plex and heterogeneous metabolic disorder of absolute or relative insulin deficiency, causing microvascular and macrovascular disease with subsequent serious end-organ complications.

Until recently, convincing evidence documenting benefits in preventing diabetic complications by the tight control of diabetes was lacking. Results from two well-designed long-term studies, the Diabetes Control and Complications Trial and the Stockholm Diabetes Intervention Study, now show that intensified insulin treatment of patients with type I or insulin-dependent diabetes mellitus (IDDM) leads to a substantially reduced frequency of retinopathy, nephropathy, and neuropathy. These studies showed a dramatic reduction of most diabetic complications in the range of 30% to 60% by using intensified insulin treatment. Although specialized diabetic centers that have the appropriate multidisciplinary support team are generally more successful in implementing intensified treatment, appropriately trained and motivated primary care physicians should be able to achieve comparable results.

The intensified treatment regimen of insulin includes keeping the fasting and premeal serum glucose levels between 4.4 and 6.7 mmol per liter (80 and 120 mg per dl) and the two-hour postprandial serum glucose level under 10.0 mmol per liter (180 mg per dl). The glycosylated hemoglobin should be kept within 10% of the upper limit of the normal range. To avoid hypoglycemia, serum glucose levels should be maintained at or above 3.0 mmol per liter (55 mg per dl). Continuous subcutaneous insulin infusions or more frequent insulin injections are required to achieve this control. The short-acting insulin can be given just before each meal and the intermediate-acting insulin given at bedtime—resulting in three to four insulin injections per day compared with the more conventional one to two injections. The yearly cost of intensified insulin treatment has been estimated to be twice that of standard therapy, but the potential cost savings from preventing diabetic complications are immense.

Based on these more recent findings, it is now generally conceded that intensified insulin treatment is indicated in pregnant women with diabetes, patients with newly diagnosed IDDM, patients with uncomplicated IDDM with a life expectancy greater than ten years, and children. Intensified insulin treatment is contraindicated in patients with unstable proliferative retinopathy, advanced nephropathy (that is, unmistakable proteinuria), a life expectancy of less than ten years, an inability to self-monitor adequately, severe recurrent hypoglycemia or hypoglycemia without warning, coronary artery or cerebrovascular disease, and those who are noncompliant.

Controversy still exists concerning the efficacy of intensive hypoglycemic therapy (by insulin or oral sulfonylurea agents) in patients with type II or non-insulin-dependent diabetes mellitus (NIDDM). Caution should be used in extrapolating from studies designed for patients with IDDM, particularly with regard to the possible atherogenic complications arising from the hyperinsulinemic states observed in patients with NIDDM. Proper diet, exercise, and weight reduction still remain the cornerstone treatment methods for patients with NIDDM. In addition, for all patients with diabetes (both type I and type II), aggressive treatment of hypertension, especially using the angiotensin-converting enzyme inhibitors, has been shown to delay or prevent nephropathy, and laser photocoagulation has been successful in substantially reducing the incidence of blindness due to diabetic retinopathy.

Clearly in selected patients with IDDM, early intervention and intensified insulin treatment will substantially decrease the incidence of diabetic complications and should be implemented if at all possible. In fact, any important reduction in the levels of glycosylated hemoglobin will benefit patients with IDDM—whether or not euglycemia is reached. Because there is now clear evidence of effective preventive therapies, clinicians should revive their efforts in appropriately treating their patients. Patients with diabetes now have reason to be more optimistic about their future, which should be increasingly free from many of the devastating complications of diabetes mellitus.

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Pharmacologic Stress Echocardiography

NUMEROUS NONEXERCISE METHODS have been developed to evaluate ischemic heart disease in patients who are unable to achieve an adequate heart rate and blood pressure response with exercise. Most tests use pharmacologic agents such as dipyridamole, adenosine, or dobutamine to induce ischemia. Ischemia can be detected by electrocardiography (ECG), nuclear perfusion scans, or echocardiography. The accuracy of ECG changes alone is limited. Adding nuclear imaging improves accuracy but is expensive and time-consuming. Recent literature has suggested that a combination of dobutamine and two-dimensional echocardiography is a reasonable and economical alternative for detecting and evaluating coronary artery disease.

