patient’s region. Attribution means that where appropriate, information contained on a Web site will be supported by clear references as to source and hyperlinks to that source. Additionally, the date when that source was last updated must be indicated (ie, timeliness of data). Justifiability specifies that any claims relating to the benefits/pesformance of a specific treatment, product, or service will be supported by appropriate, balanced evidence in the manner outlined under the “attribution” element of the HON code. Transparency of authorship addresses that the Web site will clearly provide information including contact informa-tion for all authors and the Webmaster of the site. Transparency of sponsorship makes obvious the identities of commercial and noncommercial organizations that have contributed funding services or materials for a site. Finally, the honesty in advertising and editorial policy element of the HON code speaks to the need to have a brief description on a medical site of the advertising and editorial policies of the site explicitly stated.

Despite the “dot bomb” economic downturn in the past 6 months, it is very clear that the WWW will continue to grow as an essential information delivery technology.3 Furthermore, we would expect that over the next few years, traditional sources of authoritative printed medical information, such as the American College of Chest Physicians, will develop and promulgate on-line standards of medical information for the benefit of providers and patients alike. Finally, as patient advisors, it will remain our growing responsibility and challenge to understand, interpret, and guide our patients and colleagues to the best of the WWW, to both improve the quality of on-line communication and insist on the broad adoption of quality standards of on-line medical journalism.

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Assessment of Prognosis in Idiopathic Dilated Cardiomyopathy

Determining the prognosis in each patient with idiopathic dilated cardiomyopathy (IDC) has been an important goal since the introduction of cardiac transplantation. Although heart transplants continue to be limited to critically ill patients, the triage of IDC patients will assume greater importance as the era of an implantable artificial heart nears. How successful are current approaches to identifying patients with high short-term mortality rates?

The New York Heart Association-rated class IV patient who experiences repeated hospitalizations and has a need for inotropic support is clearly at a high risk of death. Thus, the consideration for a heart replacement is straightforward. Most patients with IDC are not critically ill and do not require such an urgent intervention, yet perhaps 20% of such patients will die within 1 year. Early follow-up studies1–6 have identified a number of variables that are associated with an adverse outcome. Some of the better predictors were New York Heart Association class rating, increasing age, a low left ventricular ejection fraction (LVEF), high left ventricular filling pressures, a very dilated left ventricle, exercise peak oxygen uptake (VO2) of <11 to 16 mL/kg/min, marked intraventricular conduction delay (including a permanent pacemaker), and complex ventricular arrhythmias. Later studies that included echocardiography confirmed the importance of these factors and identified additional variables associated with adverse outcomes, including a relatively low left ventricular mass,7 the presence of moderate or greater mitral regurgitation,8 an increased left atrial size, right ventricular enlargement,9 and a reduced right ventricular ejection fraction.10 Echocardiographic parameters of diastolic function that reflect a high left atrial pressure were also predictive of adverse outcomes and included a high early diastolic mitral inflow velocity, a short early diastolic mitral inflow velocity deceleration time,11,12 and a reduced pulmonary venous inflow velocity during ventricular systole.13 A “Doppler index,” which was defined using the formula (isovolumic contraction time + isovolumic relaxation time)/ejection time, was introduced to assess both right and left ventricular function and, as would be anticipated, the reduced function of either ventricle identified patients with unfavorable outcomes.14,15

As each discipline examined patients with IDC, the number of variables associated with adverse outcomes or a high mortality rate grew. An increase
In the late potentials of the QRS complex, as seen in the signal-averaged ECG, was shown to be an independent predictor of all-cause cardiac death. The presence of chronic and excessive cardiac sympathetic stimulation implies an adverse prognosis, and can be identified by high serum levels of circulating catecholamines, a decrease in the heart rate variability during Holter monitoring, or down-regulation of the myocardial β-adrenergic receptors, as assessed by nuclear metaiodobenzylguanidine imaging. Ventricular tachycardia and complex ventricular arrhythmias during a 24-h Holter recording, when associated with a low LVEF, place patients at a higher risk of death. Markers of myocardial cell death, such as an elevation of serum troponin T levels, an increased ratio of creatine kinase MB2/MB1, and scintigraphic evidence of an abnormal myocardial uptake of a monoclonal antibody to myosin all identify IDC patients who are at high risk.

With the exception of peak VO_2, the many variables reviewed above assessed only resting cardiac function. Perhaps ventricles that are able to favorably respond to a transient inotropic stimulus (ie, contractile reserve) would be capable of long-term improvement and would be associated with a better prognosis. Conversely, the irreversibly damaged ventricle would not exhibit enhanced function, and the prognosis would be poor. The utility of assessing the contractile reserve of severely hypokinetic myocardial regions in patients with chronic ischemic heart disease is now well-established. Revascularization of the myocardial segments exhibiting contractile reserve leads to improved regional function. Whether evidence of contractile reserve in IDC patients also would identify those most likely to respond favorably to medical therapies has only been explored in the last 10 years. Dubois-Rande et al studied 36 patients and reported in 1992 that patients demonstrating an increase in left ventricular dP/dt with intracoronary dobutamine infusion had favorable responses to medical therapy. Subsequently, five reports involving a total of 223 patients have shown the utility of contractile reserve as an indicator of prognosis. Exercise was the inotropic stimulus in one study, and IV dobutamine infusion was used in the others. Protocols for the infusion of dobutamine differed, and the measurements used to assess contractile reserve varied. Nevertheless, the results of these studies are consistent in that patients exhibiting enhanced left ventricular function had better clinical outcomes over relatively short periods of follow-up (ie, 6 to 36 months). Interestingly, the report by Kitaoka et al found that the LVEF during dobutamine infusion and the LVEF at follow-up were closely related.

