years before a definitive judgement could be passed. There is difference of opinion between the members of the team as to whether it is sufficient to alter the ratio of polyunsaturates to saturates (P/S ratio) or whether the fat/calorie ratio (F/C ratio) should also be reduced.

Diets which effectively reduce F/C ratio and P/S ratio are admittedly a nuisance and inconvenience to the patient and his household. The strongest arguments in favour of such diets for CPPs who have a level of STC higher than 233 mg. per 100 ml. are: (1) that they are effective in lowering the STC, (2) that they can easily be combined with calorie restriction, (3) that there is no evidence of any harmful effect, and (4) that they tend to eliminate the more rich and sophisticated foods which characterize the diets of wealthy and self-indulgent people. The principal arguments against the use of such diets are their inconvenience and the absence of any final evidence of their effectiveness.

During the last half decade a great deal of research has been undertaken on the significance of the serum triglyceride level and its relationship to carbohydrate metabolism. The review, *Diet, Lipid Metabolism, and Atherosclerosis* of the National Heart Institute[25] indicates the extent of activity in this field. The principal references, as they affect the problem of IHD, are to be found in a recent paper from this department by L. H. Krut and R. S. Barsky.[23] The subject has been more thoroughly reviewed by Krut in a publication which is not readily available in South Africa.[24] There is no doubt that these research developments are very significant for the future, but the extent of their applicability to dietary management today is still obscure. They do suggest that a considerable proportion of CPPs have metabolic characters suggesting latent diabetes.

Dietary Sucrose

The lay press in South Africa and Great Britain has recently given considerable publicity to the views of Yudkin on the dangers of excessive consumption of dietary sucrose.[35] He made the point that among the dietary changes which have occurred in westernized nations over the last half-century, none has been more dramatic than the increase *per capita* in consumption of sucrose. In 1957 he pointed out that the statistical correlation between IHD and increasing sucrose consumption was more significant than the statistical correlation between IHD and increasing fat consumption. Although he has himself published no experimental evidence which might explain a causal association, the work on serum triglycerides referred to above does give some quite interesting theoretical correlations. It certainly reinforces the importance of dietary sucrose restriction in CPPs who are either obese or diabetic; perhaps we should give more attention to the detection of latent diabetes in CPPs.

Other environmental factors in privileged westernized living can easily be linked statistically with the prevalence of myocardial infarction, but there is little or no evidence to support causality in the relationship. The use of telephones and motor cars have been jocularly put forward by sceptics who would nevertheless admit their conceivable relationship to tension and strain and lack of exercise respectively.

Control of Associated Diseases

A number of diseases are so markedly correlated with a tendency to premature myocardial infarction that it is entirely reasonable to proceed on the assumption that their effective amelioration might improve the prognosis of CPPs. The STC of patients with essential hypercholesterolaemic xanthomatosis can, up to a point, be reduced from its ordinary very high level by the use of fat-restricted diets and drugs which will be discussed later. The progression of hypertension to left-ventricular hypertrophy can be checked by hypotensive drugs. There is no doubt about the close association between diabetes mellitus and IHD. It is generally accepted that careful control of diabetes mellitus by diet, alone or in combination with insulin or oral hypoglycaemic drugs, is worth while in the hope of preventing or modifying the accelerated rate of arterial degeneration in patients with diabetes mellitus. Final proof of effective result is still lacking. It may be worth while to direct more attention to the discovery of latent diabetes and then to treat such people as both potential diabetics and potential CPPs. There is evidence of association between gout and degenerative arterial disease. Treatment, as in the case of diabetes mellitus, is worth while for its direct results, and one is entitled to hope that effective control may decelerate arterial degeneration. The extent of causal association between exogenous or constitutional obesity and the tendency to myocardial infarction is still unsettled. A recent article by Alexander[1] goes a long way to substantiate the prophylactic value of calorie restriction. Obesity is worth treating in its own right, and there can be no doubt whatsoever of the beneficial effect of reduction of obesity on patients whose myocardial efficiency has already been impaired by IHD.

