Large granular lymphocytic leukemia: a treatable form of refractory celiac disease.
This report describes 2 cases of T-cell large granular lymphocyte leukemia (LGL) that led to resistance to gluten-free diet in celiac disease. The same clone of T-cells was identified in the peripheral blood and the intraepithelial compartment in the intestine. As opposed to the typical CD3+/CD8-/CD57- phenotype of intraepithelial lymphocytes in type II refractory celiac disease, the T-cells in LGL are CD3+/CD8+/CD57+. The distinction is important because of the excellent response of T-cell LGL to immunosuppressive therapy.

Epigenetics of colorectal cancer.
This comprehensive review covers DNA methylation, histone and chromatin structure, and alterations and expression of microRNAs in colorectal cancer. With its implications in the screening and diagnosis of sporadic and hereditary colorectal cancer, this topic has ramifications in routine pathology practice.

Prognostic value of serologic and histologic markers on clinical relapse in ulcerative colitis patients with mucosal healing.
Biologic therapy is increasingly used in ulcerative colitis and mucosal healing is considered a key endpoint in clinical trials. Since there is poor correlation between endoscopic and histologic activity, biopsy is advocated for assessment of mucosal healing. This study demonstrates that basal plasmacytosis (defined as dense plasma cell infiltrate in the basal part of the crypt) predicts relapse in patients with complete mucosal healing and advocates closer follow-up and optimization of medical therapy if this feature is present.

Non-Celiac Wheat Sensitivity Diagnosed by Double-Blind Placebo-Controlled Challenge:
Exploring a New Clinical Entity
In recent years, the entity of non-celiac wheat sensitivity has been increasingly recognized, although the existence of this entity has been questioned. The clinical features are similar to celiac disease and serology for anti-gliadin antibodies may be positive. This study shows that one-third of irritable bowel syndrome patients may have wheat sensitivity. Histologically, these
patients show intraepithelial and lamina propria eosinophil infiltration of the duodenal and colon mucosa (>60 eosinophils/10 HPF). Intraepithelial lymphocytosis and villous atrophy typical of celiac disease are not seen.


**Hum Pathology, Nov 2012**

*International study group on rectal cancer regression grading: interobserver variability with common only used regression grading systems.*


Regression grading is routinely done for rectal adenocarcinomas treated with neoadjuvant chemoradiation. The study shows that the current system is not precise and has low reproducibility. The need for a simple, reproducible regression grading system is emphasized which has precise criteria, considers all tumor sections rather than the worst area and outlines a uniform method of sampling.


**Hum Pathology, Dec 2012**

*A histopathologic scoring system as a tool for standardized reporting of chronic (ileo)colitis and independent risk assessment for inflammatory bowel disease.*


This study proposes a histopathologic scoring system for chronic colitis with the aim of standardizing terminology and providing probabilistic diagnostic statements based on total scores and their positive predictive values. This can help in more effective communication of the likelihood of inflammatory bowel disease and decrease the variability in interpretation.


**AJSP, Nov 2012**

*Acinar Cystadenoma of the Pancreas: A Clinicopathologic Study of 10 Cases Including Multilocular Lesions With Mural Nodules*

Khor TS et al. *Am J Surg Pathol.* 2012;36(11):1579-1591. Ten cases of pancreatic acinar cystadenoma are characterized, all of which were benign on follow-up. Lesions can be unilocular (n=3) or multilocular (n=7) with a mixture of mucinous or squamous epithelium. CGH shows multiple chromosomal gains, and the authors propose this as additional evidence of the neoplastic nature of this lesion.

*Ampullary Region Carcinomas: Definition and Site Specific Classification with Delineation of Four Clinicopathologically and Prognostically Distinct Subsets in an Analysis of 249 Cases*

A large cohort of ampullary carcinomas identified from malignant pancreatoduodenectomy specimens was characterized by location as Intra-AMP (25%), AMP-ductal (15%), Peri-AMP-duodenal (5%), or AC-not otherwise specified (“papilla of Vater,” 55%). Of these, the worst prognosis belongs to AMP-ductal (3-year survival of 41%) with pancreatobiliary histology/origin in the majority.

