Evaluation of the Patient with Congestive Heart Failure and Ventricular Arrhythmias

BERTRAM PITT, MD

Although vasodilators and new inotropic agents have been shown to improve ventricular function and reduce symptoms, their effect on mortality is uncertain. In view of our failure to reduce mortality in patients with congestive heart failure (CHF), the identification and amelioration of potentially reversible factors that might alter survival are crucial before initiating therapy. The first step is to establish the diagnosis of CHF and the presence or absence of dilated congestive cardiomyopathy. The extent of myocardial dysfunction, both right and left, must also be evaluated. In post–myocardial infarction patients, left ventricular ejection fraction is an important indicator of prognosis during the first 1 to 2 years. However, in patients with chronic CHF and dilated cardiomyopathy, right ventricular ejection fraction may be a more effective predictor of surviv-

al. The presence, frequency and complexity of ventricular arrhythmias must be determined, because these arrhythmias may independently increase the risk of sudden cardiac death in patients with ischemic cardiomyopathy. Their role in patients with idiopathic cardiomyopathy is less certain. In addition, myocardial ischemia, left ventricular dyskinesis or aneurysm, occult myocarditis and neurothrombosis formation must be ruled out. Detection and correction of serum electrolyte and neurohumeral abnormalities are essential. Our failure to reduce mortality in patients with CHF may not entirely lie in the lack of effective therapeutic agents but rather in our failure to apply properly the diagnostic and therapeutic approaches now available.

(Am J Cardiol 1986;57:19B–24B)

The goals of treatment in a patient with congestive heart failure (CHF) are two-fold: to improve symptoms and to increase survival (Table I). Although vasodilators and new inotropic agents improve ventricular function, reduce symptoms and enhance the quality of life, their effects on mortality are not yet clear.[1,2] Similarly, while antiarrhythmic agents obviously decrease the incidence of arrhythmias in patients with CHF, they apparently do not lead to a subsequent reduction in sudden cardiac death. In 1971, the Framingham study found that the probability of dying within 5 years from the onset of CHF was 62% for men and 42% for women.[3] The investigators stated, "despite earlier recognition and increasingly sophisticated and potent treatment of congestive heart failure, its clinical course and prognosis remains surprisingly grim and not much better than those for cancer in general." Unfortunately, this statement remains true 15 years later.

From the Division of Cardiology, Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor, Michigan.

Address for reprints: Bertram Pitt, MD, University Hospitals, University of Michigan, 1405 East Ann Street, Ann Arbor, Michigan 48109.

In view of our failure to reduce mortality in CHF patients with vasodilators, inotropic or antiarrhythmic agents, the identification and amelioration of potentially reversible factors that might alter survival are crucial before initiating therapy. This review focuses on the evaluation of patients with dilated congestive cardiomyopathy with particular emphasis on the patient whose clinical course is complicated by ventricular arrhythmias. The key points in the assessment of a patient with suspected dilated congestive cardiomyopathy are outlined in Table II.

Establishing the Diagnosis of Congestive Heart Failure and the Presence of Dilated Congestive Cardiomyopathy

The diagnosis of CHF can usually be made by history and physical examination. On the other hand, the diagnosis of dilated congestive cardiomyopathy and its differentiation from other forms of heart failure, such as restrictive or constrictive cardiomyopathy, often require laboratory investigation. It is important to ascertain whether a patient's symptoms of fatigue, shortness of breath, dyspnea on exertion and pulmonary rales, if present, are primarily due to a cardiac, pulmonary or

TABLE I   Goals in Treating a Patient with Congestive Heart Failure

To improve symptoms:
    To enhance well-being and quality of life
    To increase exercise tolerance
To improve survival:
    To prevent progressive cardiac failure
    To prevent sudden cardiac death
    To prevent thromboembolic episodes

TABLE II   Steps in the Evaluation of a Patient with Dilated Congestive Cardiomyopathy

