Long-Term Management of Patients with Coronary Artery Disease

By Laurence B. Ellis, M.D., Herrman L. Blumgart, M.D., Dwight E. Harken, M.D., Herbert S. Sise, M.D., and Fredrick J. Stare, M.D.

Dr. Laurence B. Ellis: Our conference today is on the long-term management of patients with chronic coronary artery disease, with particular emphasis on the more radical methods of therapy. This is intended to be a practical discussion for practicing physicians and our hope is to put into perspective the special methods of treatment that have been advocated, either directly or by implication, as the result of some of the more recent investigations. Anyone who reads medical journals or even any of the printed matter offered by the pharmaceutical houses is bombarded by various special methods of treating coronary disease. One can but wonder whether he may not be neglecting some useful therapeutic device that might benefit the future course of his patients. With the aid of experts in several special fields I shall attempt to separate some of the wheat from the chaff in this important and perplexing problem.

I need not remind you that coronary atherosclerosis occurs to a greater or lesser extent almost universally in human beings and its fatal consequences are so numerous that the disease is now the leading cause of death in the United States; nor need I remind you that it occurs much earlier and in a more severe form in men than in women. There appears to be undoubtedly a constitutional trait predisposing to premature coronary atherosclerosis in certain family stocks. To what extent the physical and emotional stresses and strains of life hasten the development of coronary atherosclerosis has not yet been proved. Most cardiologists however are of the opinion that coronary insufficiency as manifested either by pain or by myocardial failure may be hastened by such stresses.

In the evaluation of any studies concerned with coronary artery disease, one must remember that it is possible to make a diagnosis of this disease in life only after some breakdown in the coronary circulation has occurred, such as a myocardial infarction, the development of angina pectoris, or congestive failure. This makes it almost impossible to carry out controlled studies of the type that one would like to have concerning the value of various therapeutic or diagnostic procedures. Physicians should bear this in mind when they peruse the many articles that are written on this subject and they should also remember that coronary artery disease gives rise to no specific physical signs. The physical signs that do develop in patients with this disease reflect changes in the state of the myocardium. This is true also of the electrocardiogram which, of course, in no way is a direct measure of the state of the coronary circulation, but only an indirect index, reflecting changes in those potentials produced by excitation of the myocardium itself. The same reservations must be made in regard to the value of the ballistocardiogram, only more so. It can-
not be emphasized too much that the diagnosis of angina pectoris is chiefly made from an evaluation of a carefully taken history as given by the patient, and that physical signs and laboratory tests are only of ancillary importance in helping to support the diagnosis of this subjective symptom indicating coronary insufficiency.

In general, the first principle in the treatment of coronary disease is to adjust the energy budget of the individual so that his heart, with a limited performance capacity, will not be called upon to meet greater demands than it is capable of supplying. Every patient should be individualized because his cardiac reserve is different. The patient’s schedule of living should be so arranged that he is not called upon to do more than he can carry out, and a reasonable margin of safety should be provided. Beyond this, however, it is probably not advisable to restrict the activity of patients, and since many of them have virtually a normal cardiac reserve, there is no reason why they should not lead a normal life provided they do not go in for physical or mental excesses. The avoidance of unusually severe activity, of course, should be prescribed but regular exercise within the capacity of the patient is advisable and many patients with coronary disease who have always carried on an active physical life can still remain quite active after convalescence from a noninimacitating coronary accident. Relatively few patients after a myocardial infarction have to leave their previous occupations. The physician should always keep in front of him the goal of returning the patient to that type of life which is most economically productive and satisfactory to him, so avoiding insofar as possible the psychologic hazard of seriously disrupting a patient’s life by forcing him to give up work or to change to a less satisfactory occupation. Psychologic damage may well be as bad as physical strain. Detailed attention to the proper regulation of the patient’s life and habits with the aim of giving him a maximum of satisfaction and happiness should be the prime objective of the physician. Since this often involves time-consuming effort it is often neglected, whereas many doctors tend to overemphasize drug treatment in the attempt to control coronary artery disease.

