TREATMENT OF CORONARY ARTERY DISEASE*

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Physicians in general are familiar with the treatment of coronary artery disease; however, a review of the methods and drugs of choice should be of value.

The most common cause of death after 50 years of age is heart disease, primarily coronary artery disease. The severity of symptoms in coronary artery disease depends entirely upon the degree of arteriosclerosis involving the coronary vessels or the aorta. Although extensive arteriosclerosis of the coronary vessels has been demonstrated post mortem without history of cardiac distress, such cases are unusual.

The 5 chief manifestations of coronary artery disease are (1) angina pectoris, (2) coronary thrombosis with infarction of the myocardium, (3) cardiac asthma with paroxysmal cardiac dyspnea, (4) Morgagni-Adams-Stokes syndrome, and (5) congestive myocardial failure. The two latter manifestations are often complications of coronary thrombosis with infarction of the myocardium.

Recent studies of series of cases by Master,[1] Dack and Jaffe,[2] and Rathe[3] indicate that the prognosis of coronary artery disease, particularly myocardial infarction, is more favorable than has been believed. Only 20 per cent of patients die from the initial occlusion within the first month. Approximately 50 per cent survive the first month and live for several years. Thirty per cent recover and resume normal activity. A definite prognosis of angina pectoris is more difficult to make, but patients may live for years and carry on reasonably normal activities. Sir James Mackenzie, the well known English cardiologist, had his first attack of angina pectoris at 49, but lived for another 25 years, during which time he was very active.

ACUTE CORONARY THROMBOSIS

When the diagnosis of acute coronary thrombosis is relatively certain, absolute bedrest should be prescribed for 6 to 8 weeks. Hospitalization for the first 3 to 4 weeks facilitates treatment of complications. Nursing care, which is very important, is greatly simplified in the hospital during the early weeks. However, moving the patient to the hospital if the attack occurs at home may carry undue risk during the early course of the disease.

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Relief of pain is of first importance. Morphine sulfate is probably the most common drug used. The dose is ¼ gr. repeated in 30 minutes if necessary; 1 gr. may be given during a 2 hour period. Pain is relieved much more rapidly by intravenous administration than by subcutaneous. The intravenous dose is 1/6 gr. repeated in 15 minutes if necessary. Dilaudid may be substituted for morphine in dosages of 1/16 or 1/32 gr. and, in our experience, causes less nausea. Papaverine hydrochloride, if available, is probably the initial medication of choice in ½ gr. dosage intravenously. Morphine or dilaudid can be given later as indicated.

Nitroglycerin is contraindicated in acute coronary thrombosis. It tends to lower blood pressure and depress circulation, which may favor progression of a thrombus.

All patients suffering from pain, dyspnea, cyanosis, or restlessness should have the benefit of oxygen. Even in the absence of these symptoms oxygen is excellent therapy during the first 48 hours.

The following drugs may be indicated in the treatment of coronary artery disease, depending upon the signs and symptoms.

Atropine sulfate. Myocardial infarction may lead to reflex vasospasm, in which the vagus nerve is the afferent path of the reflex. Atropine sulfate, 1/150 gr. by mouth twice daily for 3 days, is prescribed.

Glucose. A common complication is nausea, which may be controlled by the intravenous administration of 200 to 300 cc. of a 10 per cent solution given slowly. The dose may be repeated twice daily for several days, if nausea persists. The use of 50 cc. of 50 per cent glucose is of questionable value.

Quinidine sulfate. Quinidine sulfate should be employed routinely whether or not arrhythmia is present. The drug tends to prevent cardiac arrhythmias and fatal irreversible ventricular fibrillation. A dose of 3 gr. may be administered 3 times daily. An initial dose of 3 gr. will determine the presence of any sensitivity. The use of the drug may be continued for 2 to 3 weeks.

Papaverine hydrochloride. Papaverine hydrochloride, a non-habit-forming, opium alkaloid of the benzyl-iso-quinoline group, has recently been substituted for quinidine in the initial treatment of the disease. It seems to be superior to quinidine, is of very low toxicity, and may be given intravenously with a large margin of safety.

Recent studies by Elek and Katz[4] indicate that papaverine hydrochloride is a powerful and lasting coronary vasodilator. The drug is of value in the treatment of angina pectoris and in controlling the fre-

quency of premature beat; it relieves pain following acute coronary occlusion and prevents arrhythmia following acute myocardial infarction. Papaverine hydrochloride has also been used in peripheral vascular embolism, pulmonary embolism, Raynaud's disease, and ureteral spasm.

Larger doses than ordinarily prescribed should be used. Generally, I use 1 gr. 3 times daily.

Digitalis. Digitalis is indicated in (1) congestive cardiac failure, (2) cardiac dilatation with or without failure, (3) persistent tachycardia with a pulse of over 100, and (4) arrhythmia.

