The Clinical Concept of Primary Myocardial Disease

A Classification and a Few Notes on Management and Prognosis

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A USEFUL and effective guide for therapy of any disease requires a common understanding of the disease by the author and the reader. It is essential that the disease entity be identified before therapy is discussed, prescribed or evaluated. In many disease entities, this mutual understanding is well established by familiarity with the disease as gained by similar periods of training and experience or from information that is readily available in standard reference texts. Neither the familiarity, mutual experience, or immediate reference sources presently exist in relation to the disease under discussion. Current medical conferences conducted by participants familiar with myocardial disease are characterized by a great disparity in the concepts of the diseases of the myocardium. For these reasons, it is considered that a brief description of the author’s concepts of primary myocardial disease be provided prior to a discussion of therapy.

Definition and Classification

The term primary myocardial disease as used here and in prior publications\(^1-5\) refers to groups of diseases that primarily involve the myocardium and spare or only minimally involve other important structures of the heart and the cardiovascular system. By definition, it excludes secondary forms of myocardial disease complicating occlusive coronary artery disease and systemic and pulmonary hypertensive cardiovascular diseases as the disease processes in these conditions primarily involve the coronary, systemic, or pulmonary vasculature with secondary myocardial hypertrophy, degeneration, and fibrosis. Likewise, syphilis with its primary cardiovascular lesions in the aorta and aortic valve and rheumatic heart disease with its proclivity to produce valvular lesions are not ordinarily considered as primary myocardial diseases but admittedly instances occur where rheumatic lesions are primarily and only in the myocardium. Most congenital malformations produce secondary myocardial alterations of hypertrophy, dilatation, or degeneration but there are some in which the defects involve primarily the myocardium, e.g., glycogen-storage disease. When the important cardiovascular component or complication of a systemic disease is limited to the myocardium or constitutes the major clinical component, the myocardial disease resulting therefrom is included in this category.

This concept of primary myocardial disease therefore includes acute and chronic forms of myocarditis of specific as well as nonspecific etiology and their myocardial sequelae, congenital structural and functional malformations of the myocardium, myocardial neoplasms, infiltrative cardiopathies such as occur in amyloidosis and hemochromatosis, the cardiomyopathies occurring with endocrine, metabolic, neuromuscular, and musculoskeletal diseases as well as the chronic idiopathic myocardial and endomyocardial diseases, which are probably sequelae of myocardial damage and dysfunction resulting from one of the preceding conditions which were unrecognized at an earlier stage. A useful classification is given as follows:

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1. Myocarditis, Specific, Acute and Chronic

Includes the reactions to injury, repair and immunologic responses to bacterial, viral, mycotic, protozoal, and rickettsial infections and parasitic infestations; specific bacterial toxins and toxic chemicals and drugs; physical trauma, including electrical current and radiation.

2. Myocarditis, Nonspecific, Acute and Chronic

Includes reactions to injury, repair and immunologic responses to unknown agents. Variously reported as Fiedler's, giant-cell, idiopathic, and granulomatous myocarditis. So-called autoimmune or autoallergic and hypersensitivity myocarditis are included. Also myocarditis of rheumatic fever, rheumatoid diseases, lupus erythematosus, progressive systemic sclerosis and other diseases with vasculitis and connective-tissue alteration of the myocardium are included in this group.

3. Metabolic and Nutritional Disorders of the Myocardium

Includes morphologic and functional alterations resulting from hyperthyroidism, hypothyroidism, pheochromocytomas, adrenal insufficiency, primary hyperaldosteronism, hyperinsulinism, and acromegaly; thiamin deficiency, dysproteinemias, severe chronic anemias, hypokalemia, and hyperkalemia.

4. Idiopathic Myocardiopathies

Includes cardiac hypertrophy and dilatation of obscure nature with and without myocardial or endomyocardial fibrosis. Probably residuals of repair and hemodynamic adaptation to groups 1, 2, 3 above. Reported in literature under many names: idiopathic hypertrophy, cardiomegaly or cardiomyopathy, familial cardiomyopathy, alcoholic cardiomyopathy, interstitial myocardial fibrosis, myocarditis with endomyocardial fibrosis or elastosis, congenital and adult forms of endocardial or subendocardial fibrosis, sclerosis or fibroelastosis and cardiovascular collagenosis with recurrent parietal thromboendocarditis.

