Gastrointestinal Pathology Society Newsletter
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GASTROINTESTINAL PATHOLOGY SOCIETY
1992-1993 OFFICERS AND COMMITTEE MEMBERS

Position	Term Ends
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Vice-President/President-Elect (1-year term):	
Stanley Hamilton	1993
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Robert Petras	1993
Education Committee (3-year term):	
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Alexander Brian West	1993
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Robert Pascal (Ex-officio: Chairman of Education Committee)
Stanley Hamilton (Ex-officio: President-Elect of GIPS)

Newsletter Editors (3-year term):
Harry Cooper (term ends 1994)

Presidents Message

First I want to thank our outgoing President, Frank Mitros for serving as President of the society during the past year. Frank has presided over an excellent year for the society in which we continued to present high quality educational programs at the USCAP, AGA, and ASCP meetings. I also wish to recognize several other individuals whose efforts on behalf of GIPS keep our membership informed, organized, and help to encourage research in gastrointestinal pathology by house officers and fellows.

Bob Pascal, has chaired the Education Committee again this year. His programs continue to receive high praise. At the ASCP meeting on October 10, 1992, we will present a session on "Gastrointestinal Disorders in Children and Adolescents". Also, Bob has already lined up an exciting program on "Disorders of the Esophagus" for the USCAP meeting.

Marcia Gottfried's Training Programs Committee presented the Pathologist In-Training Award at the USCAP meeting last Spring at the Tuesday afternoon GI Pathology session. We believe that presenting our award at the USCAP meeting enhances the significance of the award for the recipient.

The two other most challenging jobs in our society continue to be the Secretary-Treasurer and the GIPS Newsletter Editor. Bob Petris is our Secretary-Treasurer. He must keep our records together, take care of official correspondence, collect the all important dues, and record coherent minutes of our meetings. Harry Cooper continues to excel as Editor of the GIPS Newsletter. This task requires him to gather useful information from our membership and report it two editions of the newsletter each year. The review of gastrointestinal pathology abstracts that he presents is a favorite feature for our members. As a former Editor of the newsletter, I encourage you to write to Dr. Cooper and use the newsletter as a forum to present your ideas and concerns about our Society in the newsletter.

I urge program directors to consider application for the Microgrants Program. This program has received only five applications since 1986. Two of these applications have been funded. These funds are available for GI-related projects, especially for young investigators requiring some start-up funds.

Lastly, please feel free to write me, other officers, or committee chairpersons about items which you feel should be addressed by the Society.

Best wishes for a pleasant autumn.

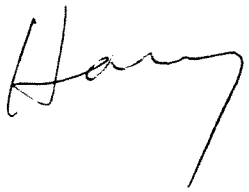
David F. Keren, M.D.
President, Gastrointestinal Pathology Society

Editor's Message

As Dave Keren mentioned in his message, I would encourage the GIPS membership to use the Newsletter as a forum for matters of Gastrointestinal Pathology and related matters. The Newsletter could also be used as a mechanism of announcements of matters of information that you feel would be of interest to the membership. I would also greatly appreciate any comments or thoughts you might have regarding any changes (additions or deletions) that you would like to see in the Newsletter.

Finally, I am attempting to get together a complete set of all Newsletters from Volume 1 through to the present. If you have back issues, would you kindly make copies and forward them to me.

Harry S. Cooper, M.D.
Editor GIPS Newsletter



IMMUNOHISTOCHEMICAL STUDY OF INFLAMMATORY FIBROID POLYP OF THE STOMACH. Pascual Abenoza, M.D., Dale Snover, M.D., Division of Surgical Pathology, University of Minnesota, Minneapolis, MN.

The authors studied a series of eight inflammatory fibroid polyps of the stomach via histochemistry and immunohistochemistry. Special stains (Leder stain) indicated that for the most part occasional mast cells were noted. Reticulin fibrils were noted, as was the presence of mature collagen, probably related to the age of the lesion. The stromal cells were negative for S-100 protein, Leu 7, chromogranin, synaptophysin, cytokeratin, neuron specific enolase, ulex, actin, and desmin, however the same cells were positive for vimentin. The study failed to demonstrate any evidence of neural differentiation in this lesion. The authors believe that the inflammatory fibroid polyp of the stomach is a non-neoplastic, reactive lesion with proliferation of stromal cells with some fibroblatic differentiation.

PROGNOSTIC VALUE OF PCNA INDEX IN GASTRIC STROMAL TUMORS: CORRELATION WITH MITOTIC COUNT AND OUTCOME. M.B. Amin, C.K. Ma, M.D., Linden J. Kubus, R.J. Zarbo, Henry Ford Hospital, Detroit, MI.

