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Steven F. Moss

Gastric Cancer: Overview 211

Pelayo Correa

This review provides a state of the art description of gastric cancer etiology, the infectious agent, host factors, the precancerous cascade, clinical aspects, and prevention strategies. The biology of *Helicobacter pylori*, the primary causative agent, is discussed as well as the environmental factors that may modulate its effects.

Gastric Cancer: Epidemiology and Risk Factors 219

Catherine de Martel, David Forman, and Martyn Plummer

Gastric cancer is one of the major malignancies in the world. This article summarizes the current understanding of the worldwide burden of this disease, its geographic variation, and temporal trends. An overview is presented of known risk factors, including genetic, dietary, and behavioral, but focuses on *Helicobacter pylori* infection as the most important factor in noncardia gastric cancer. When the data and the literature allow, we distinguish between cardia and noncardia sub-sites, as it is now clear that these two anatomic locations present distinct and sometimes opposite epidemiological characteristics.

Genetics/Genomics/Proteomics of Gastric Adenocarcinoma 241

Dushant S. Uppal and Steven M. Powell

Hereditary diffuse gastric cancer can be caused by epithelial cadherin mutations for which genetic testing is available. Inherited cancer predisposition syndromes including Lynch, Li-Fraumeni, and Peutz-Jeghers syndromes, can be associated with gastric cancer. Chromosomal and microsatellite instability occur in gastric cancers. Several consistent genetic and molecular alterations including chromosomal instability, microsatellite instability, and epigenetic alterations have been identified in gastric cancers. Biomarkers and molecular profiles are being discovered with potential for diagnostic, prognostic, and treatment guidance implications.

Pathology of Gastric Cancer and Its Precursor Lesions 261

Evgeny Yakirevich and Murray B. Resnick

Gastric cancers are a histologically heterogenous group of neoplasms arising from unique epidemiologic and molecular backgrounds. There is accumulating evidence that the intestinal type of gastric adenocarcinoma develops through a multistep process beginning with chronic gastritis triggered primarily by *Helicobacter pylori* and progressing through atrophy, intestinal metaplasia, and dysplasia (intraepithelial neoplasia) to carcinoma. Loss of E-cadherin expression resulting from *CDH1* gene alterations is the primary

carcinogenetic event in hereditary diffuse gastric cancer. Proximal gastric adenocarcinomas likely result from either gastroesophageal reflux or *H pylori* gastritis. This article provides an update of the histologic, immunohistochemical, and molecular pathways of gastric cancer and its precursors.

***Helicobacter pylori* in Gastric Carcinogenesis: Mechanisms** **285**

Lydia E. Wroblewski and Richard M. Peek Jr

Helicobacter pylori infection induces chronic inflammation and is the strongest known risk factor for gastric cancer. The genomes of *H pylori* are highly diverse and therefore bacterial virulence factors play an important role in determining the outcome of *H pylori* infection, in combination with host responses that are augmented by environmental and dietary risk factors. It is important to gain further understanding of the pathogenesis of *H pylori* infection to develop more effective treatments for this common but deadly malignancy. This review focuses on the specific mechanisms used by *H pylori* to drive gastric carcinogenesis.

Gastric Cancer Chemoprevention: The Current Evidence **299**

Victoria P.Y. Tan and Benjamin C.Y. Wong

Chemoprevention may form the cornerstone in the management of gastric adenocarcinoma of the future. *Helicobacter pylori* eradication and aspirin and/or nonsteroidal anti-inflammatory drug therapy have emerged as front-runner chemotherapeutic agents due to the putative pathogenic mechanisms that they address. Before a population-based chemopreventive strategy can be recommended on a large scale, randomized controlled trials with follow-up of more than 10 years of these 2 agents in populations at high gastric adenocarcinoma risk is urgently awaited.

Screening and Treating Intermediate Lesions to Prevent Gastric Cancer **317**

Noriya Uedo, Kenshi Yao, and Ryu Ishihara

A video of a case of superficial elevated early gastric cancer accompanies this article

Early gastric cancer is defined as adenocarcinoma confined to the mucosa or submucosa irrespective of lymph node involvement. In Japan, mucosal high-grade neoplasia is diagnosed as intramucosal early gastric cancer. Some early gastric cancers progress to advanced gastric cancer after several years of follow-up. Image-enhanced endoscopy (chromoendoscopy), narrow-band imaging, and magnifying endoscopy increase the diagnostic yield in characterizing early gastric cancer. Endoscopic resection of intramucosal early gastric cancer with endoscopic mucosal resection or endoscopic submucosal dissection is currently performed in East Asian countries to prevent the development of advanced gastric cancer and preserve patients' quality of life after treatment.

Surgical Considerations in the Treatment of Gastric Cancer **337**

Andrew M. Blakely and Thomas J. Miner

Gastric cancer is one of the most common malignancies in the world and is a leading cause of cancer death. Surgical treatment remains the best