5. Primary Idiopathic Myocardial Obstructive Hypertrophy

Includes hypertrophic myocardial lesions of the ventricle and septum which produce dynamic subvalvular obstruction. Reported in literature as asymmetrical hypertrophy, idiopathic hypertrophic subaortic stenosis, muscular subvalvular stenosis, familial muscular stenosis, idiopathic hypertrophy simulating aortic stenosis, idiopathic ventricular septal hypertrophy simulating valvular stenosis, obstructive cardiomyopathy simulating aortic stenosis, idiopathic subaortic stenosis, pseu- doaortic stenosis produced by ventricular hypertrophy or simply as functional obstruction to the left ventricle. This lesion may represent localized reaction to previous injury (myocarditis).

6. Infiltrative Diseases of the Myocardium

Includes amyloidosis, fatty infiltration, glycogenosis (glycogen-storage disease), hemochromatosis, tumor invasion and metastasis, including lymphomas, leukemias, and xanthomatosis.

7. Myocardial Lesions Associated with Neuromuscular Disorders

Includes myocardial lesions associated with muscular dystrophies and Friedreich's ataxia; lesions associated with myositis, myasthenia gravis, and the myocarditis associated with thymoma.

8. Primary Myocardial Neoplasms

Includes rhabdomyomas, sarcomas and angiosarcomas, fibromas, lipomas and tumors of the specialized tissues of the conduction system of the myocardium.

The term "primary myocardial disease" is frequently used by others in a more restricted sense to include only the idiopathic forms of myocardial disease. Others prefer simply to refer to these idiopathic forms as myocardial diseases of unknown cause. Likewise the terms cardiomyopathy and myocardiopathy are currently used to describe this group of diseases; again by some as a general term and by others in a restricted sense and referring only to the idiopathic forms of myocardial disease.

Clinical Features of Primary Myocardial Disease

The clinical features of primary myocardial
disease arise from faults in normal myocardial function. The appreciation of specific clinical features and hemodynamic alterations as manifestations of these faults of the myocardium as a functional unit of the cardiovascular system constitutes the basis for a positive clinical diagnosis. In spite of the great diversity of etiologic factors and a wide spectrum in its severity and clinical course as presented by primary forms of myocardial disease, it has been observed that they present clinical features that permit a positive diagnosis with an accuracy approaching that of the more common secondary forms of myocardial disease, valvular heart disease, or pericardial diseases. These clinical and hemodynamic features have been described in great detail elsewhere.\(^1\)\(^-\)\(^5\) Familiarity with these features is essential to the correct diagnosis, and appropriate management and a careful review are recommended.

**General Principles in Management**

The great diversity and multiplicity of causes and variations in severity as presented by primary myocardial disease make it difficult to outline a standard procedure for therapy. Individual evaluation and management are imperative. A plan of individual evaluation and management of primary myocardial disease requires the following: (1) a sound basis for a definite or presumptive clinical diagnosis; (2) establishment of the specific cause as promptly as possible and, if not obvious, a continued search for the cause or identification of the disease mechanism involved but avoiding a change of therapy with every passing idea; (3) a careful initial bedside clinical and hemodynamic assessment of the status of myocardial function, both at rest and with activity; (4) a determination as to whether the disease is one isolated to the myocardium or to the myocardium and pericardium or whether there exists an important systemic disease of which the myocardial disease is only one element of several potential fatal or crippling features, e.g., treatment of congestive failure or heart block in diphtheritic myocarditis and ignoring the systemic infection and the effect of the toxin on other organs; (5) a determination of the nature of the myocardial alteration, that is, is it an acute inflammatory or destructive process or one suggesting a hypersensitivity process or, on the other hand, is it a chronic disease state with gradual impairment of myocardial function and repeated adaptive responses; (6) an assessment of the functional alterations to include arrhythmias, conduction disorders, anemias, dysproteinemias, electrolyte and enzyme abnormalities; and (7) the nature of the peripheral effects of the malfunctioning myocardium (central pump), e.g., congestion or ischemia of the peripheral tissues and organs, the presence of a reactive systemic or pulmonary hypertension or systemic or pulmonary thromboembolism.

