Journal Watch March and April, 2015

Serrated polyps and the risk of synchronous colorectal advanced neoplasia: a systematic review and meta-analysis.

Gao Q, Tsoi KK, Hirai HW, Wong MC, Chan FK, Wu JC, Lau JY, Sung JJ, Ng SC.

Am J Gastroenterol 2015; 110(4):501-9.

http://www.ncbi.nlm.nih.gov/pubmed/25756237

This systematic review and meta-analysis included 34,084 participants from a total of 9 studies. Serrated polyps were defined as hyperplastic polyps, sessile serrated polyps/adenomas, and traditional serrated adenomas, all grouped together. The pooled prevalence of serrated polyps was 15.6%. Based on 4 of the studies, there was a 2 fold increased risk for individuals with serrated polyps to have synchronous advanced neoplasia, but no significant association was found with synchronous colorectal cancer. Patients with proximal serrated polyps (proximal to the splenic flexure) were more than twice as likely to have a synchronous advanced neoplasia. Having a large serrated polyp (> or = 10 mm) was also associated with an increased risk of synchronous advanced neoplasia. The risk was present for neoplasia occurring in both the right and the left colon. The authors conclude that surveillance colonoscopy should be offered to patients with serrated polyps, especially of if they are large or proximal.

Undifferentiated carcinoma of the esophagus: a clinicopathological study of 16 cases.
Singhi AD, Seethala RR, Nason K, Foxwell TJ, Roche RL, McGrath KM, Levy RM, Luketich JD, Davison JM.

Hum Pathol 2015; 46(3):366-75.

http://www.ncbi.nlm.nih.gov/pubmed/25634752

This is a retrospective review of 16 resections of the rare tumor: undifferentiated carcinoma of the esophagus, 94% from male patients, and 75% arising in a background of Barrett's esophagus. Tumors were centered within the distal esophagus or at the GEJ. Tumor histology included expansile growth of neoplastic cells in sheets with syncytial appearance and patchy necrosis. A few cases had sarcomatoid, rhabdoid, or <5% glandular morphology. All cases were diffusely positive for Cam5.2. Lymph node metastasis was common (81%). Mean survival after resection was about 12 months, with 67% of patients having locoregional recurrence and/or distant metastasis. These are aggressive tumors with poor prognosis.

Utility of ancillary stains for Helicobacter pylori in near-normal gastric biopsies.

Panarelli NC, Ross DS, Bernheim OE, Landzberg ZB, Schuetz AN, Jenkins SG, Landzberg BR, Jessurun J, Yantiss RK.

Hum Pathol 2015; 46(3):397-403.

http://www.ncbi.nlm.nih.gov/pubmed/25582501

In this study gastric biopsies interpreted as negative for H. pylori on H&E stain alone from 56 patients with biochemical evidence of H. pylori infection (positive Campylobacter-like organism (CLO) test) were subjected to additional testing by Giemsa, Warthin-Starry, acridine orange, and immunohistochemistry, as well as review of the original H&E. Six cases were positive with all four additional stains and on review of the H&E, which showed mild chronic inflammation. The remaining 50 cases were negative on all stains and H&E showed normal mucosa in 19 (34%), mild chronic inflammation with or without focal activity in 22 (39%), and chemical gastropathy in 15 (27%). A total of 20% of patients were taking a PPI, and 7% had received previous H. pylori treatment. Controls for this study included 10 patients with congruent CLO test positive and H&E detected H. pylori with chronic active gastritis, as well as 10 patients with congruent CLO-test negative with normal H&E gastric biopsy. This study did not find that any one ancillary test was superior to another. This study also confirmed that at least minimal chronic inactive gastritis should be present to consider ancillary testing for H.pylori. Finally, this study confirmed that H.pylori may be found in the gastric fundus without being identified in the antrum.

Aurora kinase A gene copy number is associated with the malignant transformation of colorectal adenomas but not with the serrated neoplasia progression.

Casorzo L, Dell'Aglio C, Sarotto I, Risio M.

Hum Pathol 2015; 46(3):411-8.

http://www.ncbi.nlm.nih.gov/pubmed/25596657

Eighty endoscopically resected colorectal polyps were studied, including 40 adenomas, 20 adenomas with invasive carcinoma, and 20 serrated polyps. Of the 40 adenomas, 10 were tubular adenomas and 30 were advanced adenomas (10 with villous histology, 10 with high-grade dysplasia, and 10 with size = or > than 1 cm). FISH was performed for AURKA gene amplification and IHC for AURKA protein was also performed. AURKA gene copy number was not altered in any serrated polyps, including those with conventional dysplasia, although protein expression was found. Apoptotic dysregulation is a possible explanation for the uncoupled gene status and protein expression. Protein expression corresponded with increased

gene copy number and both increased significantly in advanced adenomas as compared to tubular adenomas, and increased further in adenomas with invasive carcinoma.

