

## Journal Watch – May and June, 2015

### **Consecutive Monitoring of Fecal Calprotectin and Lactoferrin for the Early Diagnosis and Prediction of Pouchitis after Restorative Proctocolectomy for Ulcerative Colitis.**

**Yamamoto T, Shimoyama T, Bamba T, Matsumoto K.**

**Am J Gastroenterol. 2015 Jun;110(6):881-7.**

<http://www.ncbi.nlm.nih.gov/pubmed/25916224>

This was a prospective study performed in ulcerative colitis patients following total proctocolectomy, ileal pouch anal anastomosis, and ileostomy closure. Sixty patients underwent stool sample measurement every 2 months for one year to measure levels of fecal calprotectin and fecal lactoferrin. All patients underwent endoscopic examination if symptoms of pouchitis developed or at the end of the one year study. In the 10 patients (17%) who developed pouchitis, fecal calprotectin levels and lactoferrin levels were elevated 2 months prior to pouchitis diagnosis, while levels remained low in all other patients. This is the first study describing collection of consecutive fecal biomarkers in this setting, and the authors conclude that fecal calprotectin and lactoferrin monitoring is useful since elevations of these biomarkers are associated with development of pouchitis. Of note, an accompanying editorial discusses the cost-effectiveness of implementing such a monitoring program.

### **Indications and Techniques for Endoscopic Submucosal Dissection.**

**Bhatt A, Abe S, Kumaravel A, Vargo J, Saito Y.**

**Am J Gastroenterol. 2015 Jun;110(6):784-91.**

<http://www.ncbi.nlm.nih.gov/pubmed/25623656>

Helpful explanatory review of this relatively new surgical procedure for curative resection of superficial neoplasms in the GI tract.

### **The Presence of Genetic Mutations at Key Loci Predicts Progression to Esophageal Adenocarcinoma in Barrett's Esophagus.**

**Eluri S, Brugge WR, Daglilar ES, Jackson SA, Styn MA, Callenberg KM, Welch DC, Barr TM, Duits LC, Bergman JJ, Shaheen NJ.**

**Am J Gastroenterol. 2015 Jun;110(6):828-34.**

<http://www.ncbi.nlm.nih.gov/pubmed/26010308>

This case control study included 23 cases and 46 controls for assessment of the mutational load, a measure of genetic instability, and determine its utility in predicting progression to high grade dysplasia or adenocarcinoma in Barrett esophagus patients. Baseline for cases and controls was BE with no

dysplasia or with low-grade dysplasia. Epithelium was microdissected, targeting LGD if present at baseline, and made up approximately 90% of the microscopically examined cell population for genomic testing. The mean per-patient mutational load was higher in cases as compared to controls even at the time of index biopsy. Specificity and sensitivity of mutational load was tested using different cutoffs. The authors conclude that mutational load assessment can be a useful biomarker for progression to Barrett neoplasia.

### **Gastric-type expression signature in serrated pathway-associated colorectal tumors.**

Kim JH, Kim KJ, Rhee YY, Bae JM, Cho NY, Lee HS, Kang GH.

Hum Pathol. 2015 May;46(5):643-56.

<http://www.ncbi.nlm.nih.gov/pubmed/25704805>

This tissue microarray immunohistochemical study identified early gain of gastric differentiation and late loss of intestinal differentiation in 175 MSI-H colorectal carcinomas. Control tissues included 36 normal gastric and colonic mucosa, as well as 163 colorectal polyps of all types. Gastric-type markers included ANXA10, VSIG1, CLDN18, CTSE, TFF2, MUC5AC, and MUC6, and intestinal-type markers included CDX2 and CK20. All of the gastric-type markers were preferentially expressed in proximal MSI-H colon carcinomas. Expression of ANXA10, TFF2, and MUC5AC were significantly associated with sporadic MSI-H colorectal carcinomas, while about a third of these tumors lost CDX2 and CK20 expression. Microvesicular hyperplastic polyps had the highest frequency of gastric-type markers ANXA10, VSIG1, and TFF2, which were expressed in greater than two-thirds of cases. CDX2 and CK20 expression were always present in all colorectal polyps regardless of the expression of gastric-type markers. There were no marker combinations specific for distinguish among different polyp types.