The authors studied gastric stromal tumors (GST) by immunohistochemically staining formalin-fixed, paraffin-embedded tissues with anti-proliferating cell nuclear antigen (PCNA, clone PC10) in order to correlate the staining with mitotic counts and clinical outcome. Mitotic figures were counted per 50 high power fields (MC). The mitotic count and tumor size were used to categorize tumors into three groups: 1) Benign (BN) = <5 MC, <5 CM, 2) Borderline (BL) = <5 MC, >5 CM, 3) Malignant (MN) = >5 MC, >5 CM. PCNA tumor proliferating index (TPI) was assessed by the counting of 200 tumor cells per case and expressed as a percentage. Mean PCNA TPI values were significantly different between BN (9.6), BL (16.6), MN (30.9). In the MN group, mean TPI for MN with metastasis (37.9) was not significantly different from MN without metastasis (21.3). There was no correlation between PCNA, TPI, and epitheloid vs. spindle cell type of GST. The authors conclude that PCNA derived TPI correlates with MC indicating this as an additional prognostic parameter in the assesments of GST. In tumors with < 5 MC, PCNA TPI provides a qualitative parameter to potentially separate BL from BN tumors. This is not possible with MC alone, as MC for BL and BN tumors may overlap. The intermediate PCNA TPI BL lesions further justifies separation of GST into BN, BL, and MN categories.

INTESTINAL IMMUNE DEFICIENCY ASSOCIATED WITH PATHOGEN RELATED AIDS ENTEROPATHY. W. Beschorner, D. Suresch, P. Belitsos, G. Dayal, J. Greenson, J. Yardley, and J. Bartlett. The Johns Hopkins Univ. School of Medicine, Baltimore, MD.

Patients with AIDS often have diarrhea and wasting. In these patients, an occult pathogen is identified in 50% of intestinal biopsies. In this study, the authors attempted to test the hypothesis that the AIDS patients with diarrhea and a detected pathogen have a selective intestinal immunodeficiency. The authors studied the duodenal immunopathology of three groups of patients. 1. AIDS/ARC patients without diarrhea, 2. AIDS patients with diarrhea and no pathogen, and 3. AIDS patients with diarrhea and an enteric pathogen. The biopsies were immunostained for 17 phenotypes of T cells, B cells, and monocytes. HIV was also identified. The authors found no difference in immunophenotype between AIDS patients with and without diarrhea, however, those with an enteric pathogen had a deficiency of CD3 cells and CD8 cells. CD4 cells were decreased in all groups. Six of eight biopsies with enteric pathogens showed the expression of HIV in the biopsy vs. 1/10 in controls and 2/6 of the idiopathic group. Those biopsies with proven HIV positivity had fewer intraepithelial lymphocytes. The results demonstrate that AIDS patients with an enteric pathogen have a select deficiency of intestinal CD8 T cells. Those with HIV infection of duodenum itself also have a deficiency of intraepithelial lymphoctytes.

EVOLUTION AND HEALING OF DUODENAL ULCER IN A NEW EXPERIMENTAL ANIMAL MODEL. H. Bui, A. delRosario, M. Khan, M. Abdulla, J. Martini, C. Lee, and J. Ross, Albany Medical College, Albany NY.

The authors presented a time-sequence study of the development, evolution, and healing of duodenal ulcers in an animal model. Ulcers were produced in 150-200 gram male Sprague-Dawley rats by application of 50% acetic acid for 30 seconds through a 3 mm. polyethylene tube to the serosa of the duodenum. The authors observed light microscopic transmission and scanning electron microscopic changes at 15, 30, 60 minutes, 3, 24, 48, and 72 hours, and 5, 7, 10, 14, and 21 days after application of acetic acid. The earliest changes were noted at 15 minutes where there was microvascular injury to the duodenal wall with thrombosis, hemorrhage, and superficial epithelial necrosis. By three hours, progressive disintegration of the villi were noted and in 1-2 days necrosis and a distinct ulcer formed. By day 7, ulcers had gross and microscopic and ultrastructural features similar to that of human peptic ulcer disease. By day 14, the ulcers were grossly healed with prominent granular dilatation and distorted epithelial cells. The authors conclude that this new experimental duodenal ulcer models, and this model may be utilized to study the development, evolution, and healing of duodenal ulcer disease.

ASSESSMENT OF CELL PROLIFERATION IN COLORECTAL CARCINOMAS USING AN ANTI-PCNA/CYCLIN MONOCLONAL ANTIBODY IN FIXED, EMBEDDED TISSUES. A COMPARATIVE STUDY WITH Ki-67 ANTIGEN AND FLOW CYTOMETRY PARAMETERS. E. Campo, R. Miquel, A. Cardessa, A. Palacin, Hospital Clinico, Barcelona, Spain.