Gastric amyloidosis: clinicopathological correlations in 79 cases from a single institution.

Said SM, Grogg KL, Smyrk TC.

Hum Pathol 2015; 46(4):491-8.

http://www.ncbi.nlm.nih.gov/pubmed/25649008

This is a retrospective study of cases of gastric amyloidosis. In 17 of 79 patients (22%) the initial diagnosis of amyloidosis was made based on the gastric biopsy. Amyloid typing was performed by laser microdissection/mass spectrometry (44 patients), IHC (25 patients), direct immunofluorescence on a kidney biopsy (5 patients), and genetic testing (3 patients). This testing revealed that 67% had AL amyloid, 18% had ATTR, 9% had AA, and 3% had AApo A1. The majority of patients had biopsy-proven amyloid involving other GI tract sites, and many had other organs involved, including heart, kidney, liver, and nerve. Four patients had amyloid restricted to the GI tract. The muscularis mucosae was the most common location of involvement (92% of cases in which it was sampled) by any amyloid type, and lamina propria was involved in 69% of cases. Interestingly, lamina propria involvement was significantly less likely to be involved by ATTR amyloid than by AL or AA amyloid. Submucosa was involved in 28% of cases in which it was sampled, and blood vessels were involved in 77%. Other histologic findings in gastric biopsies with amyloid included gastritis, reactive gastropathy, intestinal metaplasia, H. pylori, erosions/ulcer, fundic gland polyp, invasive carcinoma, PPI-effect, and mycophenolate injury. About 35% of cases were endoscopically normal, while the others showed erythema, erosions, or nodularity, all unrelated to amyloid type. Three year survival was 60%, which was unrelated to amyloid type. The authors conclude that amyloid typing on biopsy material is important for diagnosis, prognosis and treatment.

Novel molecular insights from routine genotyping of colorectal carcinomas.

Stachler MD, Rinehart E, Lindeman N, Odze R, Srivastava A.

Hum Pathol 2015; 46(4):507-13.

http://www.ncbi.nlm.nih.gov/pubmed/25683705

This study shows that routine genotyping of colorectal carcinoma (CRC) is helpful to identify low-frequency mutations and to reveal multiplicity of concurrent mutations in a significant proportion of cases. A total of 311 CRC were genotyped for 471 mutational hot-spots in 41 cancer associated genes using the OncoMap platform. At least 1 mutation was identified in 77%

of the cases, most frequently KRAS (42%), APC (25%) and TP53 (21%). Concurrent mutations were present in a total of 40% of patients, most often 2 concurrent mutations (29%). GNAS mutations were associated with a mucinous histology (20%). Interestingly, the authors identified a subset of CRC for which the mutational profile did not fit into the CIN or CIMP pathways of carcinogenesis. The authors conclude that the genotyping data can lead to better patient selection for both oncologic management and for clinical trial enrollment.

Evaluation of human tissue kallikrein-related peptidases 6 and 10 expression in early gastroesophageal adenocarcinoma.

Grin A, Samaan S, Tripathi M, Rotondo F, Kovacs K, Bassily MN, Yousef GM.

Hum Pathol 2015; 46(4):541-8.

http://www.ncbi.nlm.nih.gov/pubmed/25649006

A stepwise increase in kallekrein-related peptidase 6 (KLK6) expression from metaplasia to dysplasia to invasive adenocarcinoma was demonstrated in Barrett's associated adenocarcinomas by immunohistochemistry in 30 patients who underwent endoscopic mucosal resection for early GEJ adenocarcinoma. KLK10 was significantly higher in dysplastic compared to metaplastic lesions, but not in invasive carcinoma. Increased staining intensity of KLK6 at the invasive front of the tumor suggests a role in tumor invasiveness. Both KLK6 and KLK10 were identified as potentially independent biomarkers, since neither was significantly associated with other known prognostic markers or other histologic markers of poor prognosis. The authors conclude that KLK6 and KLK10 are potential biomarkers and therapeutic targets in early Barrett's associated GEJ adenocarcinoma.

SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease.

Laine L, Kaltenbach T, Barkun A, McQuaid KR, Subramanian V, Soetikno R; SCENIC Guideline Development Panel.