A failure to make the above evaluation and the institution of empirical therapy for the most overt finding or symptom based only on a superficial evaluation can be disastrous or it can greatly deter the progress of recovery and rehabilitation. Such practices have resulted in erroneous concepts of therapy and prognosis. A good example is the vigorous use of digitalis in the treatment of existing congestive failure without an assessment of the status of the serum electrolytes or of an existing arrhythmia or conduction disorder. Repeated experiences and practice of this nature have resulted in therapeutic recommendations and opinions that digitalis should not be used in the treatment of primary myocardial disease or that there is an unusual degree of digitalis sensitivity or myocardial irritability present which precludes its effective use. Another frequent failure in the initial evaluation is a failure to establish the cause of an enlarged cardiac silhouette. Acute cardiac dilatation is confused with pericardial effusion or at other times with chronic hypertrophy. A third error is the reverse, namely, to deny the diagnosis of primary myocardial disease because cardiomegaly and congestive failure are not initially present and the patient is later observed to succumb to a functional disorder, such as a disorder of conduction, an arrhyth-
mia or an electrolyte disorder such as hyperkalemia.

An adequate assessment can usually be made at the bedside, utilizing the history and an evaluation of the clinical findings in light of the knowledge of the clinical course and manifestations of primary myocardial disease. The state of the cardiac output as well as the degree of cardiac dilatation and hypertrophy or the extent of the reactive pulmonary hypertension can be evaluated by the presence or absence of bedside findings. Special roentgenologic and hemodynamic studies should be selected to obtain specific information rather than made routine prior to careful bedside evaluation. Serologic, immunologic, and biochemical studies of the blood and histologic and histochemical studies of biopsy material are useful and practical only when appropriately applied after a good initial evaluation or when prior observations indicated diagnostic potentialities.

A procedure of therapeutic management based on individual evaluation permits a general plan and method of therapy that can be applied and adapted to patients with a wide spectrum of presenting symptoms and clinical states. A guide for management is suggested but flexibility is stressed.

**General Plan of Management**

1. Immediate therapy of the presenting features which are life threatening.

2. Determination of the degree of activity to be prescribed during the continuation of supportive therapy and diagnostic studies.

3. Diagnostic studies and institution of specific therapy as indicated.

4. Long-term management directed toward maximum rehabilitation consistent with the residual status of myocardial function.

5. Periodic evaluation and prevention of complications.

The presenting features which have been observed to be a threat to life are (1) myocardial insufficiency (congestive failure and circulatory failure), (2) arrhythmias or conduction disorders, or both, and (3) thromboembolic complications, chiefly in the subacute and chronic forms of primary myocardial disease. In general, conventional measures are indicated for the management of these clinical problems. Hospitalization, preferably in an intensive care unit with complete bed rest and inactivity are important.

The response to adequate therapy is usually good in the initial phase of primary myocardial disease provided it is not associated with a systemic disease, which in itself is a threat to life, and provided associated arrhythmias and conduction disorders and failures are successfully managed over a sufficient period to permit the patient to recover from the cardiac dilatation or develop adaptive hypertrophy which develops early if the patient is to survive. Complications resulting directly from therapy itself, e.g., digitalis intoxication, electrolyte problems, and thromboembolism account for the majority of failures. Therapy is less likely to be successful when the features of left-sided failure are predominant with or without congestion but with an extremely low cardiac output, systemic hypotension, and poor coronary, renal, and cerebral blood flow. The technics of mechanical cardiac assists, now in the experimental stage, may eventually prove helpful. Corticosteroids have not been found helpful in the treatment of failure per se except when the steroid has an effect on a specific type of tissue alteration, infection, or metabolic abnormality.

Refractory congestive failure is a feature of the subacute and chronic forms of primary myocardial disease, especially the idiopathic form. Complications of pulmonary embolism and electrolyte disorders of hypochloremic alkalosis, hypernatremia and hemodilution are more likely to occur at this stage, even with the best management. Conventional methods of management of these complications are used. Newer drugs such as spironolactone have seldom demonstrated a specific advantage over careful use of digitalis and mercurial diuretics but occasionally their short-term addition is helpful.

