

JOHN M. BOZDECH, MD, AND WILLIAM D. CAREY, MD, EDITORS

Gastroenterology: ongoing challenges in diagnosis and therapy

CANCER RISK IN BARRETT'S ESOPHAGUS PATIENTS

The presence of Barrett's esophagus increases the risk of esophageal adenocarcinoma by 30- to 125-fold. Nearly half of the patients with Barrett's esophagus and adenocarcinoma have no antecedent symptoms of gastroesophageal reflux disease. The most reliable sign for predicting the development of cancer in these patients is the presence of dysplasia, which is associated with adenocarcinoma in 68% to 100% of all surgical resection cases. High-grade dysplasia is most common in patients with invasive adenocarcinoma, leading to the hypothesis that low-grade dysplasia in Barrett's esophagus patients progresses to high-grade dysplasia, then to intramucosal carcinoma, and finally to invasive carcinoma.

While dysplasia is a reliable predictor of cancer, the fact that only a limited area of the esophagus is biopsied during endoscopy limits its value in screening. Furthermore, nondysplastic epithelium is endoscopically indistinguishable from dysplastic tissue, and pathological interpretations are subjective. Several other techniques, such as flow cytometry, electron microscopy, measurement of ornithine decarboxylase activity, mucin histochemistry, and endoscopic ultrasound, have been or are being developed for cancer surveillance in Barrett's esophagus patients.

GARY W. FALK, MD
Department of Gastroenterology
The Cleveland Clinic Foundation

From the Cleveland Clinic continuing medical education symposium, "Gastroenterology Update." Symposiumco-directors were John M. Bozdech, MD, and William D. Carey, MD, Department of Gastroenterology, The Cleveland Clinic Foundation.

PORTAL HYPERTENSION: WHAT ARE THE RISK INDICATORS FOR BLEEDING?

Nearly 70% of the bleeding episodes among patients with portal hypertension occur as a result of portal hypertensive gastropathy, a difficult condition to diagnose. Clinical features such as age, sex, the severity of liver disease, and the presence of esophageal varices are not reliable markers either for the disease or for the risk of hemorrhage, although prior sclerotherapy may increase the risk for bleeding.

Endoscopically, portal hypertensive gastropathy can appear as fine pink speckling, superficial reddening, cherry-red spots, or a reticulated pattern. The presence of these signs in patients with portal hypertension is a good indicator of gastropathy. Portal decompression shunting and beta blockers have considerable potential for controlling acute bleeding and as prophylaxis in portal hypertensive gastropathy. Antacids, H-2 receptor antagonists, and sucralfate have not been as effective.

MARC F. CATALANO, MD
Department of Gastroenterology
The Cleveland Clinic Foundation

MANAGEMENT OF GERD: DO LIFE-STYLE CHANGES WORK?

Changes in life-style are the first step in treating patients with frequent symptoms of gastroesophageal reflux disease. Severe dietary restrictions usually are not necessary, but the clinician should impress upon patients the need for avoiding large meals, lying down after meals, and limiting intake of coffee, tea, alcohol, and peppermint. Patients should also be

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advised to reduce fat consumption, to stop smoking, and to lose weight, if necessary. Elevation of the head of the bed 4 to 6 inches is also recommended. Physicians should stress that these changes are permanent.

Life-style changes are often sufficient treatment in mild cases. If this approach fails to achieve a reduction in symptoms, H-2 receptor antagonists are indicated. Though these agents are highly effective, they are expensive, require at least twice-daily dosing (often tid or qid), and are not curative. Failing this, prokinetic agents or omeprazole can be added. If these medical alternatives do not control the reflux disease, reassess the diagnosis and have the patient undergo esophageal motility testing and prolonged pH monitoring.

Failure of medical treatment is an indication for surgery. The short-term efficacy of surgical treatment is good, but long-term results are still equivocal.

EDGAR ACHKAR, MD
Section Head, GI Laboratory
Department of Gastroenterology
The Cleveland Clinic Foundation

EVALUATING TREATMENT OUTCOME IN IBD: COLONOSCOPY OR CLINICAL EVALUATION?

Repeat colonoscopy reveals little about the results of therapy in inflammatory bowel disease and should not be used to evaluate treatment outcomes in these patients. Clinical evaluation remains the most accurate way of assessing the results of therapy. Several studies, including one that looked at 28 different endoscopic and clinical parameters in 142 patients with Crohn's disease, showed little correlation between the presence of lesions and the advent of clinical remission. The authors of the study of 142 Crohn's disease patients concluded that the clinical severity of the attack "is not related to the nature, extent, or severity of endoscopic lesions."

Examining the bowel mucosa endoscopically will reveal more ulcers and inflammation than will radiology, but it is not certain whether this information is helpful in disease prognosis or therapeutic decisions. Prognosis is related to severity of disease, and barium studies detect more serious areas of involvement.

Of course, endoscopy will continue to have a role in inflammatory bowel disease: it can be used for evaluating strictures and mass lesions, performing biopsies in differential diagnoses, and establishing risk factors for surgery. It should not be used as the primary method of evaluating the extent of disease or for making a diagnosis in patients with mild symptoms.

JEROME D. WAYE, MD
Chief of Gastrointestinal Endoscopy Unit
Mt. Sinai Hospital
Lenox Hill Hospital
New York

LIVER TRANSPLANTATION: COSTS, SUPPLY-DEMAND DRIVE DEBATE

The demand for donor livers continues to outpace the supply, despite the introduction of new laws and techniques designed to improve harvesting. Statistics from 1990 show that there were approximately 6,110 patients waiting for a liver and a total availability—assuming no organ loss—of only 4,357. Of the estimated 37,000 deaths per year from liver disease, about 20,000 would qualify for transplantation. A government-mandated Required Request program—in which doctors are required to ask the family of a deceased patient about organ donation—was implemented in Ohio but failed to increase the availability of donors. New techniques, such as the University of Wisconsin (UW) solution, which maintains the viability of donated organs for up to 24 hours, has increased the number of organs. Grafting from a live donor is an evolving technique, but there are ethical issues involved given the morbidity and mortality risk to the donor.

The cost for a liver transplant is now $235,000. But the cost of end-stage liver disease is also significant and may exceed the cost of a transplant. The underlying presumption in liver transplantation is that the patient will return to his or her normal, pre-disease life-style, including returning to work, and some studies have shown that this occurs in up to 85% of patients. But more hard data are needed to make definite conclusions about the economies of liver disease.

D. ROY FERGUSON, MD
Department of Gastroenterology
The Cleveland Clinic Foundation

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ASCITES IN CIRRHOSIS: DUAL-DIURETIC REGIMEN HIGHLY EFFECTIVE

When combined with a sodium-restricted diet, double-agent therapy has been shown to achieve successful diuresis in over 90% of 4,000 cirrhotic patients with ascites. The best approach is a combination of spironolactone—the mainstay of treatment, but very slow to work—and furosemide. The two agents are started on the first or second day of hospitalization and are given at the same time: once-a-day dosing is pharmacokinetically optimal and maximizes outpatient compliance. The initial dose is 100 mg spironolactone and 40 mg furosemide. Amiloride at 10 mg/day can be substituted for spironolactone; it is more expensive but works faster and avoids the side effect of gynecomastia. The doses of either drug plus furosemide should be doubled simultaneously, as needed, to a maximum of 400 mg/day of spironolactone (or 40 mg/day of amiloride) and 160 mg/day of furosemide.

BRUCE A. RUNYON
University of Iowa Hospitals and Clinics
Iowa City

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Department of Continuing Education
The Cleveland Clinic Foundation
9500 Euclid Ave TT-31
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