A cardinal objective in the management of coronary artery disease is to remove or reduce the various burdens on the circulation. Although, as said, most people can continue in or return to their previous occupations, nevertheless, they should live at a more gentle pace than that to which they were formerly accustomed. With detailed attention to the regulation of the patient’s life; that is, by cutting out the unnecessary and inefficiently performed details of living, and by increasing rest periods during the day, on weekends, and in vacations, his budget of energy can be very markedly conserved. Naturally if he develops symptoms of severe angina or of cardiac insufficiency, his activity will have to be restricted further.

The second burden that should be removed is excess weight. The well-treated cardiac patient is one who is underweight. Other extrinsic burdens on the circulation should be searched for and removed whenever possible such as anemia, minor infections, etc.

There is no clear evidence that there is anything that definitely controls the progress of atherosclerosis in human beings. However, patients with coronary disease cannot wait until some future time when proof of the value of certain therapeutic measures is forthcoming. A proper therapeutic approach at the present time is to institute those therapeutic measures from which there seems a reasonable likelihood that benefit will result but to avoid highly experimental, expensive, or drastic measures that may be seriously disrupting to the person’s mode of living and happiness.

We naturally turn first to vasodilating drugs in these patients, particularly those suffering from angina pectoris. There is no question that nitroglycerin is the most effective for the acute relief of individual attacks. There is no agreement as to whether long-acting vasodilators are of specific value in
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diminishing the number of attacks of angina pectoris, and certainly there is no evidence that the routine use of such drugs in patients without symptoms is of any value in diminishing the possibility of future coronary accidents. Therefore such drugs should be given only for the relief of symptoms and not as routine measures.

Angina pectoris is notably affected by psychogenic influences. Many drugs as well as other methods of therapy if administered enthusiastically and with conviction will ameliorate the number of attacks in some patients, at least for a time. This undoubtfully explains many of the favorable reports of various methods of therapy and at the same time is a justification for a psychotherapeutic approach to the patients, including the judicious use of relaxant drugs.

What further methods are there by which we might control the advance of atherosclerosis in human beings? First of course we think of control of the diet. I shall ask Dr. Fredrick Stare if he will discuss the practical dietary management of these patients with chronic coronary disease in the light of our present knowledge.

Dr. Stare, there has been recent interest in the administration of sitosterol to patients in the endeavor to block the absorption of cholesterol as well as of other so-called lipotropic substances. Will you also tell us whether there is evidence that sitosterol or the various lipotropic substances are of value and whether we should institute such treatment in our patients?

DR. FREDRICK J. STARE: May I first dispose of the so-called lipotropes and of the various sitosterol preparations. Choline and methione are the common lipotropes. Under certain experimental and chemical conditions they may be limiting factors in fat transport and metabolism, but these conditions have not so far included atherosclerosis or coronary artery disease. I know of no evidence that they have a useful role to play in the treatment or prevention of atherosclerosis or any of its complications.

Sitosterols if taken in sufficient quantity, and each time food is consumed, will impair the absorption and reabsorption of cholesterol and hence lower the level of serum cholesterol. But the large quantities that must be taken to induce a response, together with the intolerance of many patients to the material—to say nothing of its cost—limit its usefulness appreciably. I do not think the administration of sitosterol preparations is of practical importance in decreasing the level of cholesterol.

Recent nutritional researches suggest a number of specific dietary approaches that may be helpful in the management of patients with coronary artery disease.

First, attention should be given to weight reduction, particularly if the patient is overweight. But even if he is of desirable weight, a loss of as little as 3 to 5 pounds is frequently accompanied by a decrease in serum cholesterol of the order of 10 to 15 per cent. This decrease in cholesterol may not be maintained when caloric equilibrium is re-established, but if not, other dietary therapy may be tried.