The authors studied immunohistochemically the expression of PCNA in 14 normal colons, 4 adenomas, and 34 carcinomas. The PCNA proliferative index was compared with the Ki-67 proliferative index (assessed on frozen tissue of the same cases) and with the S+G2M phase fractions measured by flow cytometry. PCNA proliferative index increased from normal mucosa (26% +/- 9) to adenomas (39% +/- 7), and carcinomas (82.5% +/- 11.7). A similar progression was noted with Ki-67 and flow cytometry. No correlation was found between PCNA, Ki-67, or flow cytometric parameters, the clinical characteristics of the patients, the size, the location, and Dukes' stage of the tumors. However, poorly differentiated carcinomas showed a higher proliferative activity with the three techniques than did the well differentiated tumors. The authors also found that tumor proliferative activity measured by flow cytometry but not by PCNA correlated with patient survival and therefore could be a prognostic factor in colorectal cancer.

NM23 SOMATIC ALLELIC DELETIONS IN HUMAN COLORECTAL CARCINOMAS. E. Campo, R. Miquel, A. Leone, A. Palacin, M. Juan, J. Vives, P. Steeg, J. Yague, A. Cardesa, Hospital Clinico, Barcelona, Spain, National Cancer Insitute, Bethesda, MD.

NM23 is a gene whose expression has been associated with low tumor metastatic potential, and has been proposed to be a metastasis supressor gene. Similar to p53, this gene has been localized to chromosome 17. The authors analzyed the loss of heterozygosity of NM23 in 58 colorectal cancers using restriction fragment length polymorphism. The authors also studied comparing the allelic deletions of NM23 to loss of heterozygosity of p53 and DNA flow cytometry. The authors concluded that: 1. somatic allelic deletions of the NM23 gene occur in 23% of colorectal carcinomas, 2. no relation could be found between the loss of heterozygosity of the NM23 and localization, degree of differentiation, invasion, lymph node metastasis, or proliferative index of tumors. However, loss of heterozygosity of NM23 in colorectal carcinomas may be involved in the development of distant metastasis (20% vs. 7%) at surgery. Aneuploidy was much more frequent in NM23 deleted (90%) than in non-deleted patients (45%).

HISTOLOGICAL SPECTRUM OF LESIONS IN EXPERIMENTAL CARCINOMA OF THE ESOPHAGUS AFTER REFLUX ESOPHAGITIS. A. Cardesa, J.A. Bombi, M. Pera, C. Pera, and U. Mohr. Univ Barcelona, Spain, and Experimental Pathology, Hannover Med School, Hannover, FRG.

The authors produced chronic reflux esophagitis (RE) by an esophagojejunostomy (EJ) with gastric preservation in eight week-old Sprague-Dawley rats. Fifteen days after the reflux procedure, the potent esophagotropic carcinogen 2-6 dimethylnitrosomorpholine (2-6 DMNM) was subcutaneously injected weekly for life. In those animals with the reflux operation, the following types of carcinomas were noted: 1. pure squamous cell carcinoma, 2. squamous cell carcinomas with focal mucin production, 3. pure adenocarcinomas, and 4. adenocarcinomas with areas of squamous differentiation. However, in the group in which a reflux procedure was not performed, only squamous cell carcinomas of the pure type without evidence of mucin or glandular differentiation were present. The authors note that the adenosquamous carcinomas of the esophagus resemble those seen in humans and that carcinomas with glandular differentiation were exclusively found only under the combined influence of reflux esophagitis plus 2/6-DMNM.

DETECTION AND SIGNIFICANCE OF HCG IN STAGE B2 AND C2 COLORECTAL CARCINOMAS. J. Connelly, D. Johnston, J. Bruner, UT M.D. Anderson Cancer Center, Houston, TX.

The authors studied a well-define group of cases with long-term follow up immunohistochemically for the detection of presence of tumoral and non-tumoral HCG. The authors studied only cases of Astler-Coller Stage B2 and C2 non-mucinous tumors. The authors reviewed the age, race, sex, site of tumor, treatment, pathological stage, and differentiation, along with the survival. Interestingly, HCG expression was noted in at least one field in 42% of the carcinomas. The staining was usually focal (<5% of tumor cells), however, some cases did stain diffusely. There was no expression of HCG in the adjacent mucosa. The authors failed to find any significant correlation of HCG expression with survival, stage, differentiation, age, race, sex, or site of tumor. The authors conclude that HCG expression is not a significant prognostic indicator in Stage B2 and C2 colorectal carcinomas.

PROGNOSTIC FACTORS IN SMOOTH MUSCLE TUMORS OF THE GASTROINTESTINAL TRACT: RESULTS FROM IMAGE CYTOMETRY AND FLOW CYTOMETRY. R.E. Cunningham, B. Federspiel, W.F. McCarthy, L. Sobin, and T.J. O'Leary, Armed Forces Institute of Pathology, Washington, DC.