Gastroenterology 2015; 148(3):639-51.

http://www.ncbi.nlm.nih.gov/pubmed/25702852

This is an international consensus statement based on a systematic review of the literature for specific clinical questions. Previous guidelines have come from older literature, and have been issued prior to the use of video endoscopy and other new endoscopic technologies, where targeted biopsies are performed for IBD-dysplasia rather than random sampling. Consensus recommendations include the use of high-definition colonoscopy for surveillance, use of chromoendoscopy if standard-definition colonoscopy is performed, use of chromoendoscopy with high –definition colonoscopy, and avoidance of narrow-band imaging in most clinical situations. Consensus was not reached regarding the utility of random biopsies, even with the availability of modern technologies for targeted biopsy, since 1-1.5% of patients with dysplasia could be missed. Surveillance colonoscopy was recommended over colectomy after complete removal of endoscopically resectable polypoid dysplastic lesions, and colonoscopy was suggested in the same situation for nonpolypoid dysplastic lesions. A recommendation was also made that patients with biopsy-proven dysplasia from a lesion not endoscopically visible (flat dysplasia) should undergo surveillance by an IBD expert using chromoendoscopy with high-definition colonoscopy.

Identification of risk loci for Crohn's disease phenotypes using a genome-wide association study.

Alonso A, Domènech E, Julià A, Panés J, García-Sánchez V, Mateu PN, Gutiérrez A, Gomollón F, Mendoza JL, Garcia-Planella E, Barreiro-de Acosta M, Muñoz F, Vera M, Saro C, Esteve M, Andreu M, Chaparro M, Manyé J, Cabré E, López-Lasanta M, Tortosa R, Gelpí JL, García-Montero AC, Bertranpetit J, Absher D, Myers RM, Marsal S, Gisbert JP.

Gastroenterology 2015; 148(4):794-805.

http://www.ncbi.nlm.nih.gov/pubmed/25557950

This genome-wide association study in a European cohort of 1090 Crohn’s patients and validated in an independent cohort of 1296 patients identified the association of 4 loci with different Crohn’s phenotypes. The MAGI1 locus was associated with a complicated structuring disease course. The CLCA2 locus was associated with disease location. The 2q24.1 locus was associated with a mild disease course. Finally, LY75 was associated with erythema nodosum. This study supports the concept that there is a genetic component for disease heterogeneity in patients with established Crohn’s disease. The authors believe that further study of these genes could reveal additional insights into the pathogenesis of Crohn’s disease.

Are patients with inflammatory bowel disease on chronic immunosuppressive therapy at increased risk of cervical high-grade dysplasia/cancer? A meta-analysis.

Allegretti JR, Barnes EL, Cameron A.

Inflamm Bowel Dis 2015; 21(5): 1089-97.

http://www.ncbi.nlm.nih.gov/pubmed/25895005

The authors analyzed pooled results of 213 studies that assessed risk of cervical high-grade dysplasia or cancer in women with inflammatory bowel disease on immunosuppressive medications compared to a healthy control population and report increased risk among the former (OR=1.34). In studies that stratified risk by medication class, higher rates of cervical neoplasia were seen among patients taking immunomodulators compared to 5-ASAs or corticosteroids.

HER2 testing in gastric and gastroesophageal adenocarcinomas.

Vakiani E.

Adv Anat Pathol 2015; 22(3):194-201.

http://www.ncbi.nlm.nih.gov/pubmed/25844677

A comprehensive review of HER2 expression in gastric and gastroesophageal adenocarcinomas, therapeutic implications, and practical issues related to interpretation of testing methodss (including immunohistochemistry and fluorescence *in situ* hybridization) used to assess HER2 expression in these tumors.

Normal villous architecture with increased intraepithelial lymphocytes: a duodenal manifestation of Crohn disease.

Patterson ER1, Shmidt E2, Oxentenko AS3, Enders FT4, Smyrk TC5.

Am J Clin Pathol 2015; 143(3):445-50.

http://www.ncbi.nlm.nih.gov/pubmed/25696804

Increased intraepithelial lymphocytes (IELs) in duodenal mucosa with normal villous architecture is a common and nonspecific finding. The authors of this article propose that inflammatory bowel disease (IBD) should be considered in the differential diagnosis of this finding, adding to a long list that includes celiac disease, CVID, H. pylori gastritis, NSAIDs, small bowel bacterial overgrowth, viral enteritis, and autoimmune disease. In a retrospective review of all duodenal biopsies reported to have increased IELs with normal villous architecture in a 10 year period (1,161 of 17,129 biopsies) 74 were from patients with confirmed IBD, the majority (58 biopsies) from patients with Crohn disease. Of these patients with Crohn disease, half had concurrent focal gastritis, another feature associated with Crohn disease. While the authors state their belief that IBD should be added to the differential diagnosis of increased IELs with normal villous architecture, they also mention that a frequently cited study by Wright and Riddell found no difference in IEL counts between patients with Crohn disease and controls.