Establish the diagnosis of congestive heart failure and the presence of dilated
    congestive cardiomyopathy
Evaluate the extent of myocardial dysfunction
Determine the presence, frequency and complexity of ventricular arrhythmias
    and the propensity for sudden cardiac death
Rule out myocardial ischemia
Rule out left ventricular dyskinesis or aneurysm
Rule out occult myocarditis
Determine serum electrolytes
Assess neurohumoral status
Detect mural thrombus formation

other cause. The standard chest x-ray may be of limited value in this regard. The electrocardiogram, while occasionally helpful, is often misleading. Evidence of myocardial infarction may be absent in patients with ischemic cardiomyopathy and, conversely, Q waves or poor R-wave progression in the anterior chest leads may frequently be present in patients with idiopathic dilated cardiomyopathy.[4] The echocardiogram is, however, especially useful in establishing the diagnosis of dilated cardiomyopathy, and in determining the presence of underlying congenital or valvular heart disease, pericardial effusion, hypertrophic cardiomyopathy or heart failure due to diastolic dysfunction.[5]

Reversible causes of heart failure—such as anemia, volume overload, uremia, hemochromatosis, sarcoid heart disease, hypophosphatemia, hypoparathyroidism, pheochromocytoma, acromegaly, arteriovenous malformations and hyper- or hypothyroidism—should be ruled out.[6-9] The history may be especially valuable in detecting doxorubicin cardiomyopathy or radiation-induced restrictive cardiomyopathy. The ingestion of alcohol or other toxins in a patient with cardiomyopathy may also result in ventricular tachycardia (the "holiday heart syndrome").[10]

Evaluating the Extent of Myocardial Dysfunction

Determination of left ventricular (LV) ejection fraction (EF) is an important indicator of survival in the post–myocardial infarction patient. Schulze et al[11,12] noted a relation between LVEFs of <40% and the occurrence of complex ventricular arrhythmias in post-infarction patients, and pointed out the importance of this relation in predicting the risk of sudden cardiac death. Results from the Multicenter Postinfarction Research Group have confirmed the value of the LVEF as a prognostic indicator in the first 1 to 2 years after infarction.[13] Recent studies have, however, suggested a poor correlation between survival and LVEF in patients with idiopathic or ischemic cardiomyopathy remote from the acute infarction.[14] Similarly a poor correlation has been reported between maximum oxygen consumption during exercise and LVEF in patients with CHF.[15] However, in a recent study of patients with CHF, Baker et al[15] found an excellent correlation between exercise performance and right ventricular (RV) EF as determined by radionuclide ventriculography. Polak et al[14] have emphasized that RVEF is a better predictor of survival than LVEF in patients with CHF. The reasons for the superiority of RVEF as a predictor of exercise performance and survival in patients with CHF remain uncertain. The development

of RV dysfunction in conjunction with LV dysfunction may impair the patient's ability to increase cardiac output during stress, thus compromising exercise performance and perhaps precipitating sudden cardiac death by secondary neurohumoral mechanisms. The recent observation that the atrial natriuretic factor is regulated at least in part by the level of right atrial pressure, and the finding of elevated levels in CHF patients,[16] raise the possibility that this and other neurohumoral mechanisms are important to our understanding of how right ventricle function affects survival in patients with CHF.

Determining the Presence, Frequency and Complexity of Ventricular Arrhythmias and the Propensity for Sudden Cardiac Death

Frequent and complex ventricular arrhythmias in a patient with ischemic cardiomyopathy appear to independently increase the risk of sudden cardiac death.[17] The prognostic value of ventricular arrhythmias in a patient with idiopathic dilated cardiomyopathy is less certain.[18] The role of ambulatory Holter electrocardiographic recordings and electrophysiologic testing in patients with CHF has been reviewed by Francis in this issue.[18]

Ruling Out Myocardial Ischemia

The presence of ischemic cardiomyopathy, as well as reversible or inducible myocardial ischemia, must be established. Exercise, emotional stress or myocardial ischemia may all trigger ventricular arrhythmias in a patient with CHF. However, antiarrhythmic therapy to prevent sudden cardiac death will probably not be effective in patients with ischemia-induced arrhythmias, unless appropriate antianginal agents or antiischemic strategies are applied.