The extent and duration of restriction prescribed for the patient during the period of

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therapy and necessary diagnostic studies or, more optimistically, the degree of activity permitted depends upon many factors. It is considered unwise to resort to a standard practice of prescribing complete bed rest for an arbitrary period for each patient with a diagnosis of primary myocardial disease. Individual evaluation and prescription is important, as in other features of management. The spectrum of activity that can be safely permitted is as wide as the clinical manifestations of the disease.

Restriction to bed status is made under the following conditions: (1) during the first episode of failure when there is an enlarged cardiac silhouette and clinical features of acute cardiac dilatation. Complete bed rest is more important and beneficial in this phase of the disease and, if appropriately applied with restoration of good myocardial function and rehabilitation, is often excellent. The duration of the prescribed bed rest is usually a matter of months and is determined by repeated clinical evaluation and not by a predetermined time table; (2) when cardiomegaly and failure are present on initial evaluation but the onset of failure as well as the relative degree of dilatation and hypertrophy is not known. While overtly the situation may be the result of a subacute or chronic process with some degree of functional adaptation, the presence of failure always suggests that an additional element of dilatation has occurred, and a period of decreased activity may permit a return to the chronic state pre-existing the current failure. Serial roentgenograms and clinical evaluations are the best guides to the duration of restriction in such cases. Experience has not demonstrated any benefits of prolonged bed rest in this type of patient over that normally practiced by allowing activity consistent with demonstrated tolerance; (3) during the treatment of episodes of acute arrhythmias, unstable block, and episodes of thromboembolism.

Although the clinical diagnosis of primary myocardial disease is usually readily made from existing faults in myocardial function, a specific cause is often not obvious on initial evaluation and treatment and some remain in the idiopathic group even after autopsy study. A continued search is however maintained for a specific cause, thereby hoping to remove the patient from the idiopathic group into one of the other classifications, as previously listed, wherein specific therapy is available or where the disease mechanism is better understood and managed. This is a diagnostic challenge that the attending physician should accept rather than to accept the label of idiopathic disease or alcoholic myocardopathy with only supportive, symptomatic, and empiric therapy.

Today the physician is provided with an increasing battery of diagnostic laboratory procedures including serologic, biochemical, immunologic, and immunochromic procedures applicable to the blood and sera and biopsy technics applicable to numerous body tissues, including the myocardium, which offer aid in specific diagnosis.

Surgery has provided beneficial results in a few forms of primary myocardial disease, such as the removal of localized tumors of the myocardium and surgical resections of hypertrophic muscle tissue in the hypertrophic muscular lesions involving the outflow tract of the left ventricle. Surgical treatment in the form of the production of poudrage has been applied to infants with endomyocardial fibroelastosis but the results have been difficult to evaluate.

An exploratory mediastinotomy has been found helpful in the study of patients with clinical features of myocardial or combined pericardial and myocardial disease of unknown etiology. Such surgical procedures permit direct visual, palpable, and biopsy examinations of the pericardium, myocardium, and coronary vessels. On other occasions, an exploratory mediastinotomy has been necessary to solve the problem of differential diagnosis between constrictive pericarditis and primary myocardial disease and at the same time provide definitive surgical therapy for the constrictive pericarditis when present.
Death from a surgically curable constrictive pericarditis has been observed to occur when such exploratory procedures were delayed or not considered in therapy.

Long-term management and therapy are necessary for the majority of patients with primary myocardial disease. There is a smaller group in whom recovery is complete or in whom the residual damage to the myocardium is such that normal activity is tolerated and in whom no therapy is required. However, the presence of minimal residual damage may become important should this individual develop obstructive ischemic coronary artery disease or have severe stress on the myocardium associated with some other form of systemic or cardiovascular disease such as systemic or pulmonary hypertensive cardiovascular disease, chronic renal disease, etc.

The nature of the long-term therapy will vary, depending upon the severity of the residual structural and functional alterations of the myocardium. Again, the most important problems are concerned with the management of myocardial insufficiency as may be manifested by (1) congestive or low-output failure; (2) arrhythmias and conduction disorders; (3) thromboembolic problems, and (4) specific therapy for the management of a systemic disease related to the primary myocardial disease.