### **HER2 status in gastroesophageal cancer: a tissue microarray study of 1040 cases.**

Cappellesso R, Fassan M, Hanspeter E, Bornschein J, d'Amore ES, Cuorvo LV, Mazzoleni G, Barbareschi M, Pizzi M, Guzzardo V, Malfertheiner P, Micev M, Guido M, Giacomelli L, Tsukanov VV, Zagonel V, Nitti D, Rugge M.

Hum Pathol. 2015 May;46(5):665-72.

<http://www.ncbi.nlm.nih.gov/pubmed/25800719>

This multi-institutional European tissue microarray immunohistochemistry study aimed to determine the prevalence of Her2 amplification, the correlation between Her2 gene amplification and clinicopathologic features, the consistency of current IHC assessment, and intratumoral Her2 variability in gastric and gastroesophageal junctional tumors. Prevalence was 11%, with 5.2% of those being restricted to nodal metastasis expression. Two IHC protocols were compared to a CISH protocol, revealing 4B5-IHC to be more sensitive than CB11-IHC (94% vs 89%), with equal specificity of about 96%. This study found good intratumoral staining consistency, although overall IHC testing failed to identify about 10% of gastric and EGJ tumors in their study.

**Clinical significance of assessing Her2/neu expression in gastric cancer with dual tumor tissue paraffin blocks.**

Ge X, Wang H, Zeng H, Jin X, Sujie A, Xu C, Liu Y, Huang J, Ji Y, Tan Y, Liu T, Hou Y, Qin J, Sun Y, Qin X.

Hum Pathol. 2015 Jun;46(6):850-7.

<http://www.ncbi.nlm.nih.gov/pubmed/25863425>

Study assessed whether false negative rate of Her2 IHC on gastric cancer due to intratumoral heterogeneity could be overcome by testing 2 different tumor blocks. The higher score of the two blocks was the final score. In the 119 cases where two blocks were tested, 36 cases (30%) showed inconsistent expression between the two blocks. When using two blocks as compared to a single block, there was a higher rate of overall cases with Her2 positive (3+) gastric cancer. Her2 status was also correlated with clinic pathologic parameters, and in the dual block group, 3+ Her2 positive was significantly associated with non-poorly cohesive histology. Costs and technical issues were addressed, including making a single IHC slide containing tissue from both tumor blocks chosen for testing.

**Granular cell tumor of the gastrointestinal tract: histologic and immunohistochemical analysis of 98 cases.**

An S, Jang J, Min K, Kim MS, Park H, Park YS, Kim J, Lee JH, Song HJ, Kim KJ, Yu E, Hong SM.

Hum Pathol. 2015 Jun;46(6):813-9.

<http://www.ncbi.nlm.nih.gov/pubmed/25882927>

This retrospective study described 98 cases of granular cell tumor from the gastrointestinal tract at a single institution. Males were twice as likely as females to have tumors, and mean age of the patients was 49 years old. All cases stained positive for S-100, 95% of cases stained positive for CD56 and for CD68, and 93% stained positive for SOX-10. Inhibin-alpha was more often positive in colorectal GCTs than in esophageal GCTs. Most GCTs were found in the esophagus, followed by colorectum, then stomach, although colorectal and gastric GCT tended to be about twice as large as esophageal GCTs, and more often showed infiltrative growth pattern. Sixty-two percent of cases showed acute and chronic inflammation of the overlying mucosa.

AJCP May 2015

**Significance of Paneth Cell Metaplasia in Barrett Esophagus: A Morphologic and Clinicopathologic Study**

Wei Chen, Wendy L. Frankel, Kevin M. Cronley, Lianbo Yu, Xiaoping Zhou, MD, Martha M. Yearsley, MD1

Am J Clin Pathol. 2015 May;143(5):665-71

<http://www.ncbi.nlm.nih.gov/pubmed/25873500>

The purpose of this study was to investigate the prevalence and significance of Paneth cell metaplasia in Barrett Esophagus. The authors retrospectively reviewed 757 esophageal biopsies of Barrett Esophagus and found that 31% (234/757) had Paneth cell metaplasia. Out of the 757 cases, 299 had further clinical information including follow-up data for at least 1 year, information regarding length of the Barrett Esophagus segment, duration of disease, and proton pump inhibitor (PPI) treatment history. The authors found that the Paneth cells were less frequent in dysplastic glands compared to non-dysplastic epithelium, that Paneth cells were more common in long segment ( $\geq 3$  cm) than short segment Barrett's, and that regression (defined as a lower degree of dysplasia or no dysplasia on follow up biopsies) was less likely to occur if Paneth cell metaplasia was present. No significant difference between the groups with and without Paneth cell metaplasia was observed with respect to progression to dysplasia or carcinoma.