Weight reduction is not a complicated matter if its importance is explained and sufficient motivation stirred up and maintained. No single food need be eliminated from the diet. It simply is a matter of eating less. Cutting down, not out—smaller portions, no seconds, common sense—and checking up on oneself by a weekly stand on the bathroom scale. As has been said earlier, “the well-treated patient is one that is underweight.”

Second, in addition to advising weight loss, the physician might propose that the patient try a diet in which the total calories derived from fat are reduced to 25 to 30 per cent. Such a diet would entail a reduction of most of the visible saturated fats. This can be accomplished by trimming fat from meat, eating more lean meats and smaller servings, more fish, and consuming less butter, margarine, whole milk, cheese (except cottage), bacon, and egg yolks.

Another dietary regimen that can be tried is one that provides our accustomed 40 to 45 per cent of calories from fat but one in which the fats that are good sources of es-
essential fatty acids are emphasized, so that they might supply about 25 per cent of the fat calories, or 10 per cent of the total calories. In our experience it has been difficult to increase the essential fatty acids any more than this without going to formula diets.

If the patient is acutely sick from one of the complications of atherosclerosis, therapy might include a very low-fat diet—one with 20 per cent or less of the calories coming from fat. Also, for the sick patient a formula-type diet might be tried containing a suitable vegetable oil as the sole source of fat.

The avoidance of excessive fat, particularly in the evening meal, may be desirable from the viewpoint of decreasing the chances of intravascular clotting. It has been established that blood is more likely to clot 2 to 7 hours following a high-fat intake. The explanation for this is as yet unknown but is not thought to be associated with the lipemia that ensues. I think it would be good judgment to advise the coronary patient under treatment, and the postcoronary individual who has completely recovered, to get the bulk of his fat and protein calories at breakfast and midday and have a light supper such as soup, cereal, and a fruit salad.

In the light of all of these developments, the physician has a real opportunity to practice good preventive medicine with regard to our leading cause of death. First, it is his responsibility to reassure the public and to prevent mass hysteria for drastic changes in our diets; and second, to guide his patients, depending on their individual status, along dietary patterns that consider advances in research.

DR. ELLIS: Dr. Stare, will you say something about the practical value of the determination of serum cholesterol or other blood tests?

DR. STARE: The determination of the serum total cholesterol is the most important single blood test I am aware of in relation to this problem. Determination of various serum lipoprotein fractions is of course a part of various research studies but does not have, so far as we know, any advantage in assisting with diagnosis or prognosis. For adult males I think we can say that a serum total cholesterol much above 225 to 235 mg. per cent is getting a little higher than we should like to see it—something below 210 to 215 is preferable. There is no question that coronary artery disease is more prevalent in individuals with an elevated serum total cholesterol. This is particularly true in males 50 years or younger.

DR. ELLIS: Recently there has developed interest in the long-term use of anticoagulants in patients suffering from coronary artery disease. This is obviously a very important problem because every doctor will want to know whether he should make the extra effort involved in instituting this difficult and expensive method of treatment that is not without some hazard. I shall ask Dr. Herbert Sise, who has made a particular study of anticoagulants, to give his opinion of the evidence concerning their routine use in patients with chronic coronary disease.

DR. HERBERT S. SISE: Long-term use of anticoagulants is still in the experimental stage. The early results are sufficiently promising to consider that this method of treatment may have considerable usefulness in selected individuals. As you have pointed out earlier, the evaluation of the effectiveness of any kind of treatment of this disease is most difficult. It is not possible to rely on symptoms alone. Consequently, to date the effects of long-term anticoagulants have been assessed by the mortality rates in treated groups versus untreated groups. This method requires a large series of patients, a strict control group, and a sufficient length of time for the mortality rates in either groups to be significantly great. To date, several studies have been reported. The mortality rates in the treated groups have varied from 7 per cent to 12 per cent and in the untreated groups from 28 per cent to 33 per cent, an improvement that is quite impressive and certainly a better result than in the short-term treatment of the acute phase of a myocardial infarction. These are gross mortality figures, however, and the control groups are
for the most part not strictly comparable to the treated ones. The results have been sufficiently uniform, however, to stimulate more extensive and better controlled studies in this country and elsewhere. I am led to believe that these studies, so far, tend to confirm the earlier and less well controlled reports. The long-term use of anticoagulants consequently offers a very encouraging avenue of treatment. It is burdensome and a procedure not without danger, but is not extraordinarily expensive and the cost probably could be made quite reasonable if large groups were followed. At the present time the routine use of anticoagulants is not justified. When employed it should be only with full knowledge of the effects and properties of the drugs.