The level of physical activity or nature of occupation permitted should be one which is tolerated without symptoms or with minimal symptoms. Graduated activity is important in the convalescent period and for successful rehabilitation. Childbearing is poorly tolerated by patients with symptomatic primary myocardial disease. The majority of so-called "postpartum heart disease" consist of instances of idiopathic primary myocardial disease, and subsequent pregnancies are frequently disastrous.

A program of combined maintenance digitalization and judicious use of diuretics combined with restriction of sodium intake and physical activity provide the best form of therapy for those with continued features of congestion or with recurring episodes of congestive failure. Periodic therapy with vigorous diuresis should be avoided as complications of hemoconcentration, dehydration, and electrolyte imbalances result in serious and often fatal complications. Fatigue, exertional dizziness, and syncope occurring from low-output failure are best managed by limitation of activity and avoidance of sudden bouts of exertion.

Troublesome arrhythmias are managed by conventional therapy. Special attention should be given to unstable rhythms associated with atrioventricular block, as such may suddenly occur in chronic primary myocardial disease. Hospitalization and therapy are indicated as previously described. The implantation of a pacemaker deserves serious consideration in long-term management of those with complete heart block.

Anticoagulant therapy is an important part of long-term management, especially in those with persistent cardiac dilatation, low-output failure, or previous embolic episodes.

When primary myocardial disease occurs as a manifestation of systemic disease and when the disease itself cannot be cured, maintenance or supportive therapy becomes important. Steroid therapy for management of sarcoid, trichinosis, hypersensitivity states and collagen diseases may be beneficial. Thyroid medication becomes an important part of the management of the myocardial faults in severe hypothyroidism. Appropriate treatment of dysproteinemias, anemias, and chronic electrolyte abnormalities is important in the management of forms of primary myocardial disease associated with chronic nutritional and metabolic disorders. The causal relationship of alcohol intake and poor nutritional intake to the so-called alcoholic cardiomyopathy is yet to be clearly established. However, the highly suggestive relationship of excessive alcohol intake to some of the chronic forms of the disease is sufficient to warrant abstinence from alcohol and for the establishment of a well-balanced diet in these instances in which the two conditions coexist.

Lastly, the prevention of infections, especially of the respiratory and urinary tracts, is
most important in these patients, as they constitute circulatory stresses that often precipitate or seriously aggravate existing congestive failure or arrhythmias in a patient otherwise doing well.

**Prognosis and Prevention**

The prognosis of primary myocardial disease has steadily improved in recent years as more has been learned as to cause, pathogenesis, and the nature of hemodynamic abnormalities. Earlier clinical recognition has altered the prognosis, e.g., many of the entities such as endomyocardial disease in infants and Fiedler's type of myocarditis in past years were considered universally fatal simply because these entities were only recognized at autopsy and survivors were not recognized. The clinical recognition of infantile endomyocardial disease has resulted in the experience of observing survival into childhood and adulthood. Myocarditis is simply an incidental feature in the total systemic disease of many infections and the over-all prognosis of myocarditis of all types is good. Myocarditis of infancy due to the Coxsackie virus, once considered a universally fatal disease, has undergone a favorable change in prognosis with the clinical and immunologic recognition of mild and occult forms of the disease.10

The prognosis of subacute and chronic forms of myocarditis and of the idiopathic forms of primary myocardial disease is the poorest. Again, this poor prognosis in the past has been related to a failure to recognize the myocardial disease until the clinical endpoint of hemodynamic failure was reached. Often the patient with myocardial disease had survived for years. The recent report of hemodynamic studies of 14 patients with idiopathic hypertrophy without evidence of myocardial failure is good evidence of the degree of adaptive mechanisms which develop and permit survival.12 The over-all prognosis as well as the prognosis of the individual type of primary myocardial disease can only be determined after a better understanding of pathogenesis and early recognition of the disease. For this reason, a plea is made to consider primary myocardial disease in the broad definition as used herein. The recognition of the clinical features of the disease provide the basis for an early and accurate diagnosis and differentiation from other forms of cardiovascular diseases. Knowledge of the various types of primary myocardial disease as given in the classification provided here permits a prompt diagnosis and the application of appropriate therapy as well as an intelligent basis for the search of the cause and therapy for those initially classified as idiopathic or simply as myocardial diseases of unknown cause.

**References**

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