A modified Lynch syndrome screening algorithm in colon cancer: BRAF Immunohistochemistry Is efficacious and cost beneficial

Roth R, Hampel H, Arnold C, Yearsley M, Marsh W, Frankel W

Am J Clin Pathol 2015; 143(3):336-43.

http://www.ncbi.nlm.nih.gov/pubmed/25696791

This study looks at the possibility of using BRAF V600E immunohistochemistry rather than PCR based mutation analysis in the algorithm for the screening for Lynch syndrome in colorectal cancer. A common algorithm, which is used at the study authors' institution, is to screen all colorectal cancers by immunohistochemistry for DNA mismatch repair proteins most commonly lost in Lynch syndrome (MSH2, MSH6, PMS2, and MLH1). If MLH1 (and it dimer PMS2) is lost, BRAF mutational analysis is performed. A BRAF mutation essentially excludes Lynch syndrome, and no additional testing for the workup of Lynch is needed, saving the cost of additional testing and genetic counseling. Mutational analysis by PCR, however, is expensive and time consuming. The authors looked at a set of cases (n = 57) known to be MLH1 and PMS2 negative by immunohistochemistry, with known BRAF mutation results and tested them by BRAF V600E immunohistochemistry. The authors found the antibody, when compared to the PCR test, to be 100% specific and 88% sensitive in the sample. By a cost-befit analysis, using Medicare reimbursement rates, the authors speculated that an overall 10% savings in cost would have been obtained by using the PCR based mutational analysis in the algorithm.

Interobserver variability of mitotic index and utility of PHH3 for risk stratification in gastrointestinal stromal tumors.

Alkhasawneh A, Reith JD, Toro T, Ayed A, Lu X, George TJ, Duckworth LV.

Am J Clin Pathol 2015; 143(3):385-92.

http://www.ncbi.nlm.nih.gov/pubmed/25696796

The grading of gastrointestinal stromal tumors (GIST) relies on mitotic count and this study looks at the use of immunohistochemistry for PHH3 (phosphorolated form of histone 3) to aid in identifying mitotic figures in a manual count. PHH3 is mitosis specific and therefore correlates more closely to mitotic count than Ki-67, which identifies cells in multiple phases of the cell cycle. The authors of the study compared interobserver and intraobserver variability of mitotic activity in GISTs using H&E and PHH3 stained slides. In addition they also looked at the correlation between H&E mitotic count (manual count) and Ki67 labeling index (quantitative image analysis), association of PHH3 and Ki67 with overall survival, and attempted to define a PHH3 cutoff value that best correlated with overall survival. A set of 50 cases, 14 cases originally reported as high grade (> 5 mitoses per 5 mm2) and 36 as low grade (</= 5 mitoses per 5 mm2). The results showed good intraobserver variability between H&E and PHH3 counts. By PHH3 staining, using established criteria, a higher grade was obtained in 38% of the cases and a lower grade in 10% of cases. Ki67 showed poor correlation with H&E mitotic counts and was a poor predictor of overall survival. By analysis of ROC curves, the authors found that a cutoff of 7 mitoses per 5 mm2 was significant. Some of the advantages of PHH3 over H&E are discussed, including ease of identification of hot spots and easier distinction between apoptotic and mitotic figures. The authors propose that revision of current grading systems to include mitosis specific markers such as PHH3 might be warranted; however, larger validation studies are needed.

Normal villous architecture with increased intraepithelial lymphocytes: a duodenal manifestation of Crohn disease.

Patterson ER, Shmidt E, Oxentenko AS, Enders FT, Smyrk TC.

Am J Clin Pathol 2015; 143(3):445-50.

http://www.ncbi.nlm.nih.gov/pubmed/25696804

Increased intraepithelial lymphocytes (IELs) in duodenal mucosa with normal villous architecture is a common and nonspecific finding. The authors of this article propose that inflammatory bowel disease (IBD) should be considered in the differential diagnosis of this finding, adding to a long list that includes celiac disease, CVID, H. pylori gastritis, NSAIDs, small bowel bacterial overgrowth, viral enteritis, and autoimmune disease. In a retrospective review of all duodenal biopsies reported to have increased IELs with normal villous architecture in a 10 year period (1,161 of 17,129 biopsies) 74 were from patients with confirmed IBD, the majority (58 biopsies) from patients with Crohn disease. Of these patients with Crohn disease, half had concurrent focal gastritis, another feature associated with Crohn disease. While the authors state their belief that IBD should be added to the differential diagnosis of increased IELs with normal villous architecture, they also mention that a frequently cited study by Wright and Riddell found no difference in IEL counts between patients with Crohn disease and controls.