Dr. Ellis: By what tests should these patients be followed?

Dr. Sise: Dr. Ellis has asked me a loaded question because he knows I have been interested in which blood clotting factors are important in the evolution of hemorrhage or of thrombosis during treatment with anticoagulants. Originally in our group of patients on long-term anticoagulant we were puzzled, as others have been, by the occasional individual who will experience hemorrhage at a prothrombin time that is within the therapeutic range or even below it. We were subsequently able to show that fluctuations in the level of the specific clotting factor called prothrombin could take place without a change in the prothrombin time. We now measure both the specific prothrombin value by Owren's 1 stage method as well as the ordinary prothrombin time by Quick's method. By keeping the prothrombin value between prescribed levels the incidence of hemorrhage in our group of treated patients has dropped from a rather high level of nearly 30 per cent down to the vicinity of 5 per cent without any increase in the incidence of thrombosis during treatment.

If measurement of the specific prothrombin value is not available, the 1-stage Quick procedure as performed widely throughout the country gives a sufficiently good guide to estimate correctly the dose in 80 per cent of cases, but bleeding and ineffective treatment in some will be experienced.

Dr. Ellis: There are 2 other types of radical therapy in current use for patients with severe angina pectoris. We are in general agreement that such treatment should be reserved for patients in whom the pain cannot be sufficiently controlled by the methods described above to permit them to live an economically satisfactory life, and even more for the patient who is having angina decubitus to such an extent that his very resting existence is miserable and whose condition is undoubtedly worsened by the continued anxiety of the anticipation of recurring pain and the fatigue resulting from lack of rest. Dr. Herrman Blumgart has made a particular study of the effect of reduction of thyroid activity in the treatment of angina pectoris and I shall ask him to tell us what his present feeling is in regard to the application of this therapy and to what type of patients it should be given; what results may be expected; and what the dangers and difficulties are, if any.

Dr. Herrman L. Blumgart: A decade of experience in the use of radiiodine in the treatment of intractable angina pectoris is now available. I shall confine my remarks today to its employment in the treatment of such patients and shall not discuss patients with intractable congestive failure. The purpose of this treatment is to reduce the circulatory requirements so that they may be within the limits of the cardiac reserve. More than 100 patients have been treated in our clinic and the evaluation of results in over 700 patients with angina pectoris is available from 49 other clinics.

The following conclusions may be stated. Hypothyroidism can be induced regularly in patients with intractable angina pectoris without risk or toxic effects. All such patients receive small doses of 6 to 30 mg. of thyroid daily to maintain them at the lowest level of metabolism consistent with comfort. Undue elevation of serum cholesterol is reduced thereby and in some patients may be only moderately increased. In most patients
with rheumatic heart disease who have died after 1 to 11 years in the hypometabolic state, little or no coronary atherosclerosis has been noted; in some, there has been no more than seen in patients not treated with \(^{131}\)I.

Approximately 3 quarters of all patients with intractable severe angina pectoris have shown worthwhile improvement; in one half of this group, the improvement has been great and many have been restored to an active gainful life. In the other half the improvement while not as marked has been considerable.

Patients should be selected who have not responded to the usual medical measures for at least 6 months, whose clinical course is not markedly progressive and who will be reasonably cooperative. Of all patients who have angina pectoris, this group comprises less than 5 per cent of the total.

Six weeks to 6 months are required to produce hypometabolism. Consequently this method of therapy should not be invoked in terminal cases.

