may be helpful in some patients with intermittent claudication.

Patients should be considered for some type of intervention if they develop rest pain, ischemic ulcerations that will not heal, or have intermittent claudication that interferes with their livelihood or lifestyle.

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AGGRESSIVE PREVENTION IS KEY TO OSTEOPOROSIS CONTROL

The diagnosis and treatment of osteoporosis are controversial. Although forearm densitometry is widely used, its value is questionable; the currently approved treatment modalities—calcium, vitamin D, and estrogen supplementation—all stabilize existing bone density, but do very little to stimulate new growth. Sodium fluoride appears to cause a linear increase in skeletal density, but there are unresolved questions about the effects of long-term use. Given this somewhat grim outlook, prevention remains the best way to control the disease.

DIAGNOSIS

Bone densitometry of the forearm, which measures mainly cortical bone density, was advocated at one time as a screening method for osteoporosis. However, measurement of trabecular bone by dual photon absorptiometry (DPA) or quantitative computed tomography (CT) is more sensitive, because trabecular bone is lost earlier and at a faster rate. The primary value of densitometry is to monitor treatment designed to stimulate bone growth and identify patients at risk. It is superfluous for diagnosis in older patients who already have radiographic evidence of osteoporosis, but it has great value in high-risk middle-aged asymptomatic patients. In this population group, bone loss is better measured in the lumbar region, where trabecular bone is lost earliest.

CT is diagnostic, but it is expensive and impractical for routine office practice. DPA machinery can be acquired for a fraction of the cost of CT equipment.

THERAPY

Most therapy in use today stabilizes existing bone density. A few experimental modalities stimulate new bone growth, but these do not correct the destruction of osteoporotic bone. Rather, they stimulate the growth of new bone over the existing framework which, in the case of osteoporosis, is weak.

Calcium

The usual calcium intake for women age 35 and older is 500 mg/d; yet the postmenopausal woman needs 1,500 mg/d, and men and premenopausal women should consume 1,000 mg/d. If dietary calcium is inadequate, then hormonal systems draw on the bone to meet daily calcium requirements. Adequate dietary calcium will block this hormonal "robbing" of the skeleton.

Calcium alone will not protect the skeleton of a woman in early menopause. Although calcium is somewhat protective of cortical bone, it has little effect on trabecular bone, which is estrogen sensitive.

Estrogen

Estrogen is the best modality for maintaining skeletal integrity in the early menopausal years. Women who are not on estrogen supplementation have a decrease in bone density. Estrogen therapy will help stabilize bone mass at its existing level, but it must be continued indefinitely. Upon discontinuation, bone mass deteriorates rapidly. Estrogen therapy has little protective value when begun in late menopause because so much bone may have already been lost. But excessive bone loss may not have occurred; density measurements can determine this.

Sodium fluoride

Long-term sodium fluoride therapy causes a linear increase in bone density at dosages ranging from 40 to 80 mg/day. Gastrointestinal side effects—primarily nausea and vomiting—are largely eliminated by a new formulation that is now being studied. However, we do not have all the answers regarding the consequences of long-term use. To minimize the risk, serum fluoride levels should be maintained at 90–195 ng/ml. Sodium fluoride appears to have little efficacy in the prevention of hip fractures, but it may help to prevent spinal fractures.

PREVENTION

The best treatment is prevention, which should begin in the early teenage years with adequate dietary calcium and reasonable physical activity. Strong bones and a vigorous lifestyle in the early years should enhance the efficacy of estrogen in the menopausal years.

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EVALUATING TREATMENT OPTIONS FOR CHRONIC LIVER DISEASE

Newer options for treating chronic liver disease are accepted by most experts, and have found their way to many internists' offices. Nevertheless, they represent a grey area, in that they have yet to appear in standard textbooks.

Three areas are of particular interest: the use of colchicine to treat primary biliary cirrhosis (PBC); alpha interferon for the treatment of chronic non-A non-B hepatitis; and nadolol therapy to prevent first variceal bleeds.

TREATING PRIMARY BILIARY CIRRHOSIS

Despite a limited number of studies that demonstrate efficacy, colchicine has been accepted for five or six years for treatment of primary biliary cirrhosis. The beneficial effects of colchicine include decreased collagen synthesis and increased collagenase activity. The drug is also safe and inexpensive. In a recent study (Kaplan et al. N Engl J Med 1986; 315:1448–54) that compared colchicine, 0.6 mg bid, with placebo, the 45 patients who received the drug showed improvements in serum albumin, bilirubin, alkaline phosphatase, cholesterol, and aminotransferases. The cumulative mortality after four years of study was 21% in the colchicine group *v* 47% in the untreated patients.

Ursodeoxycholic acid also is potentially useful for treatment of primary biliary cirrhosis. The rationale is that the underlying cause of primary biliary cirrhosis is an autoimmune process, and the accumulation of bile acids in portal areas may contribute to worsening of the disease. The replacement of these bile acids by ursodeoxycholic acid may lead to improvement in liver lesions. A recent trial (Poupon et al. Lancet 1987;1:834–6) of 15 patients showed improvements in alkaline phosphatase, transaminases, bilirubin, and pruritus, but no change in histology.

The Cleveland Clinic Foundation is now formulating a trial that will compare colchicine with ursodeoxycholic acid.

INTERFERON

Alpha interferon may be helpful in patients with chronic non-A non-B hepatitis. A recent multicenter trial (Davis et al. Hepatology 1989;9:in press), that included the Cleveland Clinic Foundation, addressed this question. Patients in one group received either 1 million or 3 million units of alpha interferon three times weekly for 24 weeks; treatment was delayed in the second group. A preliminary analysis showed marked improvement in SGPT in the treatment group, from 175 before therapy to 95 after treatment. SGPT levels normalized in 36% of the treatment group, compared to 5% of the delayed therapy group. Improvement was unlikely in patients who did not respond within 10–12 weeks. Unpublished data suggest that the lower dosage may be inadequate.

In patients with chronic active hepatitis B, alpha interferon appears to eliminate viral replication in some patients. Those patients who have active disease characterized by e antigen positivity and higher SGPT and SGOT levels are more likely to respond to therapy than are homosexuals or patients with minimally elevated enzymes, childhood onset of disease, and HIV positivity. High-dose prednisone therapy, which temporarily worsens the disease, seems to enhance the effects of alpha interferon.

Despite the potential for benefits, interferon is not easy to use. Most patients who take it have a flu-like illness for the first week or two; depression may warrant cessation of therapy; and leukopenia is potentially dangerous. The drug, which is expensive, must be administered parenterally.

PREVENTION OF FIRST VARICEAL BLEEDS

The mortality from bleeding esophageal varices may be as high as 60%–65%.

With proper patient selection, beta blocker therapy has the potential to prevent first bleeds because it re-