Peritumoral eosinophils predict recurrence in colorectal cancer.

Harbaum L, Pollheimer MJ, Kornprat P, Lindtner RA, Bokemeyer C, Langner C.

Mod Pathol 2015; 28(3):403-13.

http://www.ncbi.nlm.nih.gov/pubmed/25216222

This retrospective study aims to assess the role of intratumoral and peritumoral eosinophils as a prognostic feature in colorectal cancer. The study included 400 cases, randomly selected from a set of 7564 patients. Among other features, the number of eosinophils were recorded (intratumoral separately from peritumoral), and divided into those with absence of eosinophils, low count (<10/hpf), intermediate count (10-50/hpf), and high count (>50/hpf). Although eosinophil count correlated with overall inflammatory reaction the authors found that the degree of inflammatory reaction varied with respect to eosinophil count, and peritumoral (but not intratumoral) eosinophils were independently predictive of outcome in the study set and that this may be a relevant prognostic parameter in patients with colorectal cancer.

Distribution and variability of esophageal eosinophilia in patients undergoing upper endoscopy.

Dellon ES, Speck O, Woodward K, Covey S, Rusin S, Shaheen NJ, Woosley JT.

Mod Pathol 2015; 28(3):383-90.

http://www.ncbi.nlm.nih.gov/pubmed/25216228

This prospective study aimed to characterize the distribution of eosinophilia in eosophageal mucosa in a wide range of adult patients with dysphagia or symptoms of gastroesophageal reflux disease who underwent esophagogastroduodenoscopy at the University of North Carolina from 2009-20011 (with some exclusions described in the article). Overall 213 patient's biopsies were evaluated. It was found that most patients had little or no eosinophilia, supporting the belief that any eosinophilia is abnormal. In patients with a clinical and histologic diagnosis of eosinophilic esophagitis, the cut off of 15 eos/hpf showed good sensitivity and specificity. It was also shown that in these patients the levels of eosinophilia shows marked variation per patient, per biopsy, and per hpf supporting the suggestion that at least 3 biopsies may be needed to provide adequate analysis.

Collagenous gastritis: a morphologic and immunohistochemical study of 40 patients.

Arnason T, Brown IS, Goldsmith JD, Anderson W, O'Brien BH, Wilson C, Winter H, Lauwers GY.

Mod Pathol 2015; 28(4):533-44.

http://www.ncbi.nlm.nih.gov/pubmed/25234289

The aim of this study was to characterize inflammatory patterns in collagenous gastritis. Collagenous gastritis is rare and the article notes that even with a multi-institutional patient base only 40 patients were found to be included in the study. A part of the study looked at eotaxin and IGG4 immunohistochemistry in biopsies, but found no significant evidence that they play a part in pathogenesis. By histology, aside from the diagnostic feature of at least one biopsy with >10 microns in thickness, three associated inflammatory patterns were identified: a lymphocytic gastritis-like pattern, an eosinophil-rich pattern, and an atrophic pattern. Although no clear correlation between inflammatory pattern and clinical features was discussed in the article, the authors suggest that when one of these patterns of inflammation is seen it may be useful to more carefully look for increased subepithelial collagen. The authors suggest that immunohistochemistry for tenascin may be more sensitive than histochemical stains for more subtle cases.

Gastrointestinal pathology in transplant patients.

Wong NACS.

Histopathology 2015; 66(4): 467-9.

http://www.ncbi.nlm.nih.gov/pubmed/25195803

This review article is a comprehensive summary of post-transplant changes in solid organ and hematopoietic stem cell transplant recipients. Topics include graft-versus-host disease, infections, and cord colitis syndrome among others.

Spectrum of histopathological changes encountered in stented colorectal carcinomas.

Fryer E, Gorissen KJ, Wang LM, Guy R, Chetty R.