DRUGS

Anticoagulants

In the light of what has been said about the likelihood of increased tendency to intravascular thrombosis playing an important, if not dominant, part in the production of myocardial infarction, the long-term use of anticoagulants obviously deserves serious consideration. Views on this subject are so conflicting,[11] and there is such a mass of evidence that it cannot be reviewed here. It is clear that myocardial infarction can occur in patients under control with anticoagulants. It has been claimed that those who infarct while on anticoagulants are not less well controlled than those who do not infarct.[18] Psychological dependence on anticoagulants becomes quite a problem and can lead to severe anxiety when the need for discontinuing temporarily, as for surgery, or permanently, is broached by the medical adviser.[22] It is my personal opinion that the balance of evidence is against any useful role for the long-term use of anticoagulants in CPPs. Much of the evidence for and against causality is vitiated by the fact that *in vitro* coagulation has been used in the experiments. There are many grounds for believing that the factors affecting intravenous and intra-arterial thrombosis may be different and may not be accurately reflected by changes in *in vitro* coagulability.

Cholesterol-lowering Drugs

One's attitude to the use of these drugs should be influenced by (1) the absence of convincing evidence that lowering the STC improves prognosis in CPPs, and (2) the fact that several of them have been shown, after a year or two of use, to have serious side-effects. At the moment Atromid-S is probably the safest and most effective. Its use is certainly justified, together with diet, in patients with essential hypercholesterolaemic xanthomatosis. In the ordinary CPP a high level of STC can be effectively reduced by the prescription of a diet which is known not to have any deleterious side-effects. Why then use a cholesterol-lowering drug which may prove to have deleterious effects?

PERSONAL RECOMMENDATIONS

On the basis of the above review my personal advice to coronary-prone persons is given individually along the following lines: (1) Explanation adjusted to the educational level and personality of the patient. (2) Reassurance in the sense that those who survive the first 24 hours and the bed-rest phase have reasonable grounds for expecting a good prognosis if they re-adjust their lives. (3) Recreation and relaxation of tensions are discussed in relation to the patient's way of life. (4) Physical relaxation and recreation are emphasized as the most effective method of reducing tension and strain, even during a busy life. (5) Daily exercise is recommended up to reasonable limits of tolerance. (6) Cigarette smoking is discussed as a dirty and childish habit which is admittedly important in relation to carcinoma of the lung and which might contribute something to the risk of a CPP.

Complicating and associated diseases, including exogenous and constitutional obesity, are treated *secundum artem* and through healthy dietary customs.

A simple and healthy diet is recommended on the principle of 'everything in reasonable moderation'. Strict adjustment of dietary F/C and P/S ratios is recommended mainly for younger patients with a definitely raised level of STC. Strict application of this type of diet is recommended for patients with essential hypercholesterolaemic xanthomatosis and, after the maximum fall has been achieved, on dietary management, Atromid-S is added if necessary. For other CPPs Atromid-S (including other cholesterol-lowering drugs) is not recommended. In my opinion reduction of refined carbohydrates such as sucrose is part of a healthy natural diet and this aspect is emphasized only to patients with diabetes mellitus and obesity.

After carefully weighing the evidence over a number of years I have abandoned the long-term use of anticoagulants for the ordinary CPP. Anticoagulants are administered to patients who are confined to bed after myocardial infarction and discontinued when they are up and about. The main objective is to prevent phlebothrombosis of the legs.

Finally, in spite of many uncertainties I think it should still be said that the strong statistical correlation between increasing morbidity and mortality from myocardial infarction and what is called privileged Western living is highly significant and ultimately hopeful.

Other Drugs

Space does not allow of the consideration of other drugs which have a proved place in the management of various aspects of IHD. Many of them are covered in standard texts and there have been no recent significant developments.

Two recent developments might briefly be referred to because of their future possibilities; both are at present under critical review. I refer to long-awaited progress in the development of a long-acting derivative of the nitrites and nitrates,[30] and to the development of the beta-adrenergic blockade drugs in the control of certain varieties of arrythmia and possibly of recurrent angina pectoris.[20]

This paper represents an expansion of one part of a paper read at the Medical Congress in Port Elizabeth in a Symposium on Atherosclerosis and its Effects. The views expressed arise out of the programme of the Clinical Nutrition Unit supported in the University of Cape Town and Groote Schuur Hospital by the Council for Scientific and Industrial Research and supported also by USPHS Grant HE 03316-08.

POSTSCRIPT

Platelet Adhesiveness; Fibrinolysis

Discussion of the intensive recent activity in these fields was deliberately avoided because it is still at the research stage. Personally I am inclined to believe that a solution to the problem of coronary thrombosis might well be found in developments along some such lines. There have, however, been too many false starts from premature application of recent research data and this article was intended to be utilitarian. For those who are interested in these recent trends two articles will serve:

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