Dobutamine is a sympathomimetic amine that has primarily a β_1 effect. At low infusion doses (<10 μg per kg per minute), dobutamine has a predominant inotropic effect. Doses greater than 10 μg per kg per minute can also cause substantial tachycardia. Hence, dobutamine increases myocardial oxygen demand by causing an increase in contractility and heart rate. In the presence of coronary artery stenosis, myocardial oxygen supply fails to increase sufficiently, and ischemia is produced. Dobutamine stress echocardiography incorporates the use

of two-dimensional echocardiographic wall-motion analysis at baseline and during increments of intravenous dobutamine infusion. If an adequate chronotropic response (heart rate ≥ 85% of predicted maximum) is not achieved, small aliquots of atropine sulfate are administered intravenously to augment the heart rate further. Heart rate, echocardiographic images, blood pressure, and an ECG are recorded at the end of each stage. Myocardial ischemia is detected if substantial ST segment changes develop or a regional wall-motion abnormality is seen on two-dimensional echocardiography. Interpretation of stress echocardiography studies has been further enhanced by digital technology, which displays the images side by side for easy comparison. Diagnostic studies can be obtained in most patients, but may be limited by inadequate images or adverse side effects.

The specificity and sensitivity of detecting the presence of coronary artery disease by dobutamine stress echocardiography are comparable to exercise-stress nuclear studies when done by experienced laboratory technicians. The overall sensitivity and specificity of detecting coronary artery disease in patients with normal resting regional wall motion are 87% and 91%, respectively. The sensitivity increases to 97% in patients with multiple vessel disease. By localizing the region of inducible myocardial abnormalities, two-dimensional echocardiography can also identify a stenosed major coronary artery.

Dobutamine stress echocardiography has been used in evaluating patients after myocardial infarction for the detection of residual viable myocardium. Immediately after a prolonged ischemic insult, it is important to distinguish between necrotic and stunned but viable myocardium. This question becomes important clinically in determining the need for revascularization procedures. Low-dose dobutamine (5 to 10 μg per kg per minute) improves regional myocardial function in the area of viable myocardium but not in an area of myocardial necrosis.

The noninvasive detection of multivessel coronary artery disease and residual jeopardized myocardium is essential after myocardial infarction. If the patient has multivessel disease, dobutamine stress echocardiography will show a regional wall-motion abnormality in an area remote to the primary infarct site. Substantial residual stenosis in an infarct-related artery results in worsening of the preexisting regional myocardial abnormality. In addition, patients with an abnormal dobutamine stress echocardiogram after myocardial infarction have a higher incidence of future cardiac events compared with those who had a normal study.

Dobutamine stress echocardiography can be used to stratify the degree of risk in patients who are referred for a noncardiac vascular surgical procedure. The absence of an inducible new wall-motion abnormality with dobutamine stress echocardiography is an excellent negative predictor for postoperative cardiac events. A positive test, however, does not necessarily predict the development of postoperative cardiac complications.

The safety of dobutamine stress echocardiography has been shown in a large series of patients. Noncardiac side effects are usually minor and include nausea, anxiety, headache, and tremor. Cardiac side effects such as angina and supraventricular and ventricular arrhythmias do occur, but are usually well-tolerated and rarely require treatment. In more than 1,000 patients who have had dobutamine stress echocardiography, serious complications from myocardial ischemia did not occur. Symptomatic ischemia or arrhythmias were effectively treated with test termination, sublingual nitroglycerin, or short-acting β-blocker drugs.

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Tuberculosis and Human Immunodeficiency Virus Disease

THE ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS) epidemic has exposed persons with the human immunodeficiency virus (HIV) and those who care for them to new dangers from an old pathogen, tuberculosis. Individual and public health risk can be reduced by conscientious adherence to reasonable exposure precautions, early screening, and informed selection of antituberculous regimens to treat both exposure and active disease.

It is estimated that 3 million people worldwide are infected with both *Mycobacterium tuberculosis* and HIV. In the United States, 5% to 10% of the 1 million persons infected with HIV are also infected with *M tuberculosis.* This rate is probably higher in areas with large homeless, injection drug using, or immigrant groups. The increasing incidence of tuberculosis (TB) in the United States since 1984 is generally attributed to cases associated with the AIDS epidemic. Further, in recent outbreaks on the East Coast, 96% of cases of multidrug-resistant TB occurred in HIV-infected persons. Unlike most opportunistic pathogens, *M tuberculosis* is contagious and causes potentially serious illness in immunocompetent as well as immunocompromised hosts.

Nosocomial transmission of tuberculosis to both staff and patients has been well documented. Of particular concern is the transmission of TB or multidrug-resistant TB (infection with *M tuberculosis* resistant to both isoniazid and rifampin) to patients and health care workers with HIV. Tuberculosis in HIV-infected hosts rapidly progresses, disseminating to extrapulmonary sites in as many as 70% of patients. DNA analysis of *M tuberculosis* organisms has shown that primary TB developed within five months of exposure in 37% of HIV-infected persons exposed to a source patient, compared with the 2% to 4% of immunocompetent contacts in whom TB develops within a year of exposure. Of patients with advanced HIV dis-