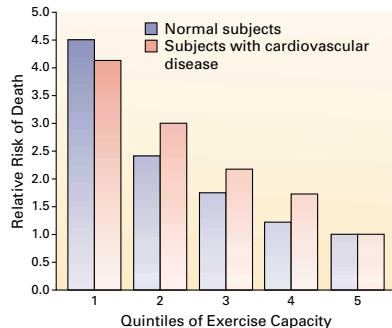




# This Week in the Journal

March 14, 2002



## Exercise Capacity and Mortality

In this study, more than 6000 men, some with and some without cardiovascular disease, underwent treadmill exercise testing and were followed for six years. Exercise capacity, as measured in metabolic equivalents, was a strong predictor of overall mortality, whether or not there was clinical evidence of cardiovascular disease.

*The findings, which demonstrate a strong association between reduced exercise capacity and higher mortality, are subject to two different interpretations. One is that reduced exercise capacity is simply a marker of a higher risk of death. The other is that reduced exercise capacity is part of the chain of causation and that increasing physical fitness through regular exercise may reduce mortality.*

see page 793 (editorial, page 852)

*“Impaired glucose tolerance is highly prevalent among children and adolescents with severe obesity.”*

## Impaired Glucose Tolerance in Obese Children and Adolescents

Childhood obesity, now epidemic in the United States, has been accompanied by an increased prevalence of type 2 diabetes among children and adolescents. This study used the two-hour oral glucose-tolerance test, along with measurements of insulin and C peptide, to identify impaired glucose tolerance. Impaired glucose tolerance was present in 25 percent of obese children and 21 percent of obese adolescents; silent type 2 diabetes was identified in 4 percent of obese adolescents.

*This study suggests that insulin resistance is an important risk factor linked to the development of impaired glucose tolerance in severe childhood obesity.*

see page 802 (editorial, page 854)

## PERSPECTIVE

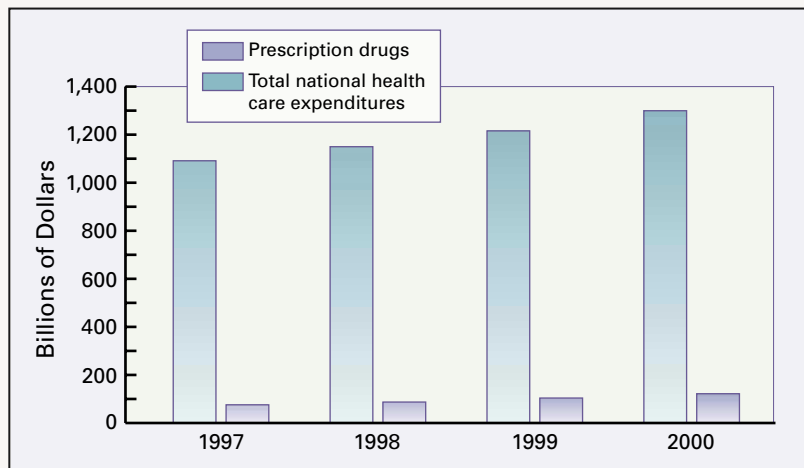
## The Prescription-Drug Problem

The soaring cost of prescription drugs has caused two interrelated problems — the expense for those who can afford to pay for them and the limited access to medications for those who cannot. These problems are particularly severe for the elderly and people with chronic illness.

From 1999 to 2000, spending for prescription drugs grew by 17.3 percent, the sixth consecutive year with a double-digit increase (Fig. 1). The rate of growth is greater than for any other health service. There are many reasons for this, including the introduction of new treatments and the aging of the population. Direct-to-consumer advertising by drug companies has also fueled greater use of newer medications, which often cost more than older drugs.

About a quarter of the nation's 40 million Medicare beneficiaries have no prescription-drug coverage. Large health insurers recruited the elderly into Medicare health maintenance organizations by promising them free prescriptions. Now they are raising copayments and scaling back coverage, blaming rising drug costs and inadequate federal payments. Unless current trends change — and there is no expectation that they will — more patients will have to choose between buying medications and buying food or paying their rent.

In this issue of the *Journal*, two studies provide information about approaches to cost control. The report by Schneeweiss et al. is about reference pricing of drugs in British Columbia, Canada (see pages 822–829). Under reference pricing, insurance fully covers the cost



**Figure 1.** Growth of Health Care Expenditures in the United States. Data are from the Centers for Medicare and Medicaid Services.

up to the reference price for medications within a specific class, and patients pay the extra cost of more expensive medications. The assumption is that costs can be lowered without detrimental clinical effects if physicians prescribe less expensive alternatives.

The other report, by Lewis et al., is about a prescription-drug discount program for Medicare beneficiaries in California (see pages 830–835). Similar programs are being considered in other states and nationally. The study found that although the mandated discounts offer substantial savings, they are not always being offered, particularly by independent pharmacies and pharmacies in low-income neighborhoods.

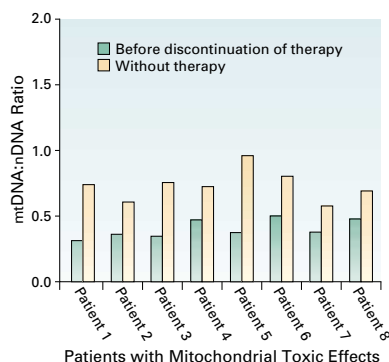
Democrats and Republicans in Washington, D.C., have promised to improve access to prescription drugs. In his State of the Union address in January, President George W. Bush asked Congress to join him to “give seniors a sound and modern Medicare system that includes coverage for prescription drugs.” But given the fragile economy, the cost of the war on terrorism, and intense lobbying by the pharmaceutical industry and other interest groups, the prospects are uncertain.