To delineate the potential roles of flow cytometry (FCM) and image morphometry in gastrointestinal smooth muscle tumors (GISMTs) the authors performed a variety of morphometric and FCM measurements on paraffin blocks from 122 patients with GISMTs. None of the morphometric measurements (nuclear perimeter, area, form factor, longest diameter, average ferret diameter, equivalent diameter, and DNA index) was a significant prognostic factor when analyzed using a univariate Cox model. In contrast, the FCM mean channel number, the fraction of cells and G2M, ploidy of the G0/G1 peak, and ploidy of the G2M peak were statistically significant in univariate models. Together with the patient age and sex, and whether or not the patient presented with metastasis. In a multivariate model, age > 59, >10% of cells in G2M, and metastasis indicated a poor prognosis, while epitheloid histology portended a somewhat improved prognosis. If metastasis was not allowed to enter this model, age >59, and a fraction of cells in G2M and the ploidy of the G0/G1 peak portended a poor prognosis.

PLASMA LEVELS AND TISSUE LOCALIZATION OF PLASMINOGEN ACTIVATORS IN COLORECTAL CARCINOMA. D. Dawson and K. Kottke-Marchant, Cleveland Clinic Foundation, Cleveland, OH.

In this study the investigators evaluate the presence of tissue type (tPA) and urokinase (uPA) plasminogen activator in patients with colorectal cancer and inflammatory bowel disease. Plasma serum showed normal values for PT, APTT, fibrinogen, D-dimer, tPA, and uPA. In tissue specimens PT, APTT, fibrinogen, and D-dimer levels were normal. uPA levels were slightly but not significantly higher in cancers compared to inflammatory bowel disease. tPA levels in both groups were similar. There was no correlation of tPA or uPA levels with disease progression. In immunohistochemical staining of all normal colon and IBD specimens, tPA stained focal goblet cells and endothelial cells, while goblet cells were negative for uPA. In contrast, tumor associated stromal and inflammatory cells were positive for uPA (15/16), while tumor cells were positive (4/16). The strongest uPA staining occurred at the advancing tumor front with associated inflammation. In summary, uPA is increased in colorectal tumor tissue, and in comparison to normal colon and in IBD. In contrast to some studies, uPA activity appears primarily localized in the stromal, may reflect presence of macrophage activity in their receptors as well as increased uPA production by adjacent tumor cells. Although uPA was increased in tumor stroma, there was no increased plasma uPA in cancer patients which may reflect lack of uPA released by sites of tumor invasion.

CONNECTIVE TISSUE DISEASE (CTD) -ASSOCIATED GASTROINTESTINAL MAST CELL-EOSINOPHIL (mc-eo) INFILTRATES ASLO INVOLVE LIVER, GALLBLADDER, AND APPENDIX. K. DeSchryver-Kecskemeti and R.E. Clouse, Departments of Pathology, CWRU, Cleveland OH and Medicine, Washington Univ. Medical School, St. Louis MO.

Gastrointestinal involvement in patients with scleroderma and connective tissue diseases can be noted. An early morphological lesion as an mc-eo infiltrate in the deep portions of the mucosa and stomach, duodenum or colon which are usually detected in patients with diarrhea and a normal endoscopy. To determine whether other sites in the GI tract could also yield clues to connective tissue disease, gallbladder, liver, and appendix specimens obtained prior to the onset of diarrhea were retrospectively reviewed for a similar mc-eo lesion. Three patients presented with clinically signficiant symptoms of accessory gastrointestinal organs. In all three patients all specimens (gallbladder, liver, and appendix) contained significant mc-eo infiltrate and antedated other diagnostic material by up to two years. In the GI specimen, mc-eo in an unusual distribution warrant consideration of idiopathic and/or chemically-induced connective tissue disease.

SURFACTANT-LIKE PARTICLES (SLP) IN HUMAN DUODENAL MUCOSA. K. DeSchryver-Kecskemeti, R. Eliakim, P. Winkle, D.H. Alpers. Departments of Pathology, CWRU, Cleveland, OH, and Medicine, H adassah University, Jerusalem, Israel, and Washington Univ. School of Medicine, St. Louis, MO.

It has been shown that enterocyte secreted particle previously identified in rats is surfactant-like in its morphology, biochemistry, and functional characteristics. The authors examined human intestinal biopsies for SLP:19. Duodenal endoscopic biopsies were fixed in glutaraldehyde, post-fixed in tannic acid and ossmium for optimal phospolipid staining and were processed for ultrastructural study. The relative intra- and extra-cellular number of SLP was scored electron micrographs of coded specimens. The degree of mucosal inflammation on corresponding Toluidine Blue sections yield no correlation with SLP. However, SLP is a product of human enterocyte present intra- and extra-cellularly. SLP is decreased almost threefold in duodenal ulcer disease. The primary or secondary defect in SLP production may be an index of epithelial secretory/metabolic integrity.

THE PRESENCE OF K-RAS-2 GENE MUTATION IN COLORECTAL TUMORS: A COMBINED HISTOPATHOLOGI/GENETIC STUDY OF 50 CASES. S. Finkelstein, R. Sayegh, S. Christensen, P. Swalsky, A. Rogers. Rhode Island Hospital, Brown University, Providence, RI.

