An understanding of the pathogenesis of reflux esophagitis and Barrett’s esophagus requires knowledge of the noxious elements in gastric juice and the three major esophageal defenses designed to protect against them. When the esophageal epithelium cannot prevent gastric acid from acidifying the intercellular spaces, the foundation is set for the development of the major symptoms, signs, and complications of reflux esophagitis. Inadequate defense by the epithelium can occur by exposure to the acidic refluxate for a prolonged period of time, because of defects in the antireflux or luminal clearance mechanisms, or by exposure to ingested products that directly impair the epithelium’s intrinsic defenses, rendering it vulnerable to injury from even physiologic levels of acid reflux.

Gastroesophageal reflux disease has immense consequences to American society in terms of disease prevalence, economic costs, psychologic toll, and quality of life, and occasionally causes life-threatening complications, such as esophageal adenocarcinoma. Although the clinical presentation is fairly characteristic for this disease, the internist must recognize the limitations of an empiric therapeutic trial and refer patients for definitive diagnosis and management when patients experience severe symptoms,
experience symptoms refractory to therapy, have alarm symptoms, are in high-risk groups, or suffer potential complications. Acid-suppressive medical therapy is highly effective in the treatment of reflux esophagitis. Novel endoscopic therapies may have an increasingly important clinical role in preventing or treating this chronic disease. Recently promulgated endoscopic surveillance protocols to detect dysplasia in Barrett’s esophagus may help reduce the mortality from esophageal adenocarcinoma, the fastest increasing type of cancer in the United States.

Epidemiology, Pathophysiology, and Treatment of Barrett’s Esophagus: Reducing Mortality from Esophageal Adenocarcinoma

Richard E. Sampliner

The definition of Barrett’s esophagus (BE) has evolved over time. BE is the key premalignant lesion at risk for developing esophageal adenocarcinoma (EAC). In this article the epidemiology and pathophysiology of BE are outlined, and risk factors for BE and EAC are reviewed. Detection of early neoplasia is the present approach to reduce EAC mortality. Novel technology should assist in the early detection of dysplasia to enable targeted therapy. Effective chemopreventive strategies may reduce the risk of progression to EAC.

The Relation of Helicobacter pylori to Gastric Adenocarcinoma and Lymphoma: Pathophysiology, Epidemiology, Screening, Clinical Presentation, Treatment, and Prevention

Barry J. Marshall and Helen M. Windsor

*Helicobacter pylori* infection may be the most common chronic bacterial infection worldwide; however, the prevalence varies between countries and is usually linked to socioeconomic conditions. Gastric cancer is one of the most frequent cancers in developing countries and usually about the seventh most common in developed countries. This article explores the relation of *H pylori* to gastric adenocarcinoma and lymphoma. The pathophysiology, epidemiology, screening, clinical presentation, treatment, and prevention are discussed.

Precancerous Hepatic Lesions and Hepatocellular Carcinoma

The Progression of Hepatitis B– and C–Infections to Chronic Liver Disease and Hepatocellular Carcinoma: Presentation, Diagnosis, Screening, Prevention, and Treatment of Hepatocellular Carcinoma

Paul H. Hayashi and Adrian M. Di Bisceglie

Patients with or at risk for hepatocellular carcinoma (HCC) present special challenges to the clinician. Despite improving understand-
ing of HCC, current guidelines and treatment algorithms are still inadequate. Team coordination and expertise are highly important. In this article, some of the challenging and controversial issues regarding HCC detection, diagnosis, prevention, and care are reviewed, with particular emphasis on hepatitis B– and C–associated HCC. Although not always evidenced-based, practice guidelines or standard of care practices are summarized.

The Progression of Hepatitis B– and C–Infections to Chronic Liver Disease and Hepatocellular Carcinoma: Epidemiology and Pathogenesis 371
Paul H. Hayashi and Adrian M. Di Bisceglie

Hepatocellular carcinoma (HCC) is a relatively common cancer worldwide. Chronic viral hepatitis, with progression to cirrhosis, remains the predominant risk factor for HCC. Although most HCC cases arise in hepatitis B–endemic areas outside North America, the United States is experiencing a significant rise in cases associated with cirrhosis from hepatitis C. This article reviews the link between chronic viral hepatitis B and C and HCC. Advances in the understanding of HCC epidemiology, pathogenesis, clinical presentation, prevention, screening, and treatment are reviewed.

Relation of Hemochromatosis with Hepatocellular Carcinoma: Epidemiology, Natural History, Pathophysiology, Screening, Treatment, and Prevention 391
Stephen A. Harrison and Bruce R. Bacon

Hereditary hemochromatosis is a common inherited disorder of iron metabolism affecting about 1 out of 250 individuals of Northern European descent. Some patients develop progressive iron overload and cirrhosis. These individuals are at risk of developing hepatocellular carcinoma. With increasing clinical recognition, hemochromatosis should be diagnosed earlier and progression to cirrhosis and hepatocellular carcinoma should be minimized. This article includes an overview of hereditary hemochromatosis with a focus on the relationship to hepatocellular carcinoma in reference to epidemiology, natural history, pathophysiology, screening, treatment, and prevention.

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