AJCP June 2015

### **Low-Cost Workflow Improvement Reduces Gastrointestinal Block Use 17% by Altering Classic Histotechnology Testing**

Bryan Steussy, Michael Gailey, Kent Becker, Emily Fuller, Melissa Jans, Sue Lewis, Leana Guerin, Patricia Kirby, Robert Robinson

Am J Clin Pathol. 2015 Jun;143(6):861-4

<http://www.ncbi.nlm.nih.gov/pubmed/25972328>

This article describes the evaluation of three changes to the workflow for GI biopsy grossing and embedding at the author's institution that were implemented to try and reduce the number of paraffin blocks and ease embedding steps as a potential cost saving measure. First, the limit to the number of biopsy pieces per block was increased from four to ten. Second, histotechnologists would no longer orient the GI specimens. And lastly, embedding would be in a straight line rather than on a diagonal in the block. Overall, the authors state that quality of slides was unchanged, job satisfaction was unchanged or increased in some cases, and a 17% reduction in blocks was calculated. Pathologists and residents generally reported satisfaction with the finished product.

### **Endoscopic ultrasound fine-needle aspiration cytology mutation profiling using targeted next-generation sequencing: personalized care for rectal cancer.**

Gleeson F, Kipp B, Voss J, Campion M, Minot D, Tu ZJ3, Klee E, Sciallis A, Graham R, Lazaridis K, Henry M, Levy M

Am J Clin Pathol. 2015 Jun;143(6):879-88.

<http://www.ncbi.nlm.nih.gov/pubmed/25972331>

The purpose of this study was to evaluate cytology samples obtained by endoscopic ultrasound fine-needle aspiration (EUS-FNA) by next generation sequencing (NGS), specifically using Ion AmpliSeq Cancer Hotspot Panel v2 and MiSeq sequencers. Out of 606 lower GI EUS procedures performed at the authors' institution over a nearly 10 year period, 231 patients were identified who had untreated, primary colorectal cancer with positive lymph nodes that were identified by EUS-FNA. Out of these cases, 131 were deemed to have adequate tumor cell quantity and density to attempt DNA analysis, and 102 of these eventually yielded quality sequencing results. The article discusses the details of the findings in depth, and ultimately proposes that application of this NGS platform on cytology specimens holds promise.

Modern Pathology May 2015

**Expression of SOX9 and CDX2 in nongoblet columnar-lined esophagus predicts the detection of Barrett's esophagus during follow-up**

Xuefeng Zhang, Maria Westerhoff and John Hart

Mod Pathol 28: 654-661 May 2015

<http://www.ncbi.nlm.nih.gov/pubmed/25412842>

The purpose of this study was to investigate biomarkers that might help identify patients who have nongoblet cell columnar lined epithelium in the esophagus that are at higher risk of progression to Barrett's esophagus. Currently the diagnosis of Barrett's esophagus is restricted to those patients who have columnar epithelium in the esophagus with pathologically identified goblet cells, and only Barrett's patients are considered to be at significant risk for adenocarcinoma. The management of patient's with nongoblet cell columnar epithelium of the esophagus is uncertain. In this study immunohistochemistry for several possible biomarkers were evaluated in nongoblet cell cases that eventually developed Barrett's esophagus and compared to a control group of nongoblet cell cases that did not progress. SOX9 and CDX2 were found to be more frequently expressed in the columnar epithelium from patient's who eventually developed Barrett's esophagus, and the authors suggest the markers may be useful in identifying patients who might warrant closer follow up.

Modern Pathology June 2015

**Overdiagnosis of high-grade dysplasia in Barrett's esophagus: a multicenter, international study.**

Sangle NA1, Taylor SL2, Emond MJ3, Depot M4, Overholt BF5, Bronner MP6.

