# NEWER THERAPEUTIC TOOLS IN CARDIOVASCULAR DISEASE

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THE most important advances in the treatment of cardiovascular disease in the last several years have been the use of the low-sodium diet in congestive heart failure, improvements in the management of acute myocardial infarction and its complications, the development of effective prophylactic measures for rheumatic fever, the use of antibiotics in the treatment and prevention of bacterial endocarditis, the surgical correction or alleviation of certain congenital cardiovascular anomalies and acquired valvular lesions, and the development of technics for aorta-iliac and segmental arterial grafting. In addition, significant progress has been made in the medical management of essential hypertension, and a number of drugs of secondary importance have been introduced for use in other cardiovascular problems. As a result, the over-all prognosis of cardiovascular disease has been greatly improved, and many patients now remain comfortable and self-supporting for considerably longer periods than heretofore.

## Congestive Heart Failure

Congestive heart failure, the most common cause of death in patients who have organic heart disease, can be treated more effectively today than ever before and can be prevented from recurring for longer lengths of time. The principal factor responsible for this improvement has been the addition of the low-sodium diet to the older and well-established measures of drug therapy. Formerly, it was customary to strictly limit the fluid intake of patients suffering from cardiac decompensation and pay no attention to the amount of salt in the food. This was changed entirely about 15 years ago as a result of the demonstration that sodium retention on a renal basis is a cardinal feature of congestive failure and the most important factor responsible for water retention and the development of edema. There is uniform agreement today that the diet of patients with myocardial failure should not contain more than 500 mg. of sodium per 24 hours. Restriction of fluids is unnecessary and may even be harmful. The most satisfactory results are obtained when the patient takes between two and three liters of water daily. In persons who respond well to treatment and maintain a satisfactory state as they increase their activities, the limitation on sodium often can be lightened. Only occasionally, however, can the daily allowance be increased beyond 2000 mg.

Digitalis and the mercurial diuretics continue to be the most valuable drugs

in the treatment of congestive failure. Every patient suffering from failure should be completely digitalized, and with few exceptions the digitalized state should then be maintained permanently. Pills, tablets or capsules of standardized digitalis leaf are the preparations of choice. The purified glycosides have no special advantage over whole digitalis leaf either in clinical effectiveness or in simplicity of dosage. The best course for the physician to follow is to become thoroughly familiar with the action of one or two preparations and to confine himself to the use of those. For intravenous administration in cardiac emergencies or in the treatment of paroxysms of supra-ventricular tachycardia, Cedilanid is a safe and effective preparation. It usually is given in doses of 0.8 mg. (4 cc.) initially, followed in two to six hours by a second injection of 0.4 mg. to 0.8 mg., if necessary.

Although many persons who have cardiac decompensation will recover satisfactorily when treated only by rest, digitalis, and a low-sodium diet, the additional use of diuretic drugs hastens improvement and more promptly restores the patient to a state of comfort. Their administration, therefore, is indicated in every case. The most satisfactory preparations for routine use are the organic mercurial compounds given by intramuscular injection. Similar preparations for oral administration are available but are not as effective as those given intramuscularly. They are helpful at times, however, in prolonging the intervals between intramuscular injections in patients with chronic failure. More recently two non-mercurial oral diuretics, Diamox and Mictine, have been introduced. These are not so consistently helpful as the intramuscular mercurial preparations but are useful substitutes in persons who are unable to tolerate the latter. As with ammonium chloride, the administration of either Diamox or Mictine may reduce the need for further injections of mercurial diuretics after congestive failure has once been controlled. In addition, either preparation may at times restore the effectiveness of the mercurial drugs after the latter have ceased to cause diuresis. Diamox and Mictine owe their diuretic action to depression of sodium reabsorption by the renal tubules, Diamox by inhibition of carbonic anhydrase activity and Mictine by some as yet unexplained mechanism.