The differentiation of ischemic from idiopathic dilated cardiomyopathy has proven difficult by noninvasive techniques. The detection of a large LV dyskinetic area or aneurysm by chest x-ray, echocardiography or radionuclide ventriculography is highly suggestive of ischemic cardiomyopathy. Patients with idiopathic dilated cardiomyopathy, especially those with alcoholic cardiomyopathy, may have abnormalities of regional myocardial wall motion and focal thallium-201 defects.[19] Conversely, patients with ischemic cardiomyopathy may have diffuse LV hypokinesis. In an early

study using thallium-201 myocardial imaging, we evaluated the possibility of distinguishing patients with ischemic cardiomyopathy from those with idiopathic dilated cardiomyopathy.[19] Patients with ischemic cardiomyopathy were found to have relatively large defects in thallium-201 uptake corresponding to large areas of myocardial scarring, while those with idiopathic cardiomyopathy had uniform thallium-201 uptake or only relatively small defects in uptake. However, subsequent studies have had difficulty distinguishing ischemic cardiomyopathy from idiopathic dilated cardiomyopathy using thallium-201.[20] Radionuclide ventriculography and echocardiography have also been used in differentiating ischemic from idiopathic dilated cardiomyopathy. Shen et al[21] recently used rest-exercise radionuclide ventriculography to compare 24 patients with dilated cardiomyopathy (13 patients had idiopathic cardiomyopathy, 11 had prior myocardial infarction) to 6 age-matched control subjects. The LVEF during exercise increased significantly in patients with idiopathic dilated cardiomyopathy compared with an insignificant increase in those with ischemic cardiomyopathy. On the basis of this study, the authors suggest that idiopathic cardiomyopathy can be distinguished from ischemic cardiomyopathy. It is, however, likely that patients with idiopathic dilated cardiomyopathy have variable LVEFs in response to exercise; in some patients LVEFs are increased during exercise, while in others they are decreased or maintained.[22]

At the moment, coronary angiography may be the only reliable means of distinguishing idiopathic from ischemic cardiomyopathy. I do not, however, believe that coronary angiography is justified in all patients with dilated cardiomyopathy. Although patients with ischemic cardiomyopathy appear to have a worse prognosis than those with idiopathic cardiomyopathy, the critical question for clinical decision-making is not whether ischemic cardiomyopathy is present, but whether there is evidence of residual reversible myocardial ischemia. A new defect in thallium-201 uptake or the redistribution of thallium-201 after exercise suggests reversible myocardial ischemia and requires further investigation by coronary angiography, antiischemic therapy or both. Although this approach may yield a number of false-positive results, (i.e., a reversible defect in thallium-201 uptake may occur in a patient with idiopathic dilated cardiomyopathy due to relative myocardial wall thinning), it generally avoids the need for coronary angiography in most patients with idiopathic dilated cardiomyopathy. Thus, the detection of reversible myocardial ischemia or a discrete LV aneurysm is more therapeutically important in preventing sudden cardiac death than the anatomic detection of diffuse coronary artery disease or myocardial scarring.

Ruling Out Left Ventricular Dyskinesis or Aneurysm

Evaluation for a possible discrete LV aneurysm is particularly important in a patient with dilated cardiomyopathy and ventricular arrhythmias. A recent study by Meizlish et al[23] suggested that a discrete area of LV dyskinesis or aneurysm formation in a post-infarction patient may be a more significant predictor of sudden cardiac death than the LVEF alone. In a group of 51 patients who had experienced anterior myocardial infarctions, 18 developed functional LV aneurysms. Although the LVEF was similar in both groups (27 ± 10% versus 31 ± 12%, respectively), 1-year mortality was significantly different. Those with an LV aneurysm had a 61% mortality rate at 1 year compared with only 19% in those without an aneurysm (p <0.001). Six of the 11 deaths (55%) in patients with aneurysm were sudden. In fact, an LV aneurysm in a patient with dilated cardiomyopathy and ventricular arrhythmias is one of the most significant preventable causes of sudden death. Resection of the aneurysm in conjunction with endocardial mapping and ablation of the ventricular arrhythmia has been effective in preventing sudden death in some patients.[24]