Using histopathological features, the authors then selected areas of tissue from paraffin blocks from which tumor DNA was extracted. This was amplified by PCR reaction and directly sequenced using standard protocols. Amplifying primers were situated in intron regions immediately flanking the first exon of the K-ras-2 gene. The authors found the presence of mutations was heterogeneous in the primary colonic tumors being most prevalent in the area of deepest invasion. 15/36 primary and 9/14 metastatic tumors contained mutations which altered positions 34, 35, and 38 of the DNA coding sequence. The authors also found that the incidence of mutations paralleled increasing depth of invasion (0/3 in-situ tumors, 2/6 submucosally invasive tumors, 3/9 tumors limited to the muscularis propria, and 9/17 tumors involving the serosa, 4/6 pericolonic metastatic tumors, and 4/4 hepatic metastasis exhibited mutations. These results indicate a trend in which mutations occur with increasing invasion and metastasis.

MUSCLE DIFFERENTIATION AND CLINICOPATHOLOGIC FEATURES OF GASTROINTESTINAL STROMAL TUMORS (GIST). D.W. Franquemont, H.F. Frierson, Jr., University of Virginia Health Sciences Center, Charlottesville, VA.

The authors looked at 46 GISTs immunohistochemically to determine the frequency of smooth muscle differentiation, most sensitive muscle antibody, and correlation if any with anatomic site, size, cellularity, nuclear pleomorphism, necrosis, mitotic rate, and clinical behavior. The staining for the GISTs were as follows: vimentin 45/46 positive, desmin 9/45 positive, muscle specific actin 36/46 positive, alpha smooth muscle actin 34/46 positive, chicken gizzard actin 0/38 positive, cytokeratin 2/46 positive, s-100 protein 6/46 positive, GFAP 0/46 positive, synaptophysin 0/46 positive, and chromogranin 1/46 positive. At least one muscle marker was positive in 39 of the 46 tumors. Of interest, all vimentin positive only GISTs were malignant. Immunoreactivity did not correlate with site, cellularity, pleomorphism, or mitotic rate. The authors conclude that 85% of GISTs react with at least one muscle antibody, immunoreactivities unrelated to anatomic site. Muscle specific actin is slightly more sensitive than smooth muscle actin, while desmin is less sensitive. The simultaneous expession of desmin, muscle specific actin, and smooth muscle actin positively correlates with benign outcome.

LEUKEMIC INFILTRATES OF THE ESOPHAGUS: A CYTOLOGY, BIOPSY, AND AUTOPSY STUDY. K.R. Geisinger, B.L. Powell, S.R. Fulp, B.R. Nestok, J.K. Evans, J.H. Gilliam, III, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, NC.

The differential diagnosis of dysphagia in patients with leukemia generally includes reflux disease, infectious esophagitis, and chemotherapy-induced mucocitis. The authors noted three patients in which they made an antemortem diagnosis of esophageal leukemic infiltrates. In all three there were numerous isolated blasts in the cytologic brushing specimens. This prompted the authors to review all leukemics autopsied from 1976-1988 at their institution. Of the 207 autopsies, 15 (7.2%) had leukemic infiltrates in the esophagus. Of factors analyzed, only high initial white blood cell count was significantly associated with esophageal involvement. Esophageal infiltrates were associated with involvment of many other organs. Esophagitis in leukemics may be due to tumor cell infiltrates which can be documented by both cytology and biopsy.

LYMPHOID AGGREGATES IN GASTRIC MUCOSA: STRONG ASSOCIATION WITH H. PYLORI INFECTION. RM Genta and DY Graham, VAMC and Baylor College of Medicine, Houston, TX.

The authors examined multiple antral fundic and duodenal biopsy specimens from 57 asymptomatic volunteers aged 20-62. They wanted to assess the distribution of gastric lymphoid aggregates with germinal centers (LAGCs) in subjects with or without H. pylori. H. pylori was detected in the stomach of 29 subjects. 26 of these had LAGCs in the antrum, and 11 had LAGCs in the body also. None had LAGCs in the duodenal bulb mucosa. Of the 26 subjects in whom H. pylori was not visualized, 2 had LAGCs in the antrum and 1 in the body. These 3 patients all had high titers of serum anti-H. pylori, suggesting recent past infection. The authors found the higher prevalence of LAGCs in t he gastric mucosa of subjects infected with H. pylori than previously reported. No subject without evidence of past or current infection with H. pylori had LAGCs. Gastric LAGCs may represent the expression of local immune responses directed at H. pylori and may represent a useful histological marker of the infection.

GASTRIC MUCOSAL CALCINOSIS (GMC) IN ENDOSCOPIC BIOPSIES FROM ORGAN TRANSPLANTS (OTP). J.K. Greenson, S.B. Trinidad, S.A. Pfeil, J.G. Lucas, The Ohio State University Hospital, Columbus, Ohio.