One other therapeutic aid in congestive heart failure should be mentioned, namely, the position of the patient's bed. In persons with cardiac decompensation, the recumbent position, through the effect of gravity, brings about a shift of edema fluid from the lower extremities to the upper portions of the body. This often results in prompt diminution in the edema of the lower extremities, but edema may simultaneously appear or increase over the back, and the evidence of pulmonary congestion may become more marked. Hydrothorax may develop for the first time, and the patient's condition may deteriorate rapidly. These undesirable effects of shifting interstitial fluid can be avoided by raising the head end of the bed on blocks 6 to 8 inches high. Fowler's position does not accomplish the same end.

## Coronary Heart Disease

The two most important clinical manifestations of coronary heart disease are angina pectoris and acute myocardial infarction. Little progress has been made in treatment of angina pectoris. None of the surgical measures thus far designed to augment coronary blood flow have been proved to be of value. For patients who become unable to perform activities of any kind without experiencing pain, the induction of hypothyroidism by means of radioactive iodine has become the treatment of choice. Induced hypothyroidism does not, of course, alleviate the underlying coronary atherosclerosis, but it does result in a reduction in the severity and frequency of the anginal seizures in approximately 75 per cent of properly selected cases.[1] It has not been established that the patient's life is prolonged. In less severe angina pectoris, the most important single measure in treatment still consists of a detailed explanation to the patient of the cause and mechanism of his symptoms with particular emphasis on the importance of doing everything possible to avoid the attacks. Full instruction should be given regarding the various factors that often exert an important effect on the ease with which the seizures occur. These factors and the use of drugs in angina have been discussed elsewhere.[2]

Several advances have been made within recent years in the treatment of acute myocardial infarction and its complications. One of the most important of these has been the demonstration of the beneficial effect of vasoconstrictor agents in management of the shocklike state that so often occurs at or soon after the onset of the attack. There is now general agreement that a preparation of this type should be administered whenever shock develops or the arterial blood pressure falls to approximately 80 mm. of mercury. The drug most widely used is norepinephrine (Levophed) diluted in 1000 cc. of 5 per cent glucose in distilled water and administered by continuous slow intravenous drip in amounts sufficient to maintain a systolic pressure of 100 mm. of mercury or somewhat higher. Cases of mild shock usually respond promptly, and occasionally even severe shock is corrected. When vasoconstrictor preparations fail to help, intravenous administration of 250 to 500 cc. of plasma or whole blood, or the intra-arterial transfusion of whole blood may be beneficial.

Although acute left ventricular failure is a well-recognized complication of the early period of acute infarction, it has been realized only of late that milder degrees of failure are much more common than was formerly supposed. If not detected and treated, the condition may have an important effect on the mortality rate. Because of this, careful auscultation of the lung bases should be carried out twice a day during the first few days of the illness, and therapy with digitalis, diuretic drugs, and a low-sodium diet should be instituted on the first appearance of râles. In the past, far too much emphasis has been placed on theoretical objections to the use of digitalis in acute myocardial infarction. These objections have not been corroborated by clinical experience, and left ventricular failure of all degrees after infarction is now regarded as an indication for administration of the drug.

The data accumulated by the Committee on Anticoagulants of the American Heart Association[3] demonstrate that anticoagulant therapy results in an important reduction in the frequency of thromboembolic complications and in the mortality rate of acute myocardial infarction. The Committee therefore recommends the use of anticoagulants in all cases except when their employment is contraindicated by the presence of hepatic or renal insufficiency or a blood dyscrasia with hemorrhagic tendencies, or when facilities are not available for making reliable measurements of the prothrombin time of the blood. These recommendations probably are being followed today in the majority of medical centers. During the past three years, however, doubt has been expressed with increasing force about the need for anticoagulant therapy in every case of infarction. Russek and others[4] have published studies which demonstrate that treatment of this kind is not actually necessary in "good-risk" cases. The main problem now is to be certain that "good-risk" cases can be reliably identified. Until we are sure on this point, it appears best to continue the routine use of the drugs.