Histopathology 2015; 66(4):480-4.

http://www.ncbi.nlm.nih.gov/pubmed/24889189

Stenting can be used to relieve obstruction of colorectal carcinoma (CRC) for palliative care or for a "bridge to surgery" in potentially curable disease. With 72 cases, this is the largest series reported thus far of stented CRCs. Stenting results in tumor necrosis (all cases) and flat ulceration (77.8%) and background changes including IBD-like changes, mimics of tumor regression post-neoadjuvant treatment, and ischemia-like changes. The authors note that the relationship of such changes to therapeutic outcome should be explored.

The correlation between endoscopic and histopathological measurements in colorectal polyps.

Levene Y, Hutchinson JM, Tinkler-Hundal Em, Quirke P, West NP.

Histopathology 2015; 66(4):485-90.

http://www.ncbi.nlm.nih.gov/pubmed/24898056

In the UK, histopathological measurement of size is mandated for adenomas obtained in the Bowel Cancer Screening Program (NHS BCSP). This program was fully implemented in the UK in 2010. Patients undergo risk stratification based on number and size of adenomas identified by

endoscopy and measured macroscopically and diagnosed by histopathology. However, fragmentation and tissue processing can impact measurement. A total of 352 polyps from 210 patients were identified for this series spanning 3 months between 2008 and 2009 prior to full implementation of the NHS BCSP regulations (235 adenomas, 107 hyperplastic polyps, 10 other lesions). Of the 53 polyps with both endoscopic and histopathological measurement documented, correlation was 0.789 ($P<0.0001$). In total, 89% of adenomas had a documented endoscopic measurement and 22% had a histopathological measurement. Overall, though, median endoscopic measurement was significantly greater, leading to risk status misclassification of 13% of patients (high to low and low to high). The authors stress the role of histopathological measurement on formalin-fixed material as the gold standard.

Coeliac-like duodenal pathology in orthotopic liver transplant patients on mycophenolic acid therapy.

Cotter MB, AbuShanab A, Merriman R, MCormick A, Sheahan K.

Histopathology 2015; 66(4):500-7.

http://www.ncbi.nlm.nih.gov/pubmed/25195696

Mycophenolate injury in the large intestine has been well-documented. Here, duodenal injury in symptomatic liver transplant patients on mycophenolate is described. Of 152 duodenal biopsies from 127 patients, 87.5% were normal. A total of 16 showed abnormal histology, of which 7 were from patients on mycophenolate. Changes resembling celiac disease (shortened villi, increased IELs) with some additional findings (increased endocrine cell counts, apoptosis, and lamina propria eosinophils in comparison to normal). Degree of mucosal damage also correlated with the presence of anti-tissue transglutaminase IgA antibody. Recognizing these changes will help pathologists address discontinuation or reduction of mycophenolate dosing.

Histology of microscopic colitis—review with a practical approach for pathologists.

Langner C, Aust D, Ensari A, Villanacci V, Becheanu G, Miehlke S, Geboes K, Münch A on behalf of the Working Group of Digestive Diseases of the European Society of Pathology (ESP) and the European Microscopic Colitis Group (EMCG).

Histopathology 2015; 66(5):613-26.

http://www.ncbi.nlm.nih.gov/pubmed/25381724

This is a comprehensive and practical review on the morphology and differential of microscopic colitis.

Anatomic distribution of sessile serrated adenoma/polyp with and without cytologic dysplasia.

Yang JF, Tang S-J, Lash RH, Wu R, Yang Q.

Arch Pathol Lab Med 2015; 139(3):388-93.

http://www.ncbi.nlm.nih.gov/pubmed/25724036

The authors identify 11,201 patients with the diagnosis of SSA/SSP over a 1-year period at Miraca Life Sciences Research Institute. The incidence and anatomic distribution are provided and noted to be proximal colon-heavy (61.2% of SSA/SSP in the proximal colon, 61.2% of SSA/SSP with low-grade dysplasia, 80% of SSA/SSP with high-grade dysplasia, and 100% of SSA/SSP with adenocarcinoma). Anatomic distribution of cytologic dysplasia is presented (most commonly ascending colon and cecum). Of note, the authors use the more recent liberal recommendation of defining SSA/SSP as requiring only "a single crypt with unequivocal dilatation, distortion, and/or horizontally branched crypt," resulting in reclassification of some lesions originally categorized as borderline or indeterminate.

Groove pancreatitis: a brief review of a diagnostic challenge.

DeSouza K and Nodit L.

Arch Pathol Lab Med 2015; 139(3):417-21.

http://www.ncbi.nlm.nih.gov/pubmed/25724040

This is a comprehensive review in the Resident Review series covering the clinical presentation, cytologic features, and surgical pathology findings in groove pancreatitis, which can mimic carcinoma.

Select biomarkers for tumors of the gastrointestinal tract.