The authors noted calcium deposits in the superficial gastric mucosa of 11 organ transplant patients (5 bone marrow, 3 liver, 2 kidney, and 1 liver and kidney transplant). These were discovered when patients underwent endoscopic biopsies to rule out CMV. The deposits were present just beneath the surface cell epithelium and the tips of the foveola. Von Kossa stains confirmed the presence of calcium crystals in 3 or 4 cases and PAS/alcian blue stain showed PAS positivity in 5/5 cases. All biopsies showed tissue injury; 7 had chemical gastritis (5 of which also had CMV inclusion), 2 had acute hemorrhagic gastritis, 1 had GVHD, and one had only CMV. The patients were on Cyclosporin and Prednisone and 10 were on Sucralfate. Gastric mucosal calcinosis in organ transplant patients is associated with Cyclosporin, glucocorticoid, and Sucralfate therapy as well as gastritis and CMV. The presence of tissue damage favors that dystrophic calcification is a mechanism in GMC. However, Cyclosporin and glucocortoid therapy is known to alter calcium balance suggesting that metastatic calcifications may also occur. It is believed that Sucralfate is not the cause of GMC. The clinical significance of GMC is unknown, but the association with CMV may be useful in assessing biopsies which have calcinosis.

COMPARISON OF THE LOCAL IMMUNE RESPONSE IN NORMAL AND CHRONIC ANTIGEN STIMULATION OF THE GASTRIC MUCOSA: A HISTOLOGIC STUDY IN HELICOBACTER PYLORI INFECTED STOMACH. M. Guindi, A. Beltrano, R.H. Stead, and R.H. Riddell. McMaster University Medical Centre, Hamilton, Ontario, Canada.

The authors were interested in examining the plasma cell immunoglobulin content in normal stomachs vs. those with chronic antigen challenge (positive for H. pylori). The authors studied immunohistochemically serial sections of gastric antrums with or without the presence of H. pylori for the expression of IgA, IgG, IgM, J chain, and secretory component. Slides were examined semi-quantitatively. In the normal gastric mucosa, there were relatively few plasma cells staining for each immunoglobulin class. In those patients with H. pylori infection, some biopsies showed a moderate to marked plasma cell response, including IgA, IgG, and IgM,while others appeared like the normal stomach. In contrast to the H. pylori negative group, secretory component staining was increased in the H. pylori group,however, this was only seen in those patients with increased immunoreactive plasma cells. Thus, it appears that H. pylori infected mucosal biopsies can be divided into two groups, with or without the marked immunogobulin

response. These may reflect different patterns of various stages or intrinsic differences in the immune systems of patients with H. pylori infection.

LOSS OF HETEROZYGOSITY AT THE p53 AND Rb LOCI IN ULCERATIVE COLITIS. Harpaz N., Yin J., Greenwald B.J., Huang Y., McDaniel T., Newkirk C., Resau J.H., Meltzer S.J. The Mount Sinai Medical Center, New York and University of Maryland and VA Hospital, Baltimore, MD.

The authors were interested in determining whether loss of heterozygosity of tumor supressor genes p53 and Rb are associated with neoplasia and ulcerative colitis. The authors examined DNA from paraffin-embedded tissues. The DNA was microdissected from the paraffin-embedded tissues and the use of restriction fragment length polymorphism and amplificaion of PCR. Loss of heterozygosity was manifested as partial or complete absence of bands corresponding to one allele in the neoplasm DNA relative to normal DNA. The authors data indicates that loss of heterozygosity of tumor supressor oncogenes, especially p53 is associated with ulcerative colitis-relatedneoplasm. It may be necessary in at least the subset of these neoplasms.

THE CROHN'S-LIKE LYMPHOID REACTION IN RIGHT COLON CANCER: RESULTS OF A MULTIVARIATE ANALYSIS. J. Harrison, S. Warner, F. El-Zeky, R. Vander Zwaag, P. Dean. University of Tennessee-Baptist Memorial Hospital, Memphis, TN.

The authors studied the Crohn's-like lymphoid reaction in right colon cancers. It was their attempt to see if this reported prognostic fact indicator was limited to univariate analytic significance, or whether in a multivariate model this would also hold significane. In total, they studied 344 right colon cancers (219 cecum and 125 ascending colon). By univariate analysis, prognostically significant variables predicting 5-year survival included: 1. lymph node metastasis, 2. Crohn's-like lymphoid reaction, 3. depth of tumor invasion, 4. metastatic tumor nodules in pericolonic fat, 5. extramural venous invasion, 6. peritumoral lymphocytic infiltrate, 7. tumor growth pattern, 8. tumor grade, 9. tubular configuration, 10. nuclear polarity, 11. fibrotic response to tumor. By Cox stepwise proportional hazard analysis, variables retaining independent prognostic significance were: 1. metastatic tumor nodules in pericolic fat, 2. lymph node metastasis, 3. depth of tumor invasion, 4. Crohn's-like lymphoid reaction. DNA ploidy and cell cycle analysis provided no additonal prognostic information. The data from t he study indicates that the Crohn's-like lymphoid reaction is a signficant independent prognosticator in right colon cancer.

