duces portal pressure in patients with alcoholic cirrhosis. In patients considered to be good risks (no ascites, Childs Class A), propranolol therapy is associated with less bleeding, but it does not significantly affect survival. The drawbacks of propranolol therapy are side effects and its reliance on hepatic metabolism for elimination.

Nadolol may be a more logical choice because it does not rely on hepatic elimination. A recent study (Ideo et al. Hepatology 1988;8:6–9) compared nadolol (30 patients) with placebo or ranitidine (49 patients). Nadolol was associated with significantly fewer episodes of bleeding, and endoscopic evaluation showed reduced variceal size in 63% of the nadolol-treated patients, compared to only 29% of control patients. Only 3% of the patients withdrew because of side effects—a much lower figure than observed in propranolol studies.

Although beta blocker therapy may benefit patients who have large esophageal varices that have never bled, the effect on mortality is less clear. For patients who are at the terminal end of disease (Childs Class C), transplantation may be the more appropriate course.

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METHOTREXATE TREATMENT OF RHEUMATOID ARTHRITIS

Dihydrofolate inhibitors including methotrexate (MTX) have been used to treat inflammatory arthritis since 1951. Following numerous reports of retrospective and prospective open trials in the late 1970s and early 1980s, five controlled, double-blind studies have confirmed its effectiveness as treatment for rheumatoid arthritis. In October 1988 the FDA approved methotrexate for that indication.

MTX is given in pulse fashion, preferably as one oral dose (7.5–15 mg) each week. Clinical improvement of rheumatoid disease is often seen within 2–4 weeks and plateaus at about six months. Because MTX is not significantly metabolized in the liver, and its half-life depends almost entirely on renal excretion, patients with elevated serum creatinine should not be given the drug.

Mild, acute adverse effects include nausea, diarrhea, minor alopecia, and oral ulcers, which occur in 10%–40% of patients, depending on the length of follow-up. These effects are usually dose related and respond to manipulation of the dose. Cytopenia is rare, occurring in less than 1% of patients reported. Acute pulmonary toxicity, which may occur in as many as 6% of patients in one report, is worrisome and does not seem to be dose related. Long-term use can result in hepatic fibrosis in a small number of patients treated for rheumatoid arthritis. For this reason, alcoholic beverages are proscribed for patients receiving the drug.

Controversy still exists in the medical literature regarding the necessity and timing of liver biopsy in patient follow-up, the mechanism(s) of action of the drug in rheumatoid arthritis, and its place on the treatment pyramid (whether it should be considered at the same time gold therapy is initiated or only after failure or intolerance to gold therapy). As further metabolic and prospective comparison studies are reported, the answers to these issues will become clearer.

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