In this issue of CHEST, Droždž and his colleagues (see page 1216) extend these observations in a larger group of 77 patients who were observed for a remarkably long (mean ± SD) period of 63 ± 7 months. The failure of ventricular function to improve during dobutamine infusion at 10 μg/kg/min was defined as either a left ventricular end-systolic volume of > 150 mL or no decrease in the left ventricular end-diastolic volume. Importantly, the failure to show improved ventricular function was a significant predictor of a fatal outcome and replaced other known clinical and echocardiographic predictors of death in a multivariate analysis. The clinical variables of male gender and atrial fibrillation remained potent indicators of a poor outcome.

Recently, Scrutinio et al reported their studies of contractile reserve in 60 IDC patients. They measured contractile reserve as the percentage change in the end-systolic volume index during dobutamine infusion, and this parameter was significantly related to the patient’s exercise capacity, which was expressed as peak VO_2. Either a small percentage decrease in the end-systolic volume index or a low peak VO_2 was predictive of the occurrence of clinical events. Unfortunately, this study was underpowered to assess the utility of these variables to predict death.

Despite all these studies, the relative value of each test remains unclear, and we continue to be uncertain as to which tests should be performed routinely. The majority of the reported observations have been in relatively small numbers of patients, the variables that were measured differ, selection bias cannot always be discerned, definitions of unfavorable outcomes have differed, and the follow-up intervals generally have been brief. Nevertheless, there are some common themes running through these and other studies that are consistent with clinical experience. A favorable prognosis is likely under the following conditions: (1) when the diseased left ventricle exhibits improved systolic function either during inotropic stimulation or in association with treatment; (2) when exercise capacity, as measured by peak VO_2 or the results of a 6-min walk test, is reasonably preserved; (3) when signs of a high left atrial pressure are absent; (4) when there is no evidence of a continued hypersympathetic state; and (5) when there are no major arrhythmic events. Although the LVEF is useful in assessing the prognosis for groups of patients, it is less helpful as a single variable in assessing the prognosis of an individual patient.

Recognition of the IDC patient who is at very high risk for death in the near term is more problematic. Confidence in our ability to identify these patients correctly will come when the many univariate predictors of death are applied to a large cohort in a
multicenter trial. This will allow a robust multivariate analysis of the relative utility of our many tests and should lead to a more focused and accurate evaluation of each patient with IDC. A measure of the contractile reserve of the left ventricle is very likely to be one of the important variables in predicting outcome. The best indicator of contractile reserve needs to be identified, but it is probable that changes in end-systolic dimensions or volume will provide useful prognostic information.

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Balancing Self and Patient in the Physician-Patient Relationship

In this issue of CHEST (see page 1337), Miller and Shorr examine the ethics of clinical trials funded by pharmaceutical companies and performed by practicing physicians. The authors describe a seven-point framework for evaluating the ethical soundness of any clinical trial. Then they use that framework to critique a recent company-sponsored study comparing a new inhaled corticosteroid, a proven inhaled corticosteroid, and a placebo for treating moderate persistent asthma. Miller and Shorr argue convincingly that, by withdrawing patients with stable asthma from proven treatment and randomizing some to placebo this study risked patients’ serious clinical deterioration.

So why was the study ever approved? Miller and Shorr speculate that self-interest was the driving force: the sponsoring company may have expected marketing advantages from the results; the participating physicians, fees for subject recruitment.

To be sure, self-interest motivates everyone at times. It is an indelible part of human nature. Especially in capitalistic cultures, self-interest rules the marketplace and is expected of companies. Business pursues profit, and customers know to protect their own interests. But physicians are held to a different standard.

Certain sensitive relationships involving unequal parties demand a higher motivation than self-interest. The stronger party has a special duty to ignore other stakeholders in the decision and know their perspective. Consider the practicing physician as a moral agent deciding whether to recruit patients into this asthma study. Using his or her actual values, the physician judges such recruitment from the perspectives, say, of the participating physician, a company official, a subject receiving active drug, a subject receiving placebo, and other asthmatics. The stakeholders most likely to be harmed deserve careful consideration. This asthma study obviously risked most harm to the subjects receiving placebo. As the study report attests, the harm turned out to be significant. Compared to subjects receiving any active drug, subjects receiving placebo had four or more times the risk of intervention failure (4 to 11% vs 44%, respectively) and more than twice the risk for adverse events (2 to 4% vs 9%). And clinical deterioration on placebo occurred quickly—in a median time of just 40 days. A physician’s values, based on the fiduciary duty to patients, typically include continuity of effective therapy and avoidance of unnecessary medical risks. Such values applied from the perspective of a subject receiving placebo argue strongly against the physician’s recruiting patients into this study.

The golden-rule test helps the moral agent recognize other stakeholders in the decision and know when the agent’s own values are at risk from different stakeholders’ perspectives. But the golden-rule test is also mired in the agent’s values. Unique combinations of personality and experience make each person’s values somewhat idiosyncratic. For instance, the physician’s particular abilities, aspirations, training, and experiences can make his or her values different from patients’. So how can the physician learn patients’ real values and incorporate them into decisions such as the one about recruiting subjects for this asthma study?

The publicity test provides a way. With this test, the moral agent seeks feedback by “publicizing” any tentative decision before implementing it. A weaker version of the test requires the agent simply to imagine the values and feedback of others. (The American College of Physicians advocates such a