Bartley AN, Hamilton SR.

Arch Pathol Lab Med 2015; 139(4):457-68.

http://www.ncbi.nlm.nih.gov/pubmed/25333834

This is a comprehensive summary of molecular testing options for esophagus, stomach, small and large intestine, and pancreas tumors. This article is part of the Cancer Biomarker Update series in Archives.

Significance of proximal margin involvement in low-grade appendiceal mucinous neoplasms.

Arnason A, Kamionek M, Yang M, Yantiss RK, Misdraji J.

Arch Pathol Lab Med 2015; 139(4):518-21.

http://www.ncbi.nlm.nih.gov/pubmed/24971927

Guidelines are unclear as to the clinical management of patients with appendiceal adenoma or LAMN and with a positive surgical margin at the time of appendectomy. A total of 15 cases of LAMN and 1 case of adenoma, all with neoplasia or dissecting mucin at the proximal margin, were included in this study. None of the patients developed recurrence or pseudomyxoma peritonei over a mean follow-up of 4.7 years, suggesting that conservative follow-up may be warranted even with an involved proximal margin.

Sporadic microsatellite instability-high colon cancers rarely display immunohistochemical evidence of Wnt wignaling activation

Panarelli NC, Vaughn CP, Samowitz WS, Yantis RK

Am J Surg Pathol 2015; 39(3):313-17.

http://www.ncbi.nlm.nih.gov/pubmed/25602793

Beta-catenin immunoexpression was evaluated in 44 sporadic microsatellite unstable adenocarcinomas and 44 microsatellite stable (MSS) colon cancers. Sporadic MSI-high carcinomas were defined as those with loss of MLH1 and PMS2 immunostaining and BRAF V600E mutations that occurred in patients 50 years of age or older without a family history of colonic adenocarcinoma or Lynch syndrome. Forty one (93%) of these carcinomas displayed membranous beta-catenin staining only, compared with 28 (64%) site-matched MSS tumors with abnormal nuclear beta-catenin staining.

Tumor budding is an independent adverse prognostic factor in pancreatic ductal adenocarcinoma

O'Conner K, Li-Chang HH, Kalloger SE, Peixoto RD, Webber DL, Owen DA, Dirman DK, Kirsch R, Serra S, Scudamore CH, Renouf DJ, Schaeffer DF

Am J Surg Pathol 2015; 39(4):472-78.

http://www.ncbi.nlm.nih.gov/pubmed/25634751

Tumor budding is a well-established adverse prognostic factor in colorectal cancer. These authors studied the significance and diagnostic reproducibility of budding in pancreatic carcinoma. The aim of this study was to assess the prognostic significance of tumor budding in pancreatic ductal adenocarcinoma, determine its relationship with other clinicopathologic features, and assess interobserver variability in its diagnosis. The authors concluded that the presence of tumor budding is an independent adverse prognostic factor in pancreatic ductal carcinoma. The assessment of budding with H&E is reliable and could be used to better risk stratify patients with pancreatic ductal adenocarcinoma.

SMAD4 Loss in esophageal adenocarcinoma is associated with an increased propensity for disease recurrence and poor survival

Singhi AD, Foxwell TJ, Nason K, Cressman KL, McGrath KM, Sun W, Bahary N, Zeh HJ, Levy RM, Luketich JD, Davison JM

Am J Surg Pathol 2015; 39(4):487-95.

http://www.ncbi.nlm.nih.gov/pubmed/25634752

In this paper the authors report that in contrast to primary esophageal adenocarcinoma, a higher prevalence of Smad4 loss was observed in metastatic disease (44% vs. 10%). Loss of Smad4 protein expression is an independent prognostic factor for time to recurrence and overall survival. Los of Smad4 correlates with increased propensity for disease recurrence and poor survival in patients with esophageal adenocarcinoma after surgical resection.

Locus/chromosome aberrations in intraductal papillary mucinous neoplasms analyzed by fluorescence in situ hybridization

Miyabe K, Hori Y, Nakazawa T, Hayashi K, Naitoh I, Shimizu S, Kondo H, Nishi Y, Yoshida M, Umemura S, Kato A, Ohara H, Joh T, Inagaki H.