Ruling Out Occult Myocarditis

A recent prospective study by Vignola et al[25] clearly pointed out the need to detect occult myocarditis in patients with ventricular arrhythmias. No obvious cause for arrhythmia was found in 17 of 65 patients referred for electrophysiologic evaluation because of an episode of sudden cardiac death, ventricular tachycardia or complex ventricular ectopy. Twelve of these 17 patients underwent myocardial biopsy. Of these, 6 (50%) had evidence of lymphocytic myocarditis. There were no clinical characteristics that could have predicted the presence of myocarditis in these patients. All 6 subsequently received immunosuppressive therapy. After 6 months, these patients underwent repeat electrophysiologic evaluation while not receiving antiarrhythmic agents. No patient had ventricular arrhythmias, and none could be induced by electrophysiologic stimulation. On repeat myocardial biopsy, lymphocytic infiltration was absent, with varying degrees of fibrosis. While the exact incidence of lymphocytic myocarditis in patients with ventricular arrhythmias and LV dysfunction is uncertain, as is the role of immunosuppressive therapy in these patients, this study suggests that myocardial biopsy may be valuable in detecting occult myocarditis and in reducing the incidence of sudden cardiac death in patients without a clear cause for their arrhythmias. Myocardial biopsy may be especially useful in evaluating patients with recent onset cardiomyopathy. Dec et al[26] detected evidence of myocarditis in 18 of 27 patients with cardiomyopathy of less than 6 months duration. In patients who had dilated cardiomyopathy for less than 4 weeks, they found an 89% incidence of myocarditis. Patients with evidence of myocarditis on biopsy tended to show improvement in LVEF; however, neither histologic nor clinical features could be correlated to increases in LVEF, regardless of whether or not immunosuppressive drugs were used.

Myocardial biopsy may also detect occult eosinophilic myocarditis. While most instances of eosinophilic myocarditis are associated with peripheral eosinophilia, active myocarditis has also been noted in patients without peripheral eosinophilia.[27]

Myocardial biopsy should be considered in all patients with recent onset dilated cardiomyopathy in order to detect occult myocarditis. Myocarditis, however, may also be detected noninvasively by gallium-67 myocardial imaging.[28] In a series of 68 consecutive patients with idiopathic dilated cardiomyopathy who underwent myocardial biopsy and gallium-67 myocardial imaging, 6 patients (8%) had biopsy evidence of myocarditis.[28] Five of these 6 (87%) had positive gallium-67 myocardial images, indicating an inflammatory process within the myocardium. The incidence of positive gallium-67 myocardial imaging in patients with negative biopsies was only 14%. The incidence of myocarditis on biopsy in patients with a positive scan was 36% compared with only 1.8% in those with a negative scan. Gallium-67 myocardial imaging may therefore be a useful screening technique for detecting occult myocarditis in patients with dilated cardiomyopathy. However, the procedure is technically demanding and a relatively large number of false-negative results may occur in institutions that do not have considerable expertise with it. Until more experience is acquired in more centers, we prefer to rely on myocardial biopsies to detect occult myocarditis. It should be emphasized that biopsy interpretation also requires an experienced pathologist. Thus, while occult myocarditis may be an important reversible cause of idiopathic dilated cardiomyopathy and sudden cardiac death, its true role cannot be known until considerably more data are gathered in a large number of patients from several centers.

Myocardial biopsies in patients with dilated cardiomyopathy may, however, gain further acceptance pending confirmation of a recent study by Figula et al.[29] In their study, 42 patients with congestive cardiomyopathy were followed for a mean of 32 ± 20 months after myocardial biopsy. On follow-up, 20 patients (48%) showed hemodynamic deterioration; 5 died of progressive CHF. Twenty-two patients (52%) showed hemodynamic improvement or stabilization on follow-up; only 1 patient died of noncardiac cause. Endomyocardial biopsy with quantification of myofibrillar cell volume showed a 96% sensitivity and 94% specificity for predicting hemodynamic deterioration or death. In view of the potential prognostic and therapeutic information obtained from myocardial biopsy in patients with recent onset or unexplained cardiomyopathy, further systematic study of this technique is clearly indicated.

Determining Serum Electrolytes

Hypokalemia is common in patients with CHF treated with diuretics, and may predispose patients to digitalis-induced arrhythmias. Johannsson[30] found a 20% to 25% incidence of hypokalemia in patients with CHF. He also pointed out that oral potassium supplementation may not be effective in CHF patients due to poor intestinal absorption, poor compliance or both. Patients with CHF who are on a low salt diet and taking diuretics may also develop hypochloremic alkalosis, which must be corrected with potassium chloride.[31] In some patients, hypokalemia can only be ame-

liorated after administration of magnesium. Dyckner et al[32] used muscle biopsies to evaluate tissue magnesium levels and reported a 65% incidence of hypomagnesemia in patients with CHF treated with diuretics. Potassium-sparing diuretics, such as amelioride, triameterene or spironolactone, correct both hypokalemia and hypomagnesemia.