Digitalis should be given slowly in the average case, although rapid administration is advisable if the patient is acutely ill with signs of severe congestive cardiac failure. Ordinarily, a patient weighing between 125 and 175 pounds requires 20 to 24 gr. for complete digitalization. The remaining 10 per cent require approximately 30 gr. The dose cannot be calculated before administration, as each patient responds differently to its use. Usually, 1½ gr. is given 3 times daily for 5 days followed by a maintenance dose of 1½ gr. daily. For more rapid digitalization 6 gr. is given every 6 hours for 3 doses, and 1½ gr. every 4 hours until digitalization is effective. Digitalis intravenously is of value in the management of cardiac emergencies resulting from acute coronary thrombosis. The preparation must be used intravenously with great caution.

Aminophylline. The intravenous administration of aminophylline seems to benefit patients suffering from acute coronary thrombosis. The usual dose is 7½ gr. every 8 hours for 2 days. Diluted with 25 cc. of isotonic sodium chloride it is administered at the rate of 5 cc. per minute. Starting the third day 3 gr. of aminophylline 3 times daily is given orally. Theobromine sodium acetate may be substituted in doses of 7½ gr. 3 times daily before meals. The use of oral aminophylline and theobromine is particularly helpful in congestive cardiac failure. This dosage is frequently maintained for 30 to 60 days.

Caffeine sodiobenzoate. This preparation is indicated only when the systolic blood pressure drops below 100 mm. of mercury; 7½ gr. may be given subcutaneously every 2 to 3 hours until the blood pressure rises above 100 mm. of mercury.

Discourmarin ((3,3'—methylene—*bis*—(4-hydroxycoumarin)). A number of observers[5] have used this preparation from sweet clover to prevent arteriothrombosis or embolism. I have used this drug in the treatment of acute coronary thrombosis and believe that it contributes to a more rapid recovery. It is too early, however, to determine its actual

value. The oral administration of dicourmarin prolongs the prothrombin time. The administration is fairly simple, but a method for calculating exact dosage has not been determined. The effect is lasting and the cost within reasonable limits. Dicourmarin is not yet available for general use.

Diet. During the first 2 weeks of bedrest, the patient should be assisted in eating, as excessive movements of the arms, neck, and trunk should be prohibited. During the first 24 hours liquids should be administered exclusively; for the next 2 or 3 days the diet should be semisoft and divided into 5 or 6 meals a day. Thereafter, a bland semisolid diet of approximately 1500 to 1800 calories is adequate. Fluid is limited to 1500 cc. daily. If the patient is overweight, a weight reduction program should be instituted. Tobacco should be eliminated if possible. Small amounts of alcohol may be good therapy.

For elimination I prefer to have patients use the bedpan. Obese patients find it less strain to use a commode next to the bed. Adequate assistance is necessary, however. Strong cathartics are not needed. Mineral oil preparations should be used chiefly; a glycerin rectal suppository may be helpful. A bowel movement every 2 days is adequate.

Duration of bedrest. Duration of bedrest is determined by clinical symptoms, such as pain, temperature, blood pressure, and pulse changes. A large severe infarction requires more prolonged bedrest than a very small infarction. Patients with congestive heart failure require even longer periods of rest. Temperature, white blood cell count, and sedimentation rate should be checked regularly. Serial electrocardiograms evaluate the management and help determine the period of bedrest. The patient should not attempt to get up until the temperature, white blood cell count, and sedimentation rate have been normal for at least one week, and if there has been no evidence of failure. Electrocardiographic changes are frequently slow, and the picture may never return to normal.

Treatment of acute coronary thrombosis does not end with carrying the patient through the first few days of the initial attack of pain. When the patient is improved, he should be told the exact nature of his condition so that he may more intelligently follow the program of treatment. A minimum of 6 to 8 weeks' bedrest should be followed by gradually progressive activity for several months. Any physical activity and nervous strain should be avoided. The psychic management is frequently more difficult than the medical management. With proper care and the complete cooperation of the patient, many patients suffering from this disease can resume reasonably normal activity.

Prognosis. Rathe[8] in a series of 274 cases of myocardial infarction reported a poor prognosis was indicated when

"1. A sinus tachycardia of 100 persisted over 5 days.
2. The age of the patient was over 55 years.
3. The systolic blood pressure dropped suddenly and failed to rise again to a level of 100 mm. mercury within 5 days.
4. Unusual fatigue and apprehensiveness were prominent during the early convalescent period.
5. Congestive heart failure developed.
6. The pulse pressure was 20 mm. of mercury or less.
7. The electrocardiogram revealed an anterior infarction or an indeterminate infarction.
8. There was a gallop rhythm present.

