SOX2 as a Novel Marker to Predict Neoplastic Progression in Barrett's Esophagus.

This case-control study was performed within a prospective cohort of 720 BE patients. Loss of SOX2 expression by immunohistochemistry was associated with an increased risk of progression to high-grade dysplasia or esophageal adenocarcinoma after adjusting for gender, age, BE length, and esophagitis. The positive predictive value for neoplastic progression was 56% when biopsy showed low-grade dysplasia, SOX2 loss, and aberrant p53 expression, as compared to 16% with low-grade dysplasia alone. Use of this marker can help stratify progression risk in these patients.

Am J Gastroenterol. 2015 Sep;110(9):1257-60.

This study used biopsies in Barrett patients obtained with the wide-area transepithelial sampling (WATS) procedure with computer assisted analysis. Four pathologists, blinded to clinical or pathologic information and experienced in WATS biopsy interpretation, evaluated 149 BE slides which were randomly chosen to have varying degrees of BE dysplasia. Of note, the original diagnosis was confirmed by a pathologist as part of the computer-assisted diagnostic procedure. There was substantial interobserver agreement in the diagnosis of indefinite/low-grade dysplasia (kappa = 0.74) and almost perfect agreement in the diagnosis of no dysplasia (kappa = 0.88) and high-grade dysplasia/adenocarcinoma (kappa = 0.95). WATS, shown in previous studies to increase BE dysplasia detection, has better interobserver variability than standard biopsy in detection of BE dysplasia.

Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE): Determining Therapeutic Goals for Treat-to-Target.
The goal of this study was to achieve international expert consensus on evidence based treatment targets for IBD that could be used in routine practice. A systematic review of the literature by 33 international IBD experts included 905 reference articles. For Crohn’s disease, Clinical symptoms together with endoscopic absence of ulceration was determined to be the recommended target; histologic remission is not a recommended target due to insufficient evidence. Imaging can be used in place of endoscopy to assess resolution of inflammation. Available biomarkers are not targets. Similar recommendations were made for ulcerative colitis, with the experts noting that although histology is a sensitive measure of inflammation, there is lack of evidence of clinical utility to recommend it as a treatment target. The authors do comment that better validation of Geboes scoring is required, and that other clinical and molecular methods of assessing histologic remission should be explored in future studies.

**Histological Response to Fluticasone Propionate in Patients With Eosinophilic Esophagitis Is Associated With Improved Functional Esophageal Mucosal Integrity.**
Am J Gastroenterol. 2015 Sep;110(9):1289-97.

This prospective study mucosal biopsies from 15 adult eosinophilic esophagitis patients tested before and 8 weeks after administration of swallowed fluticasone propionate. Pathologist assessment included eosinophil and mast cell counts, and presence of eosinophil microabscess, basal hyperplasia, and spongiosis. Additionally, in vivo tissue impedance spectroscopy was used to assess esophageal mucosal integrity, and qPCR was used to evaluate expression of inflammatory cytokines and barrier integrity proteins. The authors found that fluticasone treatment was associated with significant increase in esophageal mucosal integrity, increase in gene expression for barrier integrity proteins, and decreased inflammatory cytokine gene expression.

**Spatial Predisposition of Dysplasia in Barrett's Esophagus Segments: A Pooled Analysis of the SURF and AIM Dysplasia Trials.**
Cotton CC, Duits LC, Wolf WA, Peery AF, Dellon ES, Bergman JJ, Shaheen NJ.

This interesting study used pretreatment biopsy data from two randomized controlled trials of radiofrequency ablation of BE for dysplasia, to determine if the location of dysplasia within the
esophagus affected by Barrett’s could be determined with any greater sensitivity than the currently recommended uniformly spaced random biopsies. A post hoc analysis showed a substantial increase in dysplasia prevalence within proximal BE segments (twice as likely in the proximal half as in the distal-most quartile), and suggested that dysplasia could be found more often with targeting biopsies to 8 in the proximal cm of BE, 8 in the second cm, and 2 biopsies in each cm thereafter. Using this method, the authors suggest that a 30% increased sensitivity of dysplasia detection in short segment BE could be achieved.