A period of strict rest is an essential part of the management of every case of acute myocardial infarction, but the term "strict rest" was redefined a few years ago. Levine[5] and others have demonstrated that after the period of shock is past, and in the absence of great debility or a cerebrovascular accident, the patient may safely be permitted to sit in a chair for as long each day as he desires. He should be helped in and out of bed, however, and should be allowed no other privileges except for the use of a commode at the bedside. The length of time this program is carried out before allowing him to walk again is determined by the severity of the attack. Most patients can be permitted to take a few steps to the bathroom at the end of three weeks and can be granted gradually increasing activity after six weeks. In the absence of angina pectoris and myocardial insufficiency, a return to some form of work usually is permissible at the end of three months.

## Rheumatic Heart Disease and Bacterial Endocarditis

The ultimate aim of cardiovascular research is the prevention of all forms of heart disease. Although this goal is still far short of achievement, important progress has been made with respect to rheumatic heart disease and bacterial endocarditis. It has been established that most initial and recurrent attacks of rheumatic fever can be prevented by early and adequate treatment of beta hemolytic streptococcus infections. The treatment of choice is the intramuscular administration of penicillin, either in the form of a single injection of 600,000 to 900,000 units of benzathine penicillin G or as procaine penicillin with aluminum monostearate in oil, 300,000 to 600,000 units every third day for three doses.[6] Prophylactic treatment against streptococcal infections should be carried out in all persons who have a history of previous rheumatic fever or chorea or who present evidence of rheumatic heart disease. Sulfadiazine may

be given in doses of 0.5 to 1.0 Gm. each morning, or penicillin may be employed either by oral administration daily before breakfast in doses of 200,000 or 250,000 units or by the intramuscular injection of benzathine penicillin G, 1,200,000 units once a month. Treatment should be continued the year round until the patient is at least 21 years of age and possibly for life.

Although the majority of cases of bacterial endocarditis can now be treated successfully, the disease still has a mortality rate of 20 to 25 per cent because of delays in diagnosis and infections by penicillin-resistant organisms. In cases due to penicillin-sensitive organisms, treatment with penicillin alone usually suffices. Combined antibiotic therapy consisting of procaine penicillin 600,000 units every six or eight hours and streptomycin 1 Gm. daily has, however, become the treatment of choice because of the synergetic action of these two agents. Streptomycin is continued for 10 to 14 days, and penicillin for three weeks or longer. The same regimen often is effective in cases due to enterococci or other penicillin-resistant organisms. Only when penicillin and streptomycin have failed should bacteriostatic agents (aureomycin, terramycin, tetracycline, chloramphenicol and erythromycin) be used.

Bacterial endocarditis is, in most instances, a complication of rheumatic valvular disease or congenital heart disease. Many cases undoubtedly can be prevented by administering penicillin to patients with such cardiac problems before dental extractions, the removal of tonsils and adenoids, and obstetrical delivery. A suitable schedule consists of 600,000 units of procaine penicillin and 600,000 units of procaine penicillin with aluminum monostearate in oil administered intramuscularly approximately one hour before the operative procedure.[6] Patients who are sensitive to penicillin and those who are undergoing surgery of the urinary or lower gastrointestinal tract should be given one of the broad spectrum bacteriostatic preparations in full dosage for five days beginning the day before the surgical procedure.

## Essential Hypertension

A number of effective and fairly dependable hypotensive drugs have become available within the past few years. These preparations do not correct the underlying cause or causes of hypertension, but they reduce blood pressure in many patients and by so doing control symptoms and probably prolong life. It is fair to say that the outlook for the hypertensive person is better today than at any time in the past. Rauwolfia serpentina is the most widely applicable of the newer preparations, and, in our opinion, should be the first agent employed in the treatment of all cases except those of severe degree or in the malignant phase. The drug acts by a central tranquilizing action, and undesired side effects are infrequent and harmless. It is given in the form of the crude root (100 to 200 mg. daily), the alkaloid reserpine (0.25 to 2 mg. per day), or the total alkaloidal (alseroxylon) fraction (2 to 8 mg. daily). Because of its slow action, a decision as to its helpfulness in a given case should be postponed until after a trial of six weeks. If Rauwolfia alone proves ineffective, it may be given in combination

with phenoxybenzamine and protoveratrine (Mio-pressin). When this fails, pentolinium tartrate (Ansolysen) generally is the next preparation employed. It may be administered alone or with Rauwolfia and has largely replaced hexamethonium and Apresoline. Sympathectomy is now employed only in cases that have entered the malignant phase and fail to respond to any form of drug therapy.

