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**The Molecular Biology of Gastrointestinal Cancer:
Implications for Diagnosis and Therapy** 401
C. Richard Boland

Cancers are caused by the sequential accumulation of alterations in genes that control the growth, differentiation, and other behaviors of cells. It has long been recognized that cancers are very heterogeneous pathologically, which is a reflection of the variable genetic lesions that give rise to the variety of lesions present in the gastrointestinal tract. Despite this complexity, certain types of genetic alterations are linked to specific pathologic lesions. This review summarizes the current understanding of the molecular pathogenesis of gastrointestinal neoplasia and provides explanations for some of the pathologic variability of lesions encountered by the endoscopist.

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George K. Anagnostopoulos, Philip Kaye, and Krish Ragunath

This article introduces one of the most advanced endoscopy imaging techniques, magnification endoscopy with narrow-band imaging. This technique can clearly visualize the microvascular (MV) architecture and microsurface (MS) structure. The application of this technique is quite useful for characterizing the mucosal

neoplasia in the hypopharynx, oropharynx, esophagus, and stomach. The key characteristic findings for early carcinomatous lesions are an irregular MV pattern or irregular MS pattern as visualized by this technique. Such a diagnostic system could be applied to the early detection of mucosal neoplasia throughout the upper gastrointestinal tract.

Endoscopic Resection for Premalignant and Malignant Lesions of the Gastrointestinal Tract from the Esophagus to the Colon 435
Takuji Gotoda

The endoscopic mucosal resection and endoscopic submucosal dissection techniques, if performed with the right indications and with expertise, should be considered even in the West as elective treatment modalities for early gastrointestinal neoplasia. Because the experience is still limited, more should be done to strengthen the performance capacity and foster cooperation among skilled endoscopists.

Confocal Laser Endomicroscopy for Gastrointestinal Diseases 451
Ralf Kiesslich, Martin Goetz, and Markus F. Neurath

Confocal laser endomicroscopy enables *in vivo* microscopy of the mucosal layer of the gastrointestinal tract with subcellular resolution during ongoing endoscopy. Endomicroscopy opens the door to immediate tissue and vessel analysis. Different types of diseases can be diagnosed with optical surface and subsurface analysis. Analysis of the *in vivo* microarchitecture can be used for targeting biopsies to relevant areas, and subsurface imaging can unmask microscopic diseases or bacterial infection. Molecular imaging is becoming feasible, which will enable new indications in gastrointestinal endoscopy. This article reviews the current and rapidly expanding clinical data on endomicroscopy and gives a look into future research.

Scanning Single Fiber Endoscopy: A New Platform Technology for Integrated Laser Imaging, Diagnosis, and Future Therapies 467
Eric J. Seibel, Christopher M. Brown, Jason A. Dominitz, and Michael B. Kimmey

Remote optical imaging of human tissue *in vivo* has been the foundation for the growth of minimally invasive medicine. This article describes a new type of endoscopic imaging that has been developed and applied to the human esophagus, pig bile duct, and mouse colon. The technology is based on a single optical fiber that is scanned at the distal tip of an ultrathin and flexible shaft that projects red, green, and blue laser light onto tissue in a spiral pattern. The resulting images are high-quality color video that is expected to produce future endoscopes that are thinner, longer, more flexible, and able to directly integrate the many recent advances of laser diagnostics and therapies.

Positron Emission Tomography for the Diagnosis and Management of Patients with Gastrointestinal Malignancies 479
Tsuneo Saga, Yuji Nakamoto, Tatsuya Higashi,
and Kyosan Yoshikawa

F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) can play an important role in evaluating patients who have locally advanced diseases and in recurrence detection and restaging in patients who have gastrointestinal tract malignancies. Introduction of an integrated PET/CT system enabled the precise co-evaluation of function and morphology and improved the diagnostic ability of FDG-PET. Application of FDG-PET for treatment response evaluation and prognosis prediction is becoming important. Development of novel PET probes is expected to improve the characterization of individual cancer and to contribute to individualized patient management.

Barrett's Esophagus: Pathogenesis, Treatment, and Prevention 495
Rami J. Badreddine and Kenneth K. Wang

Esophageal adenocarcinoma is the most common type of esophageal cancer seen in the United States and Western Europe. Barrett's esophagus (BE) is a well-known risk factor for esophageal adenocarcinoma and is believed to be found in 6% to 12% of patients undergoing endoscopy for gastroesophageal reflux disease and in more than 1% of all patients undergoing endoscopy. This article focuses on the pathogenesis, treatment, and prevention of BE.