"A good prognosis was indicated . . . if (1) the patient was under 55 years of age, (2) the heart rate did not reach 100 or if it dropped within two or three days to 90 or less, (3) the blood pressure returned to a near normal level, (4) the heart was not enlarged and (5) there were no signs of cardiac insufficiency."

ANGINA PECTORIS

The treatment of angina pectoris involves the treatment of the attack itself and the prevention of an attack. An attack is usually self-limited and very seldom exceeds 15 or 30 minutes, even without medication.

At the onset of an attack the patient should have immediate and complete rest. Attacks are usually shortened by rest in the sitting or standing position rather than the supine position. Deep breathing is often helpful.

Medication, however, is indicated to relieve the symptoms and shorten the duration of the attack. Patients should carry some form of medication that can be used immediately. The most satisfactory drug is nitroglycerin; 1/100 or 1/200 gr. is necessary to relieve an attack. The smallest effective dose can be determined only by trial. Nitroglycerin under the tongue is usually effective within 15 to 30 seconds, although relief may last no longer than 30 minutes. The drug may be used as frequently as necessary and, as a rule, is without harmful effects.

Amyl nitrite by inhalation provides similar relief, but is more difficult to use and is not superior to nitroglycerin.

Prevention of attacks. Strenuous effort, sudden excitement, overeating, excessive use of tobacco, exposure to intense heat and cold, and/or excessive nervous strain tend to promote the frequency of attacks of angina pectoris. Patients soon learn their own limitations and factors which predispose to pain. The avoidance of precipitating factors is a very important part of the prevention of attacks. Patients suffering from angina pectoris need physical and mental relaxation; therefore, an ade-

quate period of rest during the day is most important. Rest for 30 minutes before and after the noon meal frequently will limit attacks during the day. It has been noted that patients are greatly benefited by a period of complete bedrest for several weeks after the initial attack of angina pectoris.

Nitrites. Nitroglycerin may be taken regularly even in the absence of attacks to prevent their occurrence. Sodium nitrite in 3 gr. doses is usually effective in 5 to 10 minutes. The effect lasts longer than that of nitroglycerin and may continue for one to 2 hours. Erythrol tetranitrate in 1½ gr. doses and mannitol hexanitrate in 3 gr. doses usually become effective after 30 minutes. The effect lasts for 4 to 6 hours. The latter drug may prevent attacks but is not as valuable as nitroglycerin in the treatment of an actual attack of angina.

Papaverine hydrochloride. A dose of ½ gr. to 1½ gr. 3 to 4 times daily frequently will reduce the number of attacks. The preparation is non-habit-forming.

Aminophylline. In my experience aminophylline and allied preparations have not been particularly satisfactory in the prevention of attacks of angina pectoris. It may be used alone in a 1½ gr. or 3 gr. dose 3 times daily, or in combination with phenobarbital. A trial of aminophylline or theobromine sodium acetate is well worth while.

Phenobarbital. Frequently, small doses of phenobarbital, ¼ gr. 3 times daily, reduce attacks of angina pectoris to a minimum. Small doses have a mild sedative effect and, no doubt, tend to reduce vasospasm.

Potassium iodide. Routine use of potassium iodide, 15 drops in water once daily after breakfast, helps to control coronary artery disease. It has no specific effect on the prevention of attacks of angina pectoris.

Glandular extracts. The literature reveals that glandular extracts are being used in the treatment of angina pectoris. I have had limited experience with these preparations, and in the few cases in which they have been used no definite benefit has been derived.

Surgical treatment. Subtotal thyroidectomy, cardiopericardiopexy, pectoral anastomosis, cervical thoracic sympathectomy, and paravertebral alcohol injection are surgical forms of treatment. Operation is advised only after careful study and then only when more conservative measures have failed. Occasionally, persons suffering from polycythemia also have typical angina pectoris. Venesection frequently relieves this particular group of patients.

SUMMARY

Because of the high mortality of coronary artery disease after middle life, the methods of treatment and the selection of drugs are important. With adequate bed rest, diet, nursing care, and proper dosage of indicated drugs the prognosis can be greatly improved.

In the treatment of acute coronary thrombosis papaverine hydrochloride, morphine sulfate, and oxygen may be used for the relief of pain. Other drugs of value are quinidine sulfate, atropine, and digitalis. Aminophylline, caffeine sodiobenzoate, and dicourmarin may be indicated in certain cases. The prognosis may be predicted by the presence or absence of certain physical signs and symptoms.

In angina pectoris consideration must be given to the treatment and prevention of attacks. Nitroglycerin is probably the medication of choice in the treatment of attacks. The nitrites, papaverine hydrochloride, aminophylline, and phenobarbital may be beneficial preventative drugs, combined with the elimination of disturbing environmental and psychic factors. Endocrine or surgical treatment of the disease may be indicated when other measures have been without benefit.

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