**Cystic Pancreatic Neuroendocrine Tumors: A Clinicopathologic Study**  

Cystic pancreatic neuroendocrine tumors are characteristic (53 in total); most were located in the pancreatic tail. All were well-differentiated with low mitotic activity and proliferation index. Comparisons with the more usual solid PanNET are provided.

**AJSP, December 2012**

**Ki67 Labeling Index in Neuroendocrine Tumors of the Gastrointestinal and Pancreatobiliary Tract: To Count or Not to Count Is Not the Question, But Rather How to Count** (Editorial)  

**Objective Quantification of the Ki67 Proliferative Index in Neuroendocrine Tumors of the Gastroenteropancreatic System: A Comparison of Digital Image Analysis With Manual Methods**  

Different methods of quantifying Ki67 are studied: digital image analysis, manual counting of >2000 cells, and eyeball estimate (EE) of labeling by pathologists, including some with prior experience counting Ki67 and others with little such prior experience. With manual counting as the gold standard, digital image analysis was highly concordant, but EE was not concordant among individual observers.

**Clinicopathologic Study of 62 Acinar Cell Carcinomas of the Pancreas: Insights Into the Morphology and Immunophenotype and Search for Prognostic Markers**  

A large series of these rare pancreatic tumors (62 in total) is characterized. Factors correlating with poor prognosis include large size (>6.5 cm), lymph node and distant metastases, and UICC stage. Vascular and perineural invasion, CK19 and p53 expression indicate poor prognosis but not to a statistically significant degree.

**Prognostic Significance of EpCAM-Positive Disseminated Tumor Cells in Rectal Cancer Patients With Stage I Disease**  

845 regional lymph nodes in 44 patients classified as negative on standard stains were reanalyzed with IHC for Ber-EP4 against EpCAM. D2-40 was used to identify the degree of lymphangiogenesis. When correlated with clinical data, 3 of the 8 patients with EpCAM-positive disseminated tumor cells relapsed, as opposed to none of the disseminated tumor cell-negative patients. The authors propose that adjuvant therapy may be beneficial for patients with disseminated tumor cells.
**Histopathology, November 2012**

*Upstaging of early colorectal cancers following improved lymph node yield after methylene blue injection (pages 788–794)*


234 colorectal cancer specimens were studied; methylene blue injection increased the number of positive nodes in pT1 or T2 tumors, impacting staging.

*Loss of succinate dehydrogenase subunit B (SDHB) expression is limited to a distinctive subset of gastric wild-type gastrointestinal stromal tumours: a comprehensive genotype–phenotype correlation study (pages 801–809)*


Most adult GISTs contain KIT or PDGFRA mutations, in contrast to the majority of pediatric GIST (“wild-type” GIST). GISTs with known genotypes were analyzed for SDHB expression, which was found to be deficient in 42% of wild-type GIST and retained in all GISTs with KIT and PDGFRA mutations.

*Atopic and non-atopic eosinophilic oesophagitis are distinguished by immunoglobulin E-bearing intraepithelial mast cells (pages 810–822)*


Eosinophilic esophagitis by maximal eosinophil count per hpf correlates with average count per square millimeter. Intraepithelial eosinophil density is higher in children than in adults. IgE-bearing mast cells are higher in atopic EoE patients than non-atopic EoE patients.

**Histopathology, December 2012**

*The utility of diagnostic biopsy specimens for predictive molecular testing in colorectal cancer (pages 1117–1124)*


Small diagnostic biopsy specimens are shown to be comparable to resection specimens for mutation analysis for KRAS, BRAF, PIK3CA, TP53, and MSI by PCR.

**Arch Pathol Lab Med, November 2012**

*Mucinous Carcinomas of the Gallbladder: Clinicopathologic Analysis of 15 Cases Identified in 606 Carcinomas*


A subset of primary invasive gallbladder carcinomas meeting WHO criteria for mucinous carcinoma are characterized. These show more aggressive behavior than typical gallbladder carcinomas, and express MUC2 in contrast to usual gallbladder carcinomas. They are microsatellite stable.

Abstract
Colorectal metastases, which overall are rare, are characterized in a multi-center study. Breast is a leading source of metastasis; these tumors have a poor prognosis and therapy tends to be palliative.

Abstract

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