HISTOPATHOLOGICAL DIAGNOSIS OF INTESTINAL REJECTION FOLLOWING CLINICAL SMALL BOWEL TRANSPLANTATION. D. Hurlbut, D. Ohene-Fianko, D. Grant, B. Garcia, University Hospital, London ON.

The authors examined the histopathological findings in the pathological criteria for rejection in small intestinal transplants. Criteria included increased enterocyte mitosis, goblet cell loss, cryptitis, lymphocytic infiltrate, flattening of intestinal villi, and villous sloughing with necrosis. The authors were able to use these criteria to diagnose rejection in two patients and successfully treat one. The authors note that these findings in some respects are non-specific andthat the findings may be patchy in nature. The authors then studied these biopsies for markers for lymphocytes (CD2, CD3, CD4, CD8) and macrophages (Ki-M1, Ki-M6, Ki-M7). The authors noted that mucosal biopsies showed Ki-M6 positive mononuclear cells in both patients with rejection episodes. The presence of these macrophages in one patient clearly predated routine histological evidence graft rejection. Also noted were changes of increased Ki-M7 and the staining of crypt epithelial cells for HLA-DR. Based on this preliminary study, selective immunohistochemical analysis of mucosal biopsies, including markers for activated macrophages and HLA-DR should be included in future intestinal transplant biopsies.

LYMPHOCYTIC GASTRITIS. A COMPARATIVE HISTOPATHOLOGIC STUDY WITH OTHER FORMS OF GASTRITIS. J Jessurun, M.D., LP Barron-Rodriguez, M.D., JJ Manrique-Ortega, M.D. Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, MN and Department of Pathology, General Hospital of Mexico City, UNAM, Mexico.

The study was undertaken to assess whether lymphocytic infiltration of the foveolar mucosal is specific for lymphocytic gastritis, to characterized other histopathological features which might be present or absent in lymphocytic and other forms of gastritis. Seven cases of lymphocytic gastritis were studied. These were among 725 consecutive gastric biopsy specimens from patients with gastritis (0.98%). These cases were compared with cases of gastritis secondary to reflux, acute hemorrhagic gastritis, chronic gastritis with helicobacter pylori, and chronic gastritis without helicobacter pylori and normal mucosa. The study was performed blindly in a semiquantitative analysis. The most distinct features were: 1. increased numbers of intraepithelial lymphocytes in the foveolar mucosa in lymphocytic gastritis compared to other forms of gastritis and normal mucosa ($p=0.001$), 2. absence of glandular atrophy in lymphocytic gastritis vs. chronic gastritis with and without H. pylori ($p<0.001$), 3. absence of foveolar hyperplasia in lymphocytic gastritis vs. reflux and paucity of active lesion lymphocytic gastrits vs. chronic gastris with H. pylori ($p<0.001$). In one case, lymphocytic gastritis was associated

with H. pylori. Because of this the authors conclude that: 1. lymphocytic gastritis is an uncommon form of gastritis, 2. inflammatory changes are almost confined to the surface epithelium and superficial lamina propria, 3. the presence of thelatter features and the absence of the other above described histological changes readily separates lymphocytic gastritis from other forms of gastritis, and 4. lymphocytic gastritis is rarely associated with H. pylori.

CECAL POORLY DIFFERENTIATED ADENOCARCINOMA, MEDULLARY TYPE. J Jessurun, M Romero-Guadarrama, JC Manivel. University of Minnesota, Minneapolis, MN and Hospital General de Mexico, U.N.A.M., Mexico.

The authors described 7 cases of cecal carcinoma of the medullary type. All tumors occurred in women, and histologically consisted of nests, trabeculae, and sheets containing small to medium sized cells with scant to moderate amounts of eosinophilic cytoplasm. Numerous mitoses and extensive lymphocytic permeation was present. Focal mucin production was noted as evidenced by positivity for the PAS, mucicarmine, and alcian blue stains. Immunohistochemical studies markers for epithelial differentiaton were positive, however, markers for neuroendocrine differentiation were negative. All patients (except for 1 who died post-operatively) are alive and well without evidence of recurrent tumor after the follow-up period of 1-49 months. The authors state that these predominantly solid poorly differentiated adenocarcinomas appear to be a distinctive entity and must be distinguished from neuroendocrine carcinomas and other more aggressive, non-glandular tumors of the colon.

A DISTINCTIVE LYMPHOCYTIC INFILTRATE IN ESOPHAGEAL AND GASTRIC MUCOSA IN H IV INFECTION. J.K. Kelly, W.S. Hwang, L.R. Sutherland, and D. Church. Departments of Pathology, Medicine and Infectious Disease, University of Calgary and Foothills Hospital, Calgary.