If radioiodine is not available, the thiourea derivatives may be used. They do not produce hypothyroidism with regularity and high dosage may be necessary. Moreover, drug reactions are not uncommon.

We believe that radioiodine therapy is the treatment of choice in these patients, restoring these incapacitated patients to comfortable and worthwhile existence without the inevitable risks of surgery.

Dr. Ellis: An alternative method of treatment with patients with severe angina pectoris has been some type of surgery, on the heart itself or the nerve supply to it. Operations designed to interrupt nerve pathways have been carried out for a number of years. I will ask Dr. Dwight Harken first to give his opinion as to the value of such operations today.

Dr. Dwight E. Harken: Many operations have been designed to interrupt the nerve pathways to relieve the pain of angina pectoris. We abandoned this type of therapy in 1952. On the whole, pain was alleviated and the fear of angina, itself capable of precipitating attacks, was abolished. Rarely, excruciating pain from trauma to the brachial plexus occurred.

Denervation has been largely abandoned because equally safe operations have been devised, which are just as effective in pain relief, and, in addition, provide at least a theoretical opportunity for increase in the blood supply to the myocardium.

Dr. Ellis: For a number of years now there have been proposed various operations that are designed to improve the vascular supply to the heart. Perhaps Dr. Harken will discuss briefly what some of these operations are and what they are designed to do and the particular type of operation that he himself favors.

Dr. Harken: Dr. Ellis, many surgical technics have been worked out in the animal laboratory that protect against coronary occlusion. Such procedures have relieved angina pectoris in many patients. The question is which one is most likely to bring a new blood supply to the heart of the human patient with coronary disease and which can be performed with the greatest safety to the patient.

A number of operations have been devised that consist of introducing some type of powder into the pericardium to produce adhesions coupled with certain other accessory procedures. The first of these was devised by Beck. In addition there have been operations in which ligation of the coronary vein and perilcoronal neurctomy have been performed, Vineberg’s procedure of implanting the left mammary artery into the myocardium, and more recently Beck’s operation in which a shunt was made between the aorta and coronary sinus in an attempt to perfuse the coronary bed in a reversed direction.

So, the list could go on with mention of any number of control experiments in which the anterior descending coronary artery was ligated to find that approximately 70 or 75 per cent of animals succumb. Conversely, after any of these and other "protective
maneuvers” the mortality after anterior descending coronary artery ligation fell to 25 per cent. It is rather interesting that these operations have uniformly protected. Such experience has thus been transferred to the human being. Again, with surprising regularity the human subjects have been relieved of pain almost immediately, long before new vessels could have grown in. Some other factor represents a common denominator in the relief and protective effect of these operations. This common denominator may well be the opening of intercoronary communications. This is important and probably related to the considerable relief of pain in people with angina. Whatever the common denominator, the fact remains that relief of pain in patients with angina has been possible and protection of animals has been uniform. The only difficulty has been that these various procedures have carried a substantial mortality rate and have not therefore been popular.

Moreover, Burchell has shown that none of these procedures designed to promote “a vascular blood supply to the myocardium” produces significant arterialization in terms of vessels that will take the Schlesinger mass. The epicardium remains a barrier.

With this basic knowledge and philosophy, more than 10 years ago we addressed ourselves to the problem of taking off the epicardium. We tried to remove the epicardium surgically and with various chemicals. After a host of experiments we finally found that the least traumatic, paradoxically enough, was 95 per cent phenol to slough off the epicardium. After de-epicardialization with phenol, tare was instilled and the lung brought to the myocardium. Blood vessels that would take the Schlesinger mass were subsequently found to run from the adhesions into the myocardium.

We thought that this operation could be performed so quickly that there would be little opportunity for tachycardia and drop in blood pressure, and therefore little opportunity for further coronary occlusion. I think this is extremely important in these patients, for a fair number of people with angina decubitus who do not respond to medical treatment are going to die before, during, or after surgery. At any rate, this simple operation of phenol de-epicardialization, poudrage, and pneumonopexy can be performed in 12 to 20 minutes. It goes quickly and the patients are rather consistently relieved of pain. Whether they have a new blood supply, as suggested in animals, I cannot say but it would appear that patients so operated upon may be exceeding their anticipated life span. At least they are living longer than the denervated patients did years ago, and the patients have been selected on the same basis.