Ladabaum U, Ford JM, Martel M, Barkun AN.

Systematic review and meta-analysis related to routine clinical practice diagnosis and management of Lynch syndrome patients; supports the AGA Guideline concurrent publication. Question 2 is pertinent to pathologists, pertaining to adult colorectal cancer patients, what is the sensitivity and specificity of tumor testing for findings LS cases, and whether age is a factor? Authors found Moderate quality of evidence of MSI testing versus no testing or IHC testing, and for IHC tumor testing versus no testing of MSI testing; and Low quality of evidence for both IHC and MSI testing versus either IHC or MSI testing. Testing was determined to be cost-effective overall. Question 3 is also pertinent to pathologists: in adult CRC patients with MLH1 loss on IHC, what is the sensitivity and specificity of further testing to identify sporadic cases? Quality of evidence is very low for MLH1 promoter methylation testing versus no further testing, and for BRAF mutation testing versus no further testing.

American Gastroenterological Association Institute Guideline on the Diagnosis and Management of Lynch Syndrome.
Rubenstein JH, Enns R, Heidelbaugh J, Barkun A; Clinical Guidelines Committee.
Gastroenterology. 2015 Sep;149(3):777-82.

This paper extends what is reported in the concurrently published technical review into AGA recommendations and suggestions. All colorectal cancer patients would have their tumor tests with either IHC or MSI to detect Lynch syndrome. For colorectal cancer patients with MLH1 loss by IHC, BRAF mutation testing or MLH1 promoter hypermethylation should be performed rather than germline genetic testing.
**Germline Mutations in FAN1 Cause Hereditary Colorectal Cancer by Impairing DNA Repair.**


The aim of this study was to identify a new hereditary colorectal cancer gene. The authors focused on 3 colorectal cancer patients with high-risk, mismatch repair proficient, Amsterdam I colorectal cancer families, and found a nonsense mutation in FAN1, c.141C>A(p.C47*), which has not been previously reported. The authors discuss the relevance of this novel finding in the current context of hereditary colorectal cancer.

**Radiofrequency Ablation Is Associated With Decreased Neoplastic Progression in Patients With Barrett's Esophagus and Confirmed Low-Grade Dysplasia.**


This retrospective study of Barrett esophagus patients with low grade dysplasia (confirmed by at least one expert pathologist) included 45 patients who underwent radiofrequency ablation (RFA) and 125 who underwent surveillance endoscopy. Annual rate of progression to high grade dysplasia or adenocarcinoma was 6.6% in the surveillance group compared to 0.77% in the RFA group. The authors emphasize the need for pathologist consensus on the LGD diagnosis, and note that in their study, 31% of patients in the surveillance group did not have future biopsies of LGD, which is similar to previously reported rates.

**Fibroblast growth factor receptor 1 gene amplification in gastric adenocarcinoma.**


Hum Pathol. 2015 Oct;46(10):1488-95.

Fibroblast growth factor receptor 1 (FGFR1) is a potential target for tyrosine kinase inhibitors. The authors performed FISH on tissue microarrays of 293 gastric adenocarcinomas and found that 2% of cases show FGFR1 gene amplification, which was significantly associated with poor 10 year survival and higher rate of distant metastases.

Acute graft-versus-host disease is more prevalent and severe in the lower than the upper gastrointestinal tract.
Ma C, Maluf HM, Liu TC.

This retrospective study of 110 cases of simultaneous upper gastrointestinal tract (UGI) and lower gastrointestinal tract (LGI) biopsies from hematopoietic stem cell transplant recipients with clinically confirmed acute GCHD of the GI tract found that 75% of cases had both UGI and LGI involvement, lowest prevalence being in the stomach (61%) and highest in the sigmoid colon (97%). Overall prevalence and grade were higher in LGI as compared to UGI (P<0.001). Esophageal biopsies were excluded from this study due to lack of a consensus grading scheme for this anatomic site. Lerner grading was otherwise applied to grade all other sites. Neither MMF therapy nor CMV infection affected the distribution or severity of GVHD in the GI tract.