The authors looked mucosal biopsies of esophagus, stomach, duodenum, and rectum in HIV-infected men and compared them to controls. The esophagus of HIV-positive cases showed a distinctive basal epithelial lymphocytic infiltration. This was CD8 predominant and was the sole abnormality in 28 HIV cases and in 0 controls ($p<0.002$). Gastric biopsies reveal focal gland destructive lymphoid infiltrates in 19 H IV cases and in 0 controls. Duodenal biopsies exhibited mean decreased villous height in HIV patients compared with controls, although most biopsies were subjectively normal. Both gastric and duodenal biopsies mean CD4 counts were significantly lower than controls and mean CD8 were significantly elevated. Rectal biopsies showed either normal findings or non-specific inflammation. The authors conclude that the CD4:CD8 ratio was

lower in tissues as well as in blood. A distinctive lymphocytic infiltrate contained mainly CD8 cells is found in esophageal epithelium and gastric mucosa of HIV-infected patients.

ROLE OF DNA CONTENT DETERMINATION BY IMAGE ANALYSIS IN CONFIRMATION OF DYSPLASIA IN BARRETT'S ESOPHAGUS. M. Khan, H. Bui, M. Abdulla, A. delRosario, F. Ballouk, Y. Sim, J.Ross, Albany Medical College, Albany NY.

Patients with Barrett's esophagus differentiation of reactive epithelial atypia from true dysplasia may often be difficult, especially with limited biopsy material. The authors examined the DNA content by use of image analysis of the following specimens: Barrett's esophagus showing reactive atypia without dysplasia, Barrett's esophagus with dysplasia, and Barrett's esophagus with invasive carcinoma. Mean DNA index (DI) of the uniformly diploid Barrett's esophagus was 1.06. The mean DI for those cases with dysplasia and those cases with carcinoma were 1.5 and 1.88 respectively. These were significantly different than that for Barrett's esophagus with reactive changes ($p<0.004$). However, they were not different from each other. Twenty percent of the cancer patients with Barrett's were diploid, while 80% were aneuploid. There was no statistically significant difference in the mean survival of diploid Barrett cancers vs. aneuploid Barrett cancers. This concludes that image analysis may be helpful in differentiating reactive changes vs. true dysplasia in biopsies of patients with Barrett's esophagus.

IMMUNODETECTION OF INTEGRINS IN THE NORMAL AND NEOPLASTIC COLON. G.K. Koukoulis, I.Virtanen, V. Quaranta, VE Gould. Rush Medical College, Chicago, IL, Scripps Clinic, LaJolla, CA and Helsinki University, Helsinki Finland.

Integrins are transmembrane glycoproteins that modulate cell matrix and cell-to-cell interactions by acting as receptors to extracellular protein ligands and as direct cell adhesion molecules. The authors immunostained samples of normal colon, tubular and villous adenomas, and adenocarcincomas with monoclonal antibodies specific for various integrin sub-units. Compared to normal mucosa, basal polarization was seen in villous adenomas. In most carcinomas, reactions were decreased as compared with adenomas. In a minority of carcinomas with poorly glandular formation, only polarized reactions of the tumor stromal interface was retained. The authors conclude that in the normal colonic mucosa the differential integrin distribution in cryptal vs. superficial cells reflects variable adhesive requirements as cells migrate from the crypts to the surface. In carcinomas, the frequently decreased and basally polarized distribution of certain integrin sub-units may be related to altered cell-to-cell and cell matrix interactions that in turn may affect the tumor's capability for invasion and metastasis.

ELASTIC STAIN POSITIVE DENSE DEPOSITS IN GASTRIC STROMAL TUMORS. ET Larsen, JK Kelly, WS Hwang, DR Sawyer, Foothills Hospital and the University of Calgary, and Reed Deer Regional Hospital, Alberta, Canada.

Homogeneous eosinophilic deposits in stromal tumors of the gastrointestinal tract were found to stain heavily with the conventional elastic tissue stains, orcein and Victoria Blue. In order to determine whether elastic staining had any specificity for GI stromal tumors the authors studied 35 GI stromal tumors, 8 gynecological smooth muscle tumors, 10 soft tissue smooth muscle tumors, and 10 neurilemmomas. Tissues were examined for the presence of a pericellular elastica fibre (framework) and for the presence of dense amorphous elastica deposits (blobs). Thirty-one percent (11/35) of the GI stromal tumors contained blobs, however, blobs were not present in any of the gynecological tumors, soft tissue tumors, and neurilemmomas ($p=0.001$). Immunostaining for elastin was consistently negative in both the blobs and the framework staining, although built in control tissue was positive. These findings may indicate that GI stromal tumors are histogenically distinct from smooth muscle tumors from other sites and also from neurogenic tumors.

BLOOD GROUP ANTIGENS IN BARRETT'S ESOPHAGUS & ASSOCIATED ADENOCARCINOMAS. G. Lauwers, J. Melamed, and R. Rojas, Memorial Sloan-Kettering Cancer Center and Impath Laboratories, New York, NY.

The authors examined