In short, we offer the patient an operation that may increase his blood supply and will usually relieve his pain. Carry in mind a low surgical risk for this operation. Thirty odd patients have had this operation, with 3 surgical deaths. Whenever the medical problem is great enough to assume this risk to relieve pain, the basis for recommending surgery is firm. You have an extra dividend in the “hope that you may increase the blood supply.”

Dr. Ellis: Dr. Harken, we have been hearing about ligation of internal mammary arteries for the possible relief of pain. What do you think of this?

Dr. Harken: Dr. Ellis, I was afraid you would ask that. I cannot give you a very good answer. Whenever an operation is advanced for the treatment of angina, one must start out with the assumption that the patients are relieved if the authors say so. The anatomist Von Hollerin suggested that occlusion of the internal mammary arteries below the pericardiophrenic branches might increase the volume of blood flow through the pericardiophrenic vessels and thence to the heart. Fieschi of Italy and his colleagues interrupted the mammary arteries bilaterally in the second interspaces. We have been conducting experiments that we hope will show us how such a mechanism may operate.
Also, because of the remarkable simplicity of the operation, we have done it in 8 patients. In all the relief of pain was spectacular. The period of observation has been too short for us to make further comment.*

In leaving this aspect of this subject, we really fade out on a feeble chord because we know little about the mechanism that may be back of the relief of pain by interruption of the mammary arteries, if indeed it exists on a permanent basis at all. It could be that there are sympathetic fibers traveling over the mammary arteries that are interrupted, and it might be that it makes a difference whether the veins are interrupted as well. Many surgeons are carrying out this procedure under general anesthesia. We view with some question any operation that is

*Thirty-five patients have now had internal mammary artery ligation. More than a third have enjoyed complete relief and there has been worthwhile pullation in almost three fourths of the group. The remainder have been total failures or have never had full return of symptoms. This seems a simple but valuable therapeutic adjunct. The associated denervation probably accounts for the relief of pain, associated with a general anesthetic because these patients are apt to have relief of pain on the nonspecific "common denominator basis" mentioned previously. Our operations have been conducted under local anesthesia. It is a safe, almost office procedure. If you have angina yourself and press firmly on your precordium, you will find that some relief of pain is produced thereby. It is entirely possible that this transverse incision is something like the blocking of reference areas of referred pain. The mechanism is not clear, the facts are not well established, but the present experience is indeed exciting.

DR. ELLIS: We have presented to you in brief form a schema for the long-term management of coronary artery disease. We have had the opinions of several experts as to the current status of certain of the so-called radical methods of therapy. We have not attempted to assess the relative value of one such treatment against another. Most methods must still be considered experimental, and their ultimate value will be established in the course of time by further studies.


In a previous study the authors demonstrated that complete, or almost complete, necrosis of the posterior papillary muscles could be produced in dogs by high ligation of the left circumflex coronary artery and that comparable samples of this region are easily obtainable for both chemical and histopathologic study. Chemical analyses of experimentally produced infarcts showed a 10 per cent loss of potassium in the first 60 to 90 minutes, and a more rapid disappearance during the subsequent 12 hours, when the level had fallen nearly to that contained in extracellular fluid. Histochemical studies using a covalent nitrite method of precipitation confirmed these results by demonstrating little or no potassium in the fibers at the end of 12 hours. The data suggest that the potassium ion leaves the irreversibly injured fibers at a slow rate during the first 2 hours after injury. Whether this is due to failure of energy-producing mechanisms involved in maintaining the normally high intracellular gradient of potassium or to delayed release of potassium containing proteins is not known.

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Circulation. 1958;17:945-952
doi: 10.1161/01.CIR.17.5.945

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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