Mod Pathol. 2015 Jun;28(6):758-65.

<http://www.ncbi.nlm.nih.gov/pubmed/25676554>

This study looks at some of the pitfalls leading to an overdiagnosis of high grade dysplasia in the setting of Barrett's esophagus. The study set was derived from cases that were previously reviewed for inclusion into an endoscopic ablation trial that enrolled patients from 1999 through 2005. On review by the study pathologists, it was found that 40% of the cases that were originally diagnosed during that time period with high grade dysplasia were overdiagnosed (negative, indefinite, or low grade dysplasia). The article has a good discussion and photos relating to the pitfalls for overdiagnosis that include, inflammatory atypia, atypia limited to the basal metaplastic glands, tangential sectioning, and reactive nuclear atypia with mucin loss. The authors stress that loss of nuclear polarity is the single most useful feature for distinguishing high grade dysplasia from low grade dysplasia.

**A three-tier classification system based on the depth of submucosal invasion and budding/sprouting can improve the treatment strategy for T1 colorectal cancer: a retrospective multicenter study.**

Kawachi H, Eishi Y, Ueno H, Nemoto T, Fujimori T, Iwashita A, Ajioka Y, Ochiai A, Ishiguro S, Shimoda T, Mochizuki H, Kato Y, Watanabe H, Koike M, Sugihara K

Mod Pathol. 2015 Jun;28(6):872-9

This study attempts to evaluate criteria to predict the risk of lymph node metastasis in T1 colorectal carcinoma. 806 patients with T1 colorectal tumors who underwent major surgery with or without prior endoscopic mucosal resection were included in the study set. A proposed tumor budding score (based on the number of single cells or less than 5 cells in a group in a 20x field) as well as depth of submucosal invasion, histologic grade, and lymphovascular invasion were used in univariate and multivariate analyses. Depth of submucosal invasion and high vs. low grade tumor budding were found to be independent predictive factors. Based on these two features the authors classified the risk of lymph node metastasis into three groups: 1) high risk group with depth of submucosal invasion greater than or equal to 1000 micrometers and high grade tumor budding (lymph node metastasis in 29%); intermediate-risk group with depth of submucosal invasion less than or equal to 1000 micrometers and low grade budding (lymph node metastasis in 9%); and low-risk group with depth of submucosal invasion less than 1000 micrometers (lymph node metastasis in 2%). The authors propose that this stratification may aid in decisions about further resection in endoscopically removed T1 tumors.

**Prevalence and Risk Factors for Therapy Escalation in Ulcerative Colitis in the Swiss IBD Cohort Study**

Safroneeva E, Vavricka SR, Fournier N, Straumann A, Rogler G, Schoepfer AM

Inflamm Bowel Dis. 2015; 21(6): 1348-1358.

<http://www.ncbi.nlm.nih.gov/pubmed/25806845>

This study analyzed data from 996 patients with ulcerative colitis and median disease duration of 9 years in order to determine which risk factors correlate with escalation of therapy through the following stages: topical anti-inflammatory drugs; systemic corticosteroids; immunomodulators; anti-TNF agents; calcineurin inhibitors; colectomy. The authors evaluated sex, age at the time of diagnosis, smoking status at the time of diagnosis, IBD family history, the presence of extraintestinal manifestations, disease location at the time of diagnosis, and disease duration. The presence of extraintestinal manifestations and pancolitis were risk factors for every level of therapeutic intervention up to and including colectomy. In addition, patient age >40 was a risk factor for immunomodulator therapy and left sided colitis at the time of diagnosis predisposed to corticosteroid therapy, immunomodulators, and anti-TNF medications, but not calcineurin inhibitors or surgery.

**Protein expression of HER2, 3, 4 in gastric cancer: correlation with clinical features and survival**  
**Xiao Xiao He, Li Ding, Yuan Lin, Man Shu, Jian Ming Wen, Ling Xue**

J Clin Pathol 2015;68:374-380

This study analyzed HER2, HER3, and HER4 expression in 498 individuals with advanced gastric carcinoma using TMAs. Overall, the expression of each individual marker correlated with expression of the other markers and with an intestinal phenotype. HER3 expression was the most frequent (21%) and expression was correlated with cardiac location, more advanced TNM stage, and poor survival. HER4 was expressed in 13% of cases and HER 2 in 9% of cases and both correlated with TNM stage.