Hypokalemia and hypomagnesemia in patients with CHF may predispose to ventricular arrhythmias and sudden cardiac death, especially in patients receiving concurrent digitalis therapy. Recent studies have shown a good correlation between serum potassium levels and the frequency of ventricular arrhythmias in patients with acute infarction.[33] The high levels of serum catecholamines found in CHF patients could further aggravate this situation and drive potassium into the cells as a result of β_2-adrenergic stimulation. Burch et al[34] called attention to the cardiac causes of hypomagnesemia, including CHF. Hypomagnesemia can result in ventricular tachycardia, torsade de pointes, digitalis-induced arrhythmias and sudden cardiac death.

Of interest is a recent study by Kay et al,[35] which reviewed 32 patients with torsade de pointes. Antiarrhythmic agents such as procainamide, quinidine, disopyramide, mexiletine and amiodarone in conjunction with hypokalemia and hypomagnesemia were associated with the development of torsade de pointes. Serum drug levels were within the therapeutic range in 20 of 26 evaluated patients. Twenty of 32 patients had prolonged QT intervals, hypokalemia or hypomagnesemia before the administration of antiarrhythmics. These arrhythmias were not benign: 5 of 32 patients died as a direct result of torsade de pointes.[35] The exact role of hypokalemia and hypomagnesemia in the development of sudden cardiac death in patients with dilated cardiomyopathy can only be speculated. In the patient with CHF, a relatively high dose of diuretics, the concurrent use of digitalis, inadequate absorption of potassium supplements, high baseline catecholamine levels and a decreased threshold for ventricular fibrillation all predispose to sudden cardiac death. These factors suggest the need for more frequent monitoring of serum potassium and magnesium levels in CHF patients, and cautious administration of antiarrhythmic agents. The use of potassium-sparing diuretics should be considered in patients with a history of poor compliance to medication, electrocardiographic evidence of prolonged QT intervals, hypokalemia or hypomagnesemia. They are not indicated in patients with renal impairment or in combination with converting enzyme inhibitors, such as captopril, which predispose to hyperkalemia. It should also be emphasized that potassium-sparing diuretics may themselves predispose the patient to hyperkalemia and ventricular arrhythmias.

Assessing Neurohumoral Status

Recent studies have shown that baseline norepinephrine levels may have prognostic value in a patient with CHF.[36] Release of norepinephrine from myocardial stores may predispose the CHF patient to ventric-

ular arrhythmias and sudden cardiac death, especially in conjunction with ischemia or hypokalemia, or it may increase myocardial cytolysis with resultant progressive heart failure. Because agents that increase serum norepinephrine levels, such as nitroprusside or hydralazine, can predispose the patient to ventricular arrhythmias, agents, such as captopril, that do not increase serum norepinephrine levels will undoubtedly be used increasingly in the future.

Other neurohumoral agents, such as renin, vasopressin and atrial natriuretic factor, are also elevated in patients with CHF.[16,37] These agents in conjunction with altered prostaglandin metabolites and elevated serum catecholamine levels are probably important in the etiology of sudden cardiac death in the patient with CHF and ventricular arrhythmias. Interestingly, the greatest reduction in sudden cardiac death in patients with a history of CHF has been observed after treatment with β blockers. Patients with a history of CHF before infarction or at the onset of infarction who were treated with propranolol had a 47% reduction in sudden cardiac death on follow-up, compared with only a 12% decrease in sudden cardiac death in those without a history of CHF.[38] Similarly, still controversial data from Sweden suggest that β-adrenergic blockade can increase exercise capacity and cardiac function in patients with dilated cardiomyopathy.[39] Therefore, the evaluation and manipulation of neurohumoral status may help reduce the incidence of sudden cardiac death and possibly progressive heart failure as well in patients with dilated cardiomyopathy.

Detecting Mural Thrombus Formation

Mural thrombus formation is relatively frequent in patients with dilated congestive cardiomyopathy, especially in those with ischemic cardiomyopathy and discrete areas of LV dyskinesis. According to Fuster et al,[40] the incidence of thromboembolic episodes in patients with CHF was 18%. A mural thrombus can be detected by echocardiography, computed tomographic imaging and indium-111 myocardial imaging. Treatment with long-term anticoagulant therapy reduced the incidence of thromboembolic events in patients with CHF and should be standard therapy if not contraindicated.[40] The role of lytic therapy with intravenous streptokinase or tissue plasminogen activator must still be determined.