Gastric Cancer: Pathogenesis, Screening, and Treatment 513
Kentaro Sugano

Early gastric cancer is a curable disease regardless of its location, histologic type, genetic changes, or the ethnicity of the patient. To improve the detection rate of early gastric cancer, intensive training of endoscopists and the use of novel endoscopic techniques have been introduced into routine examinations in Japan. In the United States, where most gastric cancer is found in advanced stages, a similar approach should be advocated. Endoscopic resection of high-grade dysplasia is also encouraged in the United States not only for proper diagnosis but also for achieving cure without surgical intervention.

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J. Steven Burdick

Intraductal papillary mucinous neoplasm (IPMN) is characterized by enhanced mucus secretion. It is a benign or low-grade neoplasm associated with a dilated main pancreatic duct, patulous ampullary orifice, and abundant mucus secretion. Foci of aggressive cancer may arise and become invasive. Surgery is the only treatment that

can cure IPMN, but the extent of pancreatic resection and the intraoperative margins remain areas of controversy. The risks of total pancreatectomy must be weighed against the risk for developing cancer in the residual pancreas. Risks must be factored against the natural course of the disease and the likelihood of malignancy developing over the life expectancy.

Screening and Surveillance Approaches in Familial Pancreatic Cancer

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Marcia Irene Canto

Screening and surveillance for pancreatic cancer and its precursors is a relatively new indication for endoscopic ultrasound. It provides an alternative approach to the ineffective treatment of mostly incurable symptomatic pancreatic cancer. It is currently reserved for individuals with an increased risk for pancreatic ductal adenocarcinoma, such as those who have inherited genetic syndromes (eg, patients who have Peutz-Jeghers syndrome or hereditary pancreatitis, germline mutation carriers of p16 and BRCA2) and at-risk relatives of patients who have familial pancreatic cancer. This article discusses the rationale for performing screening and surveillance, the types of patients who are eligible for screening, the diagnostic modalities and technique for screening, the diagnostic yield of screening, and the ongoing research.

Early Detection of Pancreatic Cancer: The Japanese Approach

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Kazuo Inui

Pancreatic cancer is the fifth leading cause of cancer-related deaths in Japan. Small pancreatic cancers have some abnormal findings on ultrasonography, and diagnosis with endosonography is useful. Positron emission tomography and contrast-enhanced ultrasonography are expected to serve as new modalities for the early detection of pancreatic cancer. The identification of high-risk individuals is necessary to perform efficient screening. Intraductal papillary mucinous neoplasms and chronic pancreatitis are important risk factors for pancreatic cancer.

Endoscopic Management of Biliary Malignancies

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Naotaka Fujita

The current status of endoscopic diagnosis and treatment of biliary malignancies is discussed. Three ways are now available to approach the bile duct endoscopically. Endoscopic diagnostic modalities are quite useful for the assessment of local changes because of their high spatial resolution and ability in tissue and bile acquisition for histologic, cytologic, and molecular biologic evaluations. Endoscopic biliary drainage is less invasive and beneficial for patients with obstructive jaundice compared with surgical or percutaneous transhepatic drainage. Continuous evolution should expand its indications.

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Recent advances in colonoscopy have enabled us to diagnose early-stage colorectal tumors. Magnifying colonoscopy is useful for diagnosing histologic types by assessing the microstructure of the mucosal surface in detail, which also helps to predict the depth. This article describes clinicopathologic features and endoscopic treatment of flat and depressed types of early colorectal carcinoma.

Screening, Surveillance, and Prevention of Colorectal Cancer	595
David Lieberman	

Colon cancer screening can be effective, but only with a high-quality program that assures adherence to all elements of the program. There is evidence in the United States of greater acceptance of screening and decreased incidence and mortality of colorectal cancer. Patient education is a key element of any effective screening program. It is hoped that future screening will develop better risk-stratification tools and enable targeting of screening to high-risk individuals.

Not Your Father's Colonoscopy: A High-tech Future for Screening and Surveillance of Colorectal Cancer	607
Michael J. Krier and Pankaj Jay Pasricha	

The 20-year technology slump in endoscopic innovation is finally giving way to a flurry of technologies, of which many are directed specifically at improving or even replacing traditional colonoscopy. These technologies include "smart" overtubes, electronically mapped and driven instruments, and completely self-propelled devices. In addition to nonendoscopic technologies such as CT, these innovations may dramatically alter the practice of colorectal cancer screening, the "bread and butter" of gastroenterologists in this country. There are multiple and complex forces driving these changes, including a mismatch between the supply and demand in colonoscopy, patient convenience and comfort, costs, and more recently, a growing concern about the miss rate of conventional colonoscopy.

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