## Cardiovascular Surgery

The value of commissurotomy for mitral stenosis has been established by extensive experience in all parts of the country. To date, 165 patients have been operated on at the Cleveland Clinic with a mortality rate of 4 per cent. Operation is not necessary in patients who have had no symptoms, nor is it advisable in patients who have significant aortic valvular disease or more than slight mitral insufficiency. Intractable congestive failure usually, but not always, is regarded as a contraindication. With these exceptions, and in the absence of active rheumatic carditis or bacterial endocarditis, commissurotomy is now recommended for all patients with mitral stenosis. The technic of commissurotomy for aortic stenosis also has been sufficiently developed that the operation should be advised in all cases of high-grade obstruction producing symptoms in persons less then 50 years of age.

Space does not permit a detailed discussion of the surgical treatment of congenital cardiovascular anomalies. The most common anomaly that can be completely corrected is a patent ductus arteriosus. In adults the recognition of this condition seldom is difficult, but in young children and especially in infants, the characteristic continuous, "machinery-type" murmur often is absent. In such patients a precise diagnosis can be established only by cardiac catheterization. Until recently this procedure was considered hazardous in infants and small children, but Dr. F. Mason Sones of our group has clearly demonstrated that such is not the case. He has performed catheterization in 108 children younger than 18 months of age, including 6 under the age of one month. All had congenital defects of such severity that survival for more than six months did not seem a reasonable expectation. Twenty-seven of the children were found to have anomalies that could be cured or corrected by surgery. Thirteen had a patent ductus arteriosus with only a nonspecific systolic murmur. Surgical division was performed in each case, and there was only one postoperative fatality. The majority of children with congenital heart disease who die before the age of two years have lesions that are not amenable to surgical correction, but a certain number have curable conditions. Because of this, cardiac catheterization is recommended for all such patients, regardless of age, who are dangerously ill.

The most recent addition to the therapy of cardiovascular disease has been arterial grafting for aneurysm or segmental arteriosclerotic obstruction of the abdominal aorta and its major branches. Discrete or segmental arteriosclerosis obliterans occurs predominantly in three locations, the aortic bifurcation, the

iliac arteries, and the superficial femoral artery. The characteristic clinical manifestation of the condition is intermittent claudication with pain in the back, buttock, thigh or calf depending on the site of the obstruction. In contrast to those with the diffuse form of arteriosclerosis obliterans, the patients usually are less than 55 years of age and seldom present evidence of severe ischemia or gangrene of the toes and feet. A rough estimate of the extent of the segmental occlusion often can be made by physical examination, but accurate evaluation requires translumbar aortography and femoral arteriography. Approximately one-half of all persons who have intermittent claudication are found by such studies to have an area of obstruction which can be replaced by a graft, but this does not mean that all should be operated on. In a considerable number adequate collateral circulation will develop spontaneously with time, and most patients therefore should have a thorough trial on conservative management. Arteriosclerotic aneurysms of the abdominal aorta and iliac arteries present a different problem. Fatal rupture of the aneurysm occurs in nearly three-fourths of all cases within three years of the time of original diagnosis. Resection and grafting, therefore, should be carried out promptly in all patients except those beyond the age of 70 years and those in poor general health. Even in the latter groups, the occurrence of symptoms referable to the aneurysm should lead to immediate surgery, although the mortality rate will be considerably higher than the 5 per cent or less which attends operation in younger patients. Dr. A. W. Humphries of our group has performed aorta-iliac grafting in 70 patients with a mortality rate of 4 per cent.

In conclusion, this discussion has not by any means touched upon all of the recent additions to the treatment of cardiovascular disease. An attempt has been made, however, to mention and partially review those that appear to be most significant. Because of these advances, the prognosis of patients suffering from many forms of cardiovascular disease is better today than at any time heretofore, and the gains of the past few years justify optimism concerning the fruits of further clinical and laboratory research.

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