In summary, new diagnostic and therapeutic approaches are necessary to reduce the mortality of patients with CHF and ventricular arrhythmias. Nevertheless, our failure to decrease mortality in these patients may not entirely lie in the lack of effective treatment but rather in our failure to apply properly the diagnostic and therapeutic approaches now available. Efforts should be increased to detect potentially reversible causes of sudden cardiac death and progressive heart deterioration. The possibility of reversible myocardial ischemia, LV aneurysm and occult myocarditis must be ruled out. Greater effort is necessary to detect and correct hypokalemia, hypomagnesemia and neurohumoral abnormalities. Although potentially reversible causes of dilated congestive cardiomyopathy may be relatively infrequent, a more aggressive diagnostic approach is justified in an attempt to detect and correct those factors that may predispose the patient to progressive heart failure and sudden cardiac death.

References

1. Furberg C, Yusuf S. Does treatment of chronic heart failure with oral vasodilators improve survival? (abstr). Circulation 1984;70:suppl II:112.
2. Simonton C, Daly P, Kereiakes D, Sata H, Parmeley W, Chatterjee K. Survival in severe congestive heart failure treated with the new non-glyco sidic, non-sympathomimetic oral inotropic agents (abstr). Circulation 1984; 70:suppl II:673.
3. McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure in the Framingham study. N Engl J Med 1971; 285:1441-1445.
4. Gau GT, Goodwin JF, Oakley CM, Olsen EGJ, Rahimtoola SH, Raphael MJ, Steiner RE. Q-waves and coronary arteriography in cardiomyopathy. Br Heart J 1972;34:1034-1041.
5. Echeverria HH, Bilsker MS, Myerberg RJ, Kessher KM. Congestive heart failure: echocardiographic insights. Am J Med 1983;75:750-755.
6. Johnson RA, Palacios I. Dilated cardiomyopathies of the adult (part I and part II). N Engl J Med 1982;307:1051-1058 and 1119-1126.
7. Garcia R, Jennings JM. Pheochromocytoma masquerading as a cardiomyopathy. Am J Cardiol 1972;29:568-571.
8. Bashoor T, Basha HS, Cheng TO. Hypocalemic cardiomyopathy. Chest 1980;78:663-665.
9. Levine SN, Rheams CN. Hypocalcemic heart failure. Am J Med 1985;78: 1033-1035.
10. Greenspan AJ, Schaal SF. The "holiday heart": electrophysiologic studies of alcohol effects in alcoholics. Ann Intern Med 1983;98:135-139.
11. Schulze RA Jr, Rouleau JR, Rigo P, Bowers S, Strauss HW, Pitt B. Left ventricular function and ventricular arrhythmias in the late hospital phase of acute myocardial infarction. Circulation 1975;52:1006-1011.
12. Schulze RA Jr, Strauss HW, Pitt B. Sudden death in the year following myocardial infarction. Relation to ventricular premature contractions in the late hospital phase and left ventricular ejection fraction. Am J Med 1977;62: 192-199.
13. The Multicenter Postinfarction Research Group. Risk stratification and survival after myocardial infarction. N Engl J Med 1983;309:331-336.
14. Polak JF, Holman L, Wynne J, Calucci WS. Right ventricular ejection fraction: an indicator of increased mortality in patients with congestive heart failure associated with coronary artery disease. JACC 1983;2:217-224.
15. Baker BJ, Wilen MM, Boyd CM, Dinh H, Franciosa JA. Relation of right ventricular ejection fraction to exercise capacity in chronic left ventricular failure. Am J Cardiol 1984;54:596-599.
16. Diltz EA, Nicklas JM, Koller PT, Shenker Y, Pitt B, Grekin RJ. Elevated atrial natriuretic factor levels in patients with severe congestive heart failure (abstr). Circulation, in press.
17. Bigger JT Jr. Relation between left ventricular dysfunction and ventricular arrhythmias after myocardial infarction. Am J Cardiol 1986;57:8B-14B.
18. Francis GS. Development of arrhythmias in the patient with congestive heart failure: pathophysiology, prevalence and prognosis. Am J Cardiol 1986;57:3B-7B.
19. Bulkley RH, Rouleau JR, Whitaker JQ, Strauss HW, Pitt B. The use of thallium-201 for myocardial perfusion imaging in sarcoid heart disease. Chest 1977;72:27-32.
20. Dunn RF, Uren RF, Sadick N, Bautovich G, McLaughlin A, Hiroe M, Kelly DT. Comparison of thallium-201 scanning in idiopathic dilated cardiomyopathy and severe coronary artery disease. Circulation 1982;66:804-810.
21. Shen WF, Roubin GS, Hirasawa K, Choong Cy-P, Hutton BF, Harris PJ, Fletcher PJ, Kelly DT. Left ventricular volume and ejection fraction response in chronic congestive heart failure: difference between dilated cardiomyopathy and previous myocardial infarction. Am J Cardiol 1985;55:1027-1031.
22. Kirlin PC, Grekin R, Das S, Ballor E, Johnson T, Pitt B. Neurohumoral activation during exercise in congestive heart failure. Am J Med, in press.
23. Meizlish JL, Berger HJ, Plankey M, Errico D, Levy W, Zaret BL. Functional left ventricular aneurysm formation after acute anterior transmural infarction: incidence, natural history, and prognostic implications. N Engl J Med 1984;31:1001-1006.
24. Josephson ME, Harken AH, Horowitz LN. Long-term results of endocardial resection for sustained ventricular tachycardia in coronary disease patients. Am Heart J 1982;104:51-57.
25. Vignola PA, Aonuma K, Swaye PS, Rozanski JJ, Blankstein RL, Benson J, Gosselin AJ, Lister JW. Lymphocytic myocarditis presenting as unexplained ventricular arrhythmias: diagnosis with endomyocardial biopsy and response to immunosuppression. JACC 1984;4:812-819.
26. Dec GW Jr, Palacios IF, Fallon JT, Aretz HT, Millo J, Lee DC-S, Johnson RA. Active myocarditis in the spectrum of acute dilated cardiomyopathies. N Engl J Med 1985;312:885-890.
27. Glass HL, Abrams G, Das S, Pitt B. Eosinophilic myocarditis without peripheral eosinophilia: terminal event in idiopathic cardiomyopathy. Am

Heart J, in review.

28. O'Connell JB, Henkin RE, Robinson JA, Subramaman R, Scanton PJ, Gunnar RM. *Gallium-67 imaging in patients with dilated cardiomyopathy and biopsy proven myocarditis. Circulation 1984;70:58-62.*

29. Figulla HR, Rahlf G, Nieger M, Luig H, Kreuzer H. *Spontaneous hemodynamic improvement or stabilization and associated hemodynamic and biopsy findings in patients with congestive cardiomyopathy. Circulation 1985;71:1095-1104.*

30. Johannsson BW. *Hypokalemia in cardiac decompensation. Acta Pharmacol Toxicol 1984;54:suppl I:103-106.*

31. Schwartz WB, van Ypersele de Strihou C, Kassirer JP. *Role of anions in metabolic alkalosis and potassium deficiency. N Engl J Med 1968;279:630-639.*

32. Dyckner T, Wester PO. *Intracellular magnesium loss after diuretic administration. Drugs 1984;28:suppl I:161-166.*

33. Nordrehaug JE, Johannessen K-A, VonDer Lippe G. *Serum potassium concentration as a risk factor of ventricular arrhythmias in early acute myocardial infarction. Circulation 1985;71:645-649.*

34. Burch GE, Giles TD. *The importance of magnesium deficiency in cardio-vascular disease. Am Heart J 1977;94:649-657.*

35. Kay GN, Plumb VJ, Arciniegas JG, Henthorn RW, Waldo AL. *Torsade de pointes: the long-short initiating sequence and other clinical features: observations in 32 patients. JACC 1983;2:806-817.*

36. Cohn JN, Levine TB, Olivari MT, Garberg V, Lura D, Francis GS, Simon AB, Rector T. *Plasma norepinephrine as a guide to prognosis in patients with chronic congestive heart failure. N Engl J Med 1985;311:819-823.*

37. Francis GS. *Neurohumoral mechanisms involved in congestive heart failure. Am J Cardiol 1985;55:15A-21A.*

38. Goldstein S, Chadda K, Byington R. *The effect of propranolol on mortality and morbidity in patients with congestive heart failure: the BHAT experience (abstr). Circulation 1984;70:suppl II:II-23.*

39. Swedberg K, Hjalmarson A, Waasgstein F, Wallentin I. *Prolongation of survival in congestive cardiomyopathy by beta receptor blockade. Lancet 1979;1:1374-1386.*

40. Fuster V, Gersh BJ, Giuliani ER, Tajik AJ, Brandenburg RO, Frye RL. *The natural history of idiopathic dilated cardiomyopathy. Am J Cardiol 1981;47: 525-531.*