Am J Surg Pathol 2015; 39(4):512-20.

http://www.ncbi.nlm.nih.gov/pubmed/25517961

The aim of this study was to retrospectively examine locus and chromosome abnormalities in intraductal papillary mucinous neoplasms (IPMNs) using fluorescence in situ hybridization. Twenty eight IPMNs were histopathologically classified as noninvasive (n= 17) or with an associated invasive carcinoma (invasive IPMN, n= 11). The authors conclude that: (1) polysomy 6 and p16 deletion may contribute to adenomatous change of IPMN; (2) polysomy 7, polysomy 18, p16 deletion, and p53 deletion play roles in malignant transformation of noninvasive IPMN; and (3) polysomy 7 and p53 deletion may be excellent diagnostic markers for invasive IPMN.

The number and distribution of eosinophils in the adult human gastrointestinal tract: a study and comparison of racial and environmental factors

Matsushita T, Maruyama R, Ishikawa N, Harada Y, Sraki A, Chen D, Tauchi-Nishi P, Yuki T, Kinoshita Y

Am J Surg Pathol 2015; 39(4):521-27.

http://www.ncbi.nlm.nih.gov/pubmed/25581733

The authors quantified the number of eosinophils from each portion of the gastrointestinal mucosa in biopsies from a Japanese adult population (132 samples), and also from surgical resections from Japanese (110 samples), Japanese Americans (64), and Caucasians (57). They suggest that when rendering a diagnosis of an eosinophilic gastrointestinal tract disease, a cutoff value for eosinophil counts should be individualized by site within the GI tract. Race and environmental factors did not seem to have a significant effect on eosinophil densities and distributions.

Strategies for Improving Diagnostic Accuracy of Biliary Strictures

Salomao M, Gonda TA, Morgolskee E, Eguia V, Romotti H, Poneros JM, Sethi A, Saqi A

Cancer Cytopathol 2015; 123:244-52

http://www.ncbi.nlm.nih.gov/pubmed/25564796

Biliary brush cytology is known for its low sensitivity (but high specificity) and may be accompanied by biopsies and/or fluorescent in situ hybridization (FISH) to improve diagnostic yield. This study aimed to identify features to enhance cytological sensitivity, and assess which sampling method(s) improve identification of pancreatobiliary adenocarcinomas (PBCa) Seventy-three biliary stricture cases were retrieved (38 PBCa and 35 control benign strictures). Biliary brushings, FISH, and biopsies were reviewed. Cytology specimens were evaluated for cellularity and presence of drunken honeycomb (DH), loosely cohesive clusters of round cells (LCCRC), large atypical cells with foamy cytoplasm (LACF), and single vacuolated malignant cells (SCs). Biopsies were examined for the presence of stromal invasion (SI). Biliary brushings were scantly cellular in 47.4% of PBCa and 51.4% of controls, resulting in 69.6% nondiagnostic/false-negative cytology diagnoses. DH, LACF, and SCs were significantly associated with adenocarcinoma ($P < .00001$, .0033, and .00002, respectively). By univariate analysis, SCs and LACF were predictors of malignancy in brushings ($P = .0002$ and .05). By multivariate analysis, only SCs were predictive of malignancy ($P = .002$). SI facilitated the diagnosis in 9 biopsies. Sensitivity/specificity of brush cytology, FISH, and biopsy were 39.5%/94.3%, 63.9%/94.3%, and 84.2%/100%, respectively. The low sensitivity of biliary brushings results from limited cellularity. Identification of LACF, DH, and SCs improves sensitivity. Sampling of stromal tissue may facilitate PBCa diagnosis. Concurrent biopsies and FISH are helpful in enhancing the diagnostic yield of PBCa.

Risk stratification of patients with Barrett's esophagus and low-grade dysplasia or indefinite for dysplasia

Thota PN, Lee H-J, Goldblum JR, Liu X, Sanaka MR, Gohel T, Kanadiya M, Lopez R.

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This retrospective study included 299 patients with Barrett esophagus and a biopsy diagnosis of low grade dysplasia or indefinite for dysplasia. During a follow-up period of 1577.4 patient-years high grade dsyplasia developed in 32 patients and adenocarcinoma developed in 10 patients. The annual incidence rate for HGD was 2/5% and was 0.6% for adenocarcinoma. No patient with an initial diagnosis of indefinite for dysplasia developed adenocarcinoma during the follow-up period. Features that were found to be associated with a high risk of progression included: prevalent LGD, male sex, multifocality, and nodules evident by endoscopy. For every 5 year increment of patient age there was a 7% increase in the chance or regression of dysplasia, while each 1 cm increase in the length of the Barrett segment decreased the risk of regression by 6%. Finally, the presence of LGD at initial biopsy decreased the chance of regression by 56% compared to cases with indefinite for dysplasia as the initial diagnosis.

Journals Reviewed (March and April 2015 Issues)

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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
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