<http://www.ncbi.nlm.nih.gov/pubmed/25731189>

**Development and Validation of a Scoring System to Identify Patients With Microscopic Colitis**

**John S. Kane, Olorunda Rotimi, Simon M. Everett, Shairoz Samji, Flurina Michelotti, Alexander C.**

Clinical Journal of Gastroenterology and Hepatology  
June 2015 Volume 13, Issue 6, Pages 1125–1131

The authors develop a clinical scoring system to identify patients that may have microscopic colitis. This retrospective study had a subset of patients used to identify risk factors and construct a scoring system and a second set of patients used to validate the scoring system. They find risk factors for microscopic colitis are age  $\geq 50$  years, female sex, use of proton pump inhibitors, use of nonsteroidal anti-inflammatory drugs, weight loss, and absence of abdominal pain. Using these parameters in their clinical scoring system, they were able to predict microscopic colitis with a sensitivity of 91% and specificity of 45%.

<http://www.ncbi.nlm.nih.gov/pubmed/25616029>

**Risk of Lymphoma in Patients With Inflammatory Bowel Disease Treated With Azathioprine and 6-Mercaptopurine: A Meta-analysis**

**David S. Kotlyar, James D. Lewis, Laurent Beaugerie, Ann Tierney, Colleen M. Brensinger, Javier P. Gisbert, Edward V. Loftus Jr., Laurent Peyrin-Biroulet, Wojciech C. Blonski, Manuel Van Domselaar, Maria Chaparro, Sandipani Sandilya, Meenakshi Bewtra, Florian Beigel, Livia Biancone, Gary R. Lichtenstein**

Clinical Journal of Gastroenterology and Hepatology  
May 2015 Volume 13, Issue 5, Pages 847–858.e4

This metaanalysis examined 18 published papers and found an overall incidence ratio for lymphoma of 4.92. An increased risk for lymphoma was seen after 1 year of usage, but returned to baseline after cessation of Azathioprine and 6-Mercaptopurine. Men had a greater risk than women for lymphoma. Age older than 50 or younger than 30 were also at increased risk for lymphoma.

<http://www.ncbi.nlm.nih.gov/pubmed/24879926>

**Clinicopathologic and Prognostic Significance of Multiple Hormone Expression in Pancreatic Neuroendocrine Tumors**

**Kim JY, Kim MS, Kim KS, Song KB, Lee SH, Hwang DW, Kim KP, Kim JH, Yu E, Kim SC, Jang HJ, Hong SM.**

Am J Surg Pathol 2015;39:592-601.

<http://www.ncbi.nlm.nih.gov/pubmed/25602797>

Immunolabeling of peptide hormones in 226 surgically resected PanNETs were studied. The authors concluded that tumors with insulin or glucagon-like peptide 1 expression and increased numbers of expressed hormones had a better survival outcome by univariate analysis. Gastrin expression was a negative prognostic indicator.

**Non-L-cell Immunophenotype and Large Tumor Size in Rectal Neuroendocrine Tumors are Associated with Aggressive Clinical Behavior and Worse Prognosis**

**Kim JY, Kim KS, Kim KJ, Park IJ, Lee JL, Myung SJ, Park Y, Park YS, Yu CS, Kim JC, Y E, Jang HJ, Hong SM.**

Am J Surg Pathol 2015;39:632-643.



<http://www.ncbi.nlm.nih.gov/pubmed/25724002>

Immunohistochemistry for GLP1 and PYY, to distinguish L-cell type tumors, using tissue microarrays was performed in 208 rectal NETs. The authors conclude that combining L-cell phenotype and tumor size determines the clinical behavior of rectal NETs more precisely than use of L-cell immunophenotyping alone.

The High-grade (WHO G3) Pancreatic Neuroendocrine Tumor Category is Morphologically and Biologically Heterogenous and Includes both Well Differentiated and Poorly Differentiated Neoplasms

**Basturk L, Yang Z, Tang LH, Hruban RH, Adsay V, McCall CM, Krasinskas AM, Jang TK, Frankel WL, Balci S, Sgel C, Klimstra DS.**

**Am J Surg Pathol 2015;39:683-690.**

<http://www.ncbi.nlm.nih.gov/pubmed/25723112>

The authors studied mitotic rate G2 pancreatic NETs which have a discordant Ki-67 index (>20%). The authors conclude that mitotic rate and Ki-67 index-based grades of PanNETs can be discordant, and when the Ki-67 index indicates G3, the clinical outcome is slightly worse. Well differentiated PanNETs which are G3 by Ki-67 index are significantly less aggressive than bona fide poorly differentiated NECs. This suggests that the current WHO G3 category is heterogeneous, and contains 2 distinct neoplasms, and can be further separated into well differentiated PanNET with an elevated proliferation rate and poorly differentiated NEC.

### **Characteristics of Gastric Mucosa in Patients with Intestinal Metaplasia**

**Genta RM, Sonnenberg A.**

Am J Surg Pathol 2015;39:700-704.

<http://www.ncbi.nlm.nih.gov/pubmed/25602799>

A large national pathology database was used to study the relative prevalence of histopathologic conditions in gastric mucosa associated with intestinal metaplasia (IM). Among other findings, the authors determined that approximately half of the patients with IM had no histopathologic evidence of current or previous Helicobacter gastritis and almost one fifth had a background of reactive gastropathy. Additional longitudinal studies are needed to determine whether these patients are at increased risk for gastric cancer and need follow-up or can be safely assumed to have no increased cancer risk above the never-infected general population.

Helicobacter pylori CagA Translocation is Closely Associated with the Expression of CagA-signaling Molecules in Low-grade Gastric Mucosa-associated Lymphoid Tissue Lymphoma

**Kuo HS, Yeh KH, Chen LT, Lin CW, Hsu PN, Wu MS, Liou JM, Tsai HJ, Tzeng YS, Cheng AL.**

**Am J Surg Pathol 2015;39:761-766.**

<http://www.ncbi.nlm.nih.gov/pubmed/25871616>

The authors expanded on previous studies to investigate 25 *Helicobacter pylori* (HP)-dependent and 22 HP-independent MALT lymphoma cases. They found that the CagA expression rate was significantly higher in HP-dependent than in HP-independent tumors. CagA expression was closely associated with CagA signaling molecule expression (p-SHP-2, p-ERK, p-p38 MAPK, Bcl-2 and Bcl-xL). The authors conclude that CagA protein expression is biologically relevant and is associated with the activation of its downstream signals in HP-dependent gastric MALT lymphoma.

### **Peculiar Histiocytic Lesions with Massive Lanthanum Deposition in Dialysis Patients Treated with Lanthanum Carbonate**

**Haratake J, Yasunaga C, Ootani A, Shimajiri S, Matsuyama A, Hisaoka M.**

Am J Surg Pathol 2015;39:767-771.

<http://www.ncbi.nlm.nih.gov/pubmed/2560800>

The authors report on 6 cases of heavy lanthanum deposition in the gastroduodenal mucosa of patients treated with lanthanum carbonate (LC, a therapeutic phosphate-binding agent). Long-standing LC administration can cause massive mucosal accumulation in mucosal histiocytes and be associated with several forms of gastroduodenal lesions.

### **Pediatric Non-*Helicobacter Pylori* Atrophic Gastritis**

**Pogorlier J, Kamin D, Goldsmith JD.**

Am J Surg Pathol 2015;39:786-792.

<http://www.ncbi.nlm.nih.gov/pubmed/25602795>

Pediatric atrophic gastritis is rare and has been primarily previously reported as single-case reports. This series reports on series of 12 patients. The authors conclude that accurate diagnosis requires a high degree of suspicion and the diagnosis should be considered in patients with a clinical history of other autoimmune diseases or iron-deficiency anemia.

A Comparative Clinicopathologic Study of Collagenous Gastritis in Children and Adults, The Same Disorder with Associated Immune-mediated Diseases

**Ma C, Park JY, Montgomery EA, Arnold CA, McDonald OG, Liu TC, Salaria SN, Limketkai BN, McGrath KM, Musahl T, Singhi AD.**

**Am J Surg Pathol 2015;39:802-812.**

<http://www.ncbi.nlm.nih.gov/pubmed/25871617>

The authors report on 10 pediatric and 21 adult cases of collagenous gastritis. The authors conclude that contrary to previous studies, no clinicopathologic differences were identified among the pediatric and adult patients. Their findings suggest that immune abnormalities and medications, such as olmesartan, may be possible triggers and that improved therapeutic regimens are needed.

### **NKX6-1 is a Novel Immunohistochemical Marker for Pancreatic and Duodenal Neuroendocrine Tumors**

**Tseng IC, Yeh MM, Yang CY, Jeng YM.**

**Am J Surg Pathol 2015;39:850-857.**

<http://www.ncbi.nlm.nih.gov/pubmed/25871618>

NKX6-1 is a homeobox transcription factor which participates in the development and regulation of endocrine function in pancreatic islets. 178 primary and 26 metastatic well differentiated neuroendocrine tumors (WDNETs) of various origins were analyzed using immunohistochemistry. The authors conclude that using a combination of NKX6-1, CDX2, TTF-1 and ISL1 is useful in identifying the primary sites of WDNETs.

### **The Concordance of Endoscopic and Histologic Findings of 1000 Pediatric EGDs**

**Sheiko MA, Feinstein JA, Capocelli KE, Kramer RE.**

**Gastrointestinal Endoscopy 2015;81:1385-1391.**

<http://www.ncbi.nlm.nih.gov/pubmed/25440693>

Pediatric gastroenterologists frequently perform routine endoscopic biopsies despite normal-appearing mucosa during EGD. This practice, however, is supported by older small studies. The authors performed retrospective cohort study at a single tertiary care center on 1000 patients to examine the concordance between endoscopic findings and histologic findings. The authors found that if biopsy specimens had only been obtained when the endoscopist identified abnormal mucosa, 48.5% of the pathologic findings would have been missed. In patients with histology consistent with eosinophilic esophagitis, 30.2% had normal-appearing mucosa. For celiac disease, 43% had normal-appearing mucosa. In the stomach, an abnormal endoscopic appearance was more likely to have normal histology. The authors conclude that these data support the routine collection of biopsy specimens in the duodenum, stomach, and esophagus during EGD in pediatric patients.

### **Solid Tumor Metastases to the Pancreas Diagnosed by FNA: A Single-Institution Experience and Review of the Literature**

**Smith AL, Odronic SI, Springer BS, Teynolds JP.**

Cancer Cytopathology 2015;123:347-355.

<http://www.ncbi.nlm.nih.gov/pubmed/25828394>

In this study, medical records were retrospectively searched for pancreatic FNAs positive for metastatic disease. Out of 2327 pancreatic FNAs over a 14 year period, 22 cases of metastatic disease were identified. There were 14 renal cell carcinomas, 2 colonic adenocarcinomas, 1 urothelial carcinoma, 1 non-small cell lung carcinoma, 1 ovarian serous carcinoma, 1 prostatic adenocarcinoma, 1 papillary thyroid carcinoma, and 1 mesenchymal chondrosarcoma. The authors conclude that in agreement with prior studies, the most common metastasis to the pancreas was renal cell carcinoma. This paper describes the first case of metastatic chondrosarcoma to the pancreas diagnosed by FNA.

## **Journals Reviewed (May and June, 2015 Issues)**

**Histopathology**

**Archives of Pathology and Lab Medicine**

**Modern Pathology**

**American Journal of Clinical Pathology**

**Journal of Pathology**

**Journal of Clinical Pathology**

**American Journal of Pathology**

**Human Pathology**

**Cancer Cytopathology**

**American Journal of Surgical Pathology**

**Advances in Anatomic Pathology**

**Journal of Molecular Diagnostics**

**Gastrointestinal Endoscopy**

**Gastroenterology Clinics of North America**

**Gastroenterology**

**Gut**

**American Journal of Gastroenterology**

**Clinical Gastroenterology Hepatology**

**Inflammatory Bowel Diseases**

## **Reviewers**

**Raga Ramachandran, MD, PhD; University of California San Francisco**

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**Ilyssa Gordon, MD, PhD; Cleveland Clinic**

**Nicole Panarelli, MD; Cornell University Medical Center**

**Cynthia D Guy, M.D.; Duke University Medical Center**

**Michael Torbenson, MD; Mayo Clinic Rochester**