Some states have enacted their

own programs. Later this year, California plans to start a second prescription-drug discount program. The goal is to convince pharmaceutical companies to offer additional rebates voluntarily to the elderly and the disabled for commonly used drugs. Michigan and Florida are seeking price concessions from manufacturers in exchange for including their products on lists of preferred drugs. Maine and Vermont have enacted laws to extend discounts from their Medicaid programs to the rest of the elderly and the uninsured. The industry organization Pharmaceutical Research and Manufacturers of America (PhRMA) has challenged some of these programs in court, and the pharmaceutical industry is promoting alternatives to more state or federal regulation. One large company, for example, is planning to offer its drugs to elderly people with low incomes for \$15 a month for each prescription.

In the United States, patients who cannot afford to pay for their medications face difficult decisions. These difficult decisions will remain until prescription-drug coverage is considered an essential part of health insurance and health insurance is available to all.

ROBERT STEINBROOK, M.D.



### Mitochondrial DNA and Nucleoside Toxicity in HIV-Infected Patients

This study analyzed changes in mitochondrial DNA relative to nuclear DNA in the peripheral-blood cells of patients infected with the human immunodeficiency virus (HIV). Symptomatic hyperlactatemia during therapy with nucleoside analogues was associated with a marked reduction in the relative amount of mitochondrial DNA, as compared with that in both uninfected controls and untreated, HIV-infected controls. In eight patients studied longitudinally, a decline in the relative amount of mitochondrial DNA preceded the increase in lactic acid.

*Nucleoside analogues can induce toxic effects on mitochondria by inhibiting DNA polymerase  $\gamma$ . The novel assay used in this study may provide a practical way to screen for this important form of toxicity, which can develop during treatment of HIV infection.*

see page 811

*“After reference pricing was implemented, there was no increase in . . . drug discontinuations.”*

### Special Article: Reference Pricing for Angiotensin-Converting–Enzyme Inhibitors

Reference pricing is a potential cost-control mechanism for prescription drugs. For medications within a specific class, health insurance typically covers the cost up to the reference price. For more expensive medications, patients pay the extra cost. This study examined the effects of reference pricing for angiotensin-converting–enzyme inhibitors, which was introduced in British Columbia, Canada, in January 1997. It found little evidence that patients stopped treatment or that health care utilization or costs increased.

*The issues of concern about reference pricing for prescription drugs include the potential for patients to switch to less effective medications, to stop taking their medications, to see their physicians more often, or to be hospitalized more frequently. This study did not substantiate such concern.*

see page 822

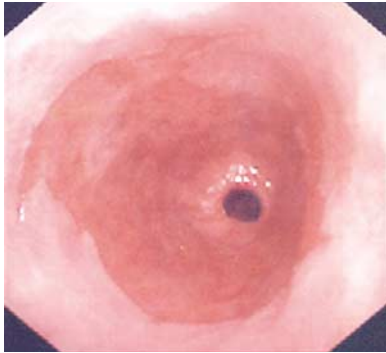


### Special Article: Prescription-Drug Discounts for Medicare Beneficiaries

Many Medicare beneficiaries lack insurance for prescription drugs and have difficulty paying for their medications. This study examined the compliance of pharmacies with a prescription-drug discount program for Medicare beneficiaries that was enacted in California in 1999. The investigators found that although 75 percent of the 494 pharmacies that were studied complied with the discount program, but only 45 percent offered the discount before it was specifically requested.

*In the absence of action by the federal government, many states are taking the initiative in making prescription drugs more affordable for Medicare beneficiaries. The results of this study suggest that, although a program that ties drug prices to rates in the Medicaid program offers substantial savings, many beneficiaries may not be receiving the specified discounts.*

see page 830 (Perspective, page 790, editorial, page 855)

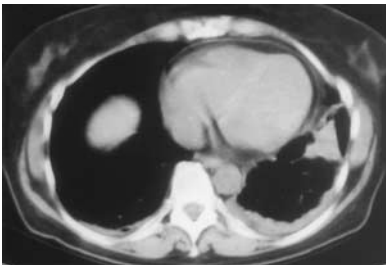


### Clinical Practice: **Barrett's Esophagus**

A 55-year-old man has had frequent heartburn for more than 10 years. Endoscopy reveals columnar epithelium lining the distal 5 cm of the esophagus. Biopsy specimens show specialized intestinal metaplasia with inflammation and possible dysplasia. How should this patient's condition be managed?

*This article reviews strategies for the management of Barrett's esophagus, which may predispose patients to esophageal carcinoma.*

**see page 836**



### Case Records of the Massachusetts General Hospital

A 56-year-old woman had pleuritic left-sided chest pain and was admitted to the hospital because of a persistent left-sided pleural effusion.

**see page 843**

*“Small, soluble molecules that can enter cells and specifically influence the production of T-bet could have considerable clinical value.”*

### Clinical Implications of Basic Research: **A New Element in the Mechanism of Asthma**

Type 2 helper T (Th2) cells, a type of CD4 T cell, trigger allergic inflammation and the production of antibodies. Type 1 helper T (Th1) cells produce interferon- $\gamma$ , which suppresses Th2 cells. Th2 cells have a prominent role in asthma. T-bet, a transcription factor required for the production of interferon- $\gamma$ , was found in a recent study to be lacking in lymphocytes from the bronchi of patients with asthma, and asthma developed in mice with experimentally disabled *T-bet* genes.

*T-bet is a key element in maintaining the balance between Th1 and Th2 cells. The absence of detectable T-bet in the bronchial lesions of patients with asthma suggests a potential new approach to the treatment of the disease.*

**see page 857**