Clinical, pathologic, and outcome study of hyperplastic and sessile serrated polyps in inflammatory bowel disease.
Hum Pathol. 2015 Oct;46(10):1548-56.

This study evaluated the clinical, pathologic, and outcome features of 65 ulcerative colitis and 50 Crohn’s patients who had at least one serrated polyp at index colonoscopy or resection and determined that these patients harbor no increased risk for flat conventional dysplasia or cancer. 96% of patients had a hyperplastic polyp, 6% of patients had a sessile serrated polyp, and none had traditional serrated adenoma. 75% of the polyps occurred within an area involved by colitis. Interestingly, 42% of the polyps were only detected microscopically, without endoscopic evidence of a polyp. Due to the low-number of SSPs and TSAs in this study, further studies are recommended to evaluate the significance of these lesions in IBD.

Expression of adhesion molecules and epithelial-mesenchymal transition factors in medullary carcinoma of the colorectum.
An immunohistochemical study was performed whereby the authors raise the possibility that the favorable outcome of medullary carcinoma despite poorly differentiated morphology may be due to preserved expression of E-cadherin in the central portion of the tumor and less frequent expression of epithelial-mesenchymal markers (Snail, Twist1) at the invasive front, which was significantly different as compared to non-medullary poorly differentiated colorectal adenocarcinomas.

**Histologic features predicting postoperative Crohn's disease recurrence.**

The European Crohn’s and Colitis Organization expects an indication of disease activity in all pathology reports for chronic colitis, but there is no standard system or validated system for grading histological activity. 102 biopsy specimens from UC patients were scored blindly by three pathologists using Geboes, Riley, Gramlich, and Gupta indices and global visual evaluation (GVE, visual scale of 0-10 for minimal to maximal activity). All methods showed good intraobserver reproducibility and agreement (agreement 75% or higher). “Chronic inflammatory infiltrate” and “eosinophils in lamina propria” showed moderate reproducibility and interobserver agreement. The best interobserver agreement was for “erosion/ulceration” (85%-96% depending on index used) and “acute inflammatory cell infiltrate/neutrophils in lamina propria” (62%-66% for various indices, 89% for Gupta index – neutrophil infiltration of >50% of sampled crypts). [Note: essentially, the worse the disease, the better the interobserver reproducibility, as might be expected.] The authors categorically state, “These findings should be taken into account for the assessment of histological disease in UC in clinical practice.”

**Real-time optical diagnosis for diminutive colorectal polyps using narrow-band imaging: the VALID randomised clinical trial.**

Diminutive polyps (less than or equal to 5mm on endoscopy) tend to be benign, either hyperplastic or adenomatous. A multi-center study of real-time optical diagnosis was investigated as to whether clinical care could be made without histopathology, i.e., can accurate
high-confidence optical diagnosis be made in comparison to central blinded pathology? 558 subjects were found to have 1309 polyps, of which 74.5% were diminutive and 60.0% neoplastic. Various optical techniques were utilized (termed “near focus” and “standard view”). Both techniques gave greater than 92% agreement with histopathological diagnosis with median diagnosis time of 14 seconds. As the authors state, “optical diagnosis would be a paradigm shift in clinical practice of colonoscopy for colorectal cancer screening.”

### Primary Anal Canal Syphilis in Men: The Clinicopathologic Spectrum of an Easily Overlooked Diagnosis.
Gopal P, Shah RB.
Arch Pathol Lab Med. 2015 Sep;139(9):1156-60.

Incidence of syphilis is increasing, particularly in HIV-positive men and men who have sex with men (MSM). Syphilis should be considered in the differential in cases of anal canal ulcers, anorectal inflammatory masses, and proctitis. Four cases of primary syphilis in the anal canal are reviewed in detail. Microscopic features include a bandlike chronic inflammatory infiltrate where squamous epithelium meets the lamina propria, dermal and perivascular chronic inflammatory infiltrate (may be plasma cell-rich), and (sometimes) poorly formed granulomas. One of the four patients had negative RPR test but positive FTA-ABS test, and the authors suggest a prozone phenomenon could be responsible for the negative RPR result; this phenomenon may be more prevalent in HIV-positive patients. Silver stains do not have good sensitivity and specificity, so Treponema pallidum IHC can be more helpful when positive (organism distribution may be variable). Despite negative T. pallidum IHC, if there is high suspicion for syphilis or other sexually transmitted infection based on histology and/or clinical presentation, the authors suggest a descriptive diagnosis with a comment suggesting clinical follow-up with appropriate lab tests to rule out STI including syphilis or lymphogranuloma venereum.

### A Comprehensive Strategy for Accurate Mutation Detection of the Highly Homologous PMS2

Accurate assessment of *PMS2* is hindered by the presence of PMS2CL, a pseudogene with 98% sequence identity with the 3’ end of *PMS2*. Furthermore, frequent sequence transfer events between *PMS2* and *PMS2CL* result identical sequence variants. Thus, distinction between the two genes and analysis of copy number variants of *PMS2* is technically difficult. These authors
describe novel technique using next-generation sequencing, multiplex ligation-dependent probe amplification, and long-range PCR to unequivocally identify sequence variants and copy number changes in PMS2 and distinguish them similar alterations in PMS2CL. Development of this and similar techniques may ultimately aid the evaluation of patients with Lynch syndrome and hereditary cancer syndromes related to biallelic PMS2 mutations.

Grading Lymph Node Metastases: A Feasible Approach for Prognostication of Patients with Stage III Colorectal Cancer
Resch A, Harbaum L, Pollheimer MJ, Kornprat P, Lindtner RA, Langner C
J Clin Pathol. 2015; 68(9):742-745.

The authors compared the prognostic importance of tumor grade within lymph node metastases to that of primary tumor grade in 145 patients with node-positive colon cancer, including 128 patients with clinical follow-up. They reported that 63% of patients with grade 2 or 3 metastatic deposits experienced disease progression compared to 55% of those with grade 1 deposits (p=0.031). Sixty-three percent of patients with grade 2 or 3 lymph node metastases died of disease compared to only 46% of those with grade 1 tumor in lymph nodes (p=0.008). In contrast, they reported no significant differences in these two prognostic parameters related to primary tumor grade. Finally, Cox’s proportional hazard regression models showed significantly lower cancer-specific survival among patients with high-grade lymph node deposits.

Tumor Budding in Colorectal Carcinoma: Confirmation of Prognostic Significance and Histologic Cutoff in a Population-based Cohort

The aim of this study was to determine a histologic cutoff for “high—tumor budding on H&E slides and confirm its prognostic significance. Incident colorectal carcinoma cases (n=553) were identified through a large cohort of women using Iowa Women’s Health Study and SEER program registry from 1986 to 2002. A scoring system described by Ueno et al was used. Briefly, the slides were scanned for areas with the maximal budding at the tumor edge and tumor buds in a 20x objective field were counted. Tumor bud is a collection of <5 neoplastic cells. Associations of tumor budding with histologic and clinicopathologic features were assessed using $\chi^2$ tests for categorical variables and analyses of variance for continuous variables. High budding ($\geq$ 10 tumor buds in x20 objective field) was present in 32% of cases, low budding (1 to
9 buds) in 46% and no budding in 22%. High tumor budding was associated with advanced pathologic stage \( (P<0.001) \), microsatellite stability \( (P=0.005) \), KRAS mutation \( (P=0.010) \) and on multivariate analysis with a \( >2 \) times risk of cancer-specific death. Interobserver agreement was \( K \) of 0.70 for 2 GI pathologists (121 randomly selected cases) and 0.72 between all 6 pathologists (20 randomly selected cases). There was no correlation between tumor budding and histologic grade, tumor site, radiation treatment, BRAF mutation, or CIMP.

**Superior Mesenteric Artery Margin (SMAM) of Posttherapy Pancreaticoduodenectomy (PD) and Prognosis in Patients with Pancreatic Ductal Adenocarcinoma (PDAC)**


This study retrospectively reviewed 411 consecutive patients (between 1999 and 2012, 183 women and 228 men, mean age: 64y) with PDAC who had received neoadjuvant therapy (various combinations of neoadjuvant chemotherapy and/or radiation) before undergoing PD. All patients had PDAC in the pancreatic head, proven on biopsy or FNA. The study correlated the distance of SMAM (aka retroperitoneal or uncinate margin) from the tumor with disease-free survival (DFS), overall survival (OS), and other parameters. PD specimens were fixed overnight (no intraoperative frozen performed) and SMAM margin was entirely submitted. No difference in either DFS or OS between the positive margin group or SMAM≤1mm was identified. By multivariate analysis, SMAM distance was an independent prognostic factor for DFS and OS and patients with an SMAM of 1.0 to 5.0mm or >5.0 mm had better prognoses that did those with positive margins or those with ≤1mm. SMAM distance correlated with lower ypT and AJCC stages, smaller tumor size, better histopathologic tumor response grade, fewer lymph node metastases and recurrences \( (P<0.05) \). There was no difference in either DFS or OS between those with positive SMAM and those with positive pancreatic or common bile duct margin. This study supports the concept that the 0-mm rule set by CAP and AJCC protocols may underestimate the real risk for local recurrence and distant metastasis and strongly support SMAM>1 mm for R0 resection in post-therapy PD specimens.

**Heterogenous MSH6 Loss Is a Result of Microsatellite Instability within MSH6 and Occurs in Sporadic and Hereditary Colorectal and Endometrial Carcinomas**

Graham RP, Kerr SE, Butz ML, Thibodeau SN, Halling KC, Smyrk TC, Dina MA, Waugh VM, Rumilla KM

The purpose of this study was to investigate cases with heterogenous (het) MSH6 loss (cases that harbored areas of definite, retained MSH6 expression within the tumor and areas of complete loss of MSH6). 13,100 IHC cases diagnosed from Jan 2001-Dec 2012 at a single institution were analyzed. 22 cases (<1 % of cases) of het MSH6 expression were identified (18 CRC, 3 endometrial carcinomas and 1 sebaceous neoplasm) by consensus of 3 pathologists. 16 cases of LS due to germline MSH6 loss were used as controls as well as 5 cases of CRC with normal MMR IHC. PCR-based MSI testing was available for 20/22 cases with het MSH6 loss. 18 of these 20 cases were MSI-H; 2 were MSS cases (these 2 cases were status post neoadjuvant chemoradiation but were microsatellite and C8 tract stable). 15 cases showed MLH1 and PMS2 loss and 3 isolated loss of PMS2. Normal MLH1 and PMS2 was noted in 4 cases. No cases showed loss of MSH2 expression. Sanger sequencing of tumor DNA derived from areas of MSH6 loss and MSH6 retention was also performed. Somatic C8 instability was seen in cases with het loss and in 2 of 4 cases with LS due to germline mutation. Het MSH6 loss cases showed mucinous or signet-ring zones in ¼ of cases. In conclusion, het MSH6 loss is a manifestation of somatic instability (frameshift mutations) within a polycytosine tract in MSH6 exon 5. MSH6 polycytosine tract instability is not useful to distinguish between germline and somatic mutations. Patients with het MSH6 loss pattern may have LS due to a defect in a different MMR gene but is not associated with germline MSH6 mutations.

"Mass-forming" Variant of Ischemic Colitis is a Distinct Entity with Predilection for the Proximal Colon
Khor TS, Lauwers GY, Odze RD, Srivastava A
Am J Surg Pathol. 2015 Sep; 39(9):1275-81

This retrospective study evaluated the clinicopathologic features of a variant of ischemic colitis (IC) that presents as a mass lesion (mass-forming variant). 19 patients were identified, mainly elderly (mean age 71.8 y) women (63.2%) with a marked predilection for the right colon (13/19), particularly cecum (n=6). Presenting symptoms were abdominal pain, hematochezia and diarrhea. Colonoscopic and/or CT findings revealed a polypoid or fungating mass (16/19) and a stricturing/apple-core-type lesion (3/19). Mean size of mass: 4.6 cm. Biopsies obtained from mass lesion showed features of IC (15/17 patients) and 2 cases showed only granulation tissue and necroinflammatory debris (subsequent resection specimens showed features of IC in both cases).15 patients underwent conservative management and 4 cases underwent surgery. In these last 4 patients, the mass-like effect could be ascribed to marked submucosal and mural edema (n=2) (polypoid mass) and marked submucosal fibrosis (n=2)(stricture-like appearance). One of the 2 cases in this last group showed intravascular cholesterol emboli. No malignancy was
identified on follow-up (mean follow-up: 39.9 months). In summary, the finding of an IC in the context of a well-sampled mass lesion, particularly in cecum or right colon, in an elderly woman with known risk factors for IC, should raise the suspicion for a mass-forming variant of IC.

Clinicopathologic Analysis of 6 Lymphomatoid Gastropathy Cases: Expanding the Disease Spectrum to CD4-CD8+ Cases

Am J Surg Pathol. 2015 Sep; 39(9):1259-66

This article analyzes 6 cases (3 men, 3 women, median age: 64.5 y, search between 1989 and 2013 in Okayama University) of lymphomatoid gastropathy (a benign NK-cell proliferation of cyCD3+, CD4-, CD5-, CD8-, CD56+ phenotype with unknown etiology that regresses without any therapy). 4 hematopathologists reviewed the cases. All lesions were located in stomach (4 presented with superficial erythematous mucosa, 1 with a superficial depression and 1 with an ulceration). 3 of 6 patients underwent lower GI examination with no findings. 2 cases showed previously unreported unique immunophenotypes of CD4-CD8+ (with no obvious difference of histology or clinical behavior). Helicobacter pylori was found in all 6 cases. EBER-1-ISH, TRG and betaF1(IHC) were negative in all cases. PCR study showed polyclonal results for TCRγ. Median follow-up was 35 months. Disease regressed without therapy confirmed by endoscopic biopsy in 4 patients. In another patient lesion regressed in 1 month but relapsed in 6 months and resection showed a small residual lesion. Of interest, 1 other case demonstrated an EATL in jejunum but gastric lesion was confirmed to be lymphomatoid gastropathy. The significance of this finding was uncertain. In summary, knowledge of this entity is important since it is a mimicker of lymphoma, mostly extranodal NK/T-cell lymphoma (negativity for EBER is the most important point in its differentiation) and EATL (absence of clonal TCRγ gene rearrangements, the non-aggressive histologic features, and the benign clinical course of the disease argue against EATL).

Knowledge and Predictors of Dysplasia Surveillance Performance in Inflammatory Bowel Diseases in Australia
This study performs a nationwide evaluation of the quality of IBD surveillance practiced by Australian endoscopists and determines the predictors of quality practice. A survey was developed by a focus group of 3 gastroenterologists and comprised 22 self-administered questions. A total of 264 responses were received (218 gastroenterologists and 46 CRC surgeons). Gastroenterologists were significantly more likely to undertake surveillance ($P<0.01$), adhere to guidelines ($P=.02$), use advanced imaging modalities ($P=.04$), and have greater surveillance knowledge that colorectal surgeons ($P<.001$). Knowledge score and gastroenterologists were independent predictors of dysplasia screening, guideline adherence and advanced endoscopic imaging technique use.

**Single-operator Cholangioscopy and Targeted Biopsies in the Diagnosis of Indeterminate Biliary Strictures: a Systematic Review**
Gastrointest Endosc. 2015 Oct;82(4):608-614

Spy Glass peroral cholangioscopy can provide endoscopic direct visualization of the biliary system and allows also targeted biopsies under direct vision. In this systematic review of PubMed and Embase databases published from Jan 1980 to October 2014, a total of 10 studies involving 456 patients were selected. The aim of this article was to study the utility of Spy Glass peroral cholangioscopy in indeterminate (benign or inconclusive with strong suspicion for malignancy) strictures. This study suggests that SpyGlass Cholangioscopy with SpyBite biopsies has moderate sensitivity for the diagnosis of malignant biliary strictures. The pooled sensitivity and specificity of cholangioscopy-guided biopsies in the diagnosis of malignant biliary strictures was 60.1% and 98.0% respectively. Only 1 study directly compared the yield of SpyBite biopsies with standard brushings and biopsies. Spybite biopsies had a sensitivity of 76.5% compared with brushings (5.8%) and biopsies (29.4%).

**Recurrence Rates after EMR of Large Sessile Serrated Polyps**
Rex KD, Vemulapalli KC, Rex DK
Gastrointest Endosc. 2015 Sep; 82(3):538-41

This retrospective cohort study reviewed a total of 362 consecutive patients referred for resection of large (>20 mm) polyps in the colorectum and particularly focused on the recurrence rate after
EMR of large SSA/Ps. All EMRs were performed with a submucosal contrast agent and all subjects had a follow-up surveillance examination (inspection and biopsy of the EMR). The procedures were performed by a single experienced endoscopist (between 2006 and 2014). The first follow-up examination was performed 4 to 6 months after EMR. This study found that EMR of large SSA/Ps performed with a submucosal contrast agent and high-definition colonoscope leads to high endoscopic cure rates (residual polyp in 8.7% of cases, 4/46) at first follow-up comparable with those achieved with conventional adenomas (residual polyp in 11.1% of cases, 39/351). On univariate analysis, only size (P = .02) predicted residual polyp at follow-up.

**Frequency of Mitogen-activated Protein Kinase and Phosphoinositide 3-kinase Signaling Pathway Pathogenic Alterations in EUS-FNA Sampled Malignant Lymph Nodes in Rectal Cancer with Theranostic Potential**


Gastrointest Endosc. 2015 Sep; 82(3):550-6


The objective of this study was to assess the frequency and distribution of pathogenic alterations in malignant LN cytology specimen in sporadic treatment naive, locally advanced primary rectal cancer by EUS-FNA (n=76, 49 men and 27 women, Feb 2002 to Dec 2011) who subsequently completed neoadjuvant therapy with on-site oncologic surgery. Multigene molecular profiling of archived malignant EUS-FNA LN cytology specimens using the Ion Ampliseq Cancer Hotspot Panel v2 (targeting 2855 possible mutations within 50 cancer-associated genes) was performed. Eleven patients were 50-gene panel wild-type and 65 patients had 139 pathogenic alterations in 13/50 evaluated genes (52 in TP53, 36 in APC, 22 in KRAS, 8 in FBXW7, 6 in NRAS, 4 in PIK3CA, 3 in SMAD4 and 3 in BRAF). Pathogenic alterations were identified in the MAPK and PI3K signaling pathways in 41% and 5% of patients. In summary, molecular EUS LN assessments using cancer “hotspot” panels can identify pathogenic alteration frequency and distribution. A limitation of this study is the inability to assess the multigene mutation profile concordance or discordance between primary lesion and malignant LN.

**Lymphangiomatous Lesions of the Gastrointestinal Tract: A Clinicopathologic Study and Comparison Between Adults and Children.**


Lawless ME, Lloyd KA, Swanson PE, Upton MP, Yeh MM.


The aim of this study was to define the morphologic and clinical features of GI tract lymphangiomas (primary lymphatic malformations) in adults and pediatric patients based on surgical excision and endoscopically removed specimens and to contrast the histologic features
with those of lymphangiectasia. Because lymphangiectasia, due to obstruction of existing lymphatics, can be associated with an unsampled tumor or other conditions that require medical attention, the distinction is important. The authors look at some clinical differences between adult and pediatric lymphangiomas, but find the histologic features are more or less similar. The authors conclude that the most important distinction between lymphangioma and lymphangiectasia is that the cystic spaces in lymphangiomas have a distinct and complete endothelial lining and are associated with a smooth muscle component, while lymphangiectasia lack both.

**Sporadic Fundic Gland Polyps With Low-Grade Dysplasia: A Large Case Series Evaluating Pathologic and Immunohistochemical Findings and Clinical Behavior.**
Levy MD, Bhattacharya B.
The purpose of this study was to evaluate clinical, morphologic, and immunohistochemical features of a series of sporadic fundic gland polyps with dysplasia (FGPD). 62 sporadic and 23 syndromic cases were pulled from the author’s database over the course of 4 years. The prevalence of dysplasia in fundic gland polyps overall was 0.3%. Immunohistochemistry for p53, Ki67, B-catenin, showed no statistically significant differences between the sporadic and syndromic polyps. Clinical follow up in the sporadic group, in a subset in which it was available, found 15% of cases with additional fundic gland polyps with dysplasia but none were found to have high grade dysplasia or other adverse outcomes.

**Performance characteristics of next-generation sequencing in clinical mutation detection of colorectal cancers.**
The main purpose of this article is to report performance characteristics of a next-generation sequencing panel (AmpleSeq Cancer Hotspot panel) as evaluated in a retrospective study of 310 colorectal cancer cases. Among other points the benefits of the multiplex platform over single gene tests for identifying predicted resistance to anti-EGFR therapy are discussed.
Grading lymph node metastasis: a feasible approach for prognostication of patients with stage III colorectal cancer
Annika Resch, Lars Harbaum, Marion J Pollheimer, Peter Kornprat, Richard A Lindtner, Cord Langner
J Clin Pathol 2015;68:742-745

In this study, the authors examine the question of whether grading the degree of differentiation in colonic lymph node metastases predicts prognosis. They studied 145 individuals with stage III colorectal cancer. Metastases were graded G1 in 77 cases (53.1%), G2 in 41 cases (28.3%) and G3 in 27 cases (18.6%) cases, respectively. Statistical analysis showed that lymph node tumor grade was significantly associated with N classification (p=0.009), tumor size (p=0.024) and lymphovascular invasion (p=0.004), and with primary tumor grade (p<0.001). Finally, multivariable analysis showed that lymph node grade was an independent predictor of cancer-specific survival.

Features of Gastric Carcinoma With Lymphoid Stroma Associated With Epstein-Barr Virus.
Lim H1, Park YS2, Lee JH3, Son da H2, Ahn JY1, Choi KS1, Kim do H1, Choi KD1, Song HJ1, Lee GH1, Jung HY1, Kim JH1, Yook JH4, Kim BS4.

The authors examine 274 cases of gastric carcinoma that were diagnosed as “gastric carcinoma with lymphoid stroma”, using the criteria of the tumor having at least some areas of undifferentiated carcinoma with a prominent lymphoid infiltration. The undifferentiated component ranged in frequency from 70% to 100% of the carcinoma. Of these 274 cases, 236 were positive for EBV (86.1%), with EBV found in both undifferentiated areas and in gland forming areas of the carcinoma. In comparing EBV positive cases to EBV negative cases, EBV positive cases were more likely to be found in younger individuals and were more likely to have a proximal location. The 10-year, disease-specific rate of survival was 89%, versus 67% for patients with EBV-negative gastric carcinomas with lymphoid stroma (p = .009). Also, cases of EBV-negative gastric carcinomas with lymphoid stroma had overall survival times similar individuals with conventional adenocarcinoma. On multivariate analysis, better survival was associated with EBV-positive tumors (p= .007), younger age (p = .002), smaller tumor size (p = .046), lower stage (p P < .001), and lack of lymphovascular invasion (p = .012). In contrast, the percent of the carcinoma showing undifferentiated morphology was not associated significantly with patient survival time.
Detection of Dysplasia or Cancer in 3.5% of Patients With Inflammatory Bowel Disease and Colonic Strictures.


This very large, multicenter study examined the frequency of dysplasia in colonic strictures complicating inflammatory bowel disease. The study examined 12,013 patients with IBD in France who underwent surgery for strictures at 16 centers. The median age at stricture diagnosis was 38 years. The strictures had a median length of 6 cm and were symptomatic in 70% of patients. On histological examination, 3.5% had dysplasia or cancer.
Journals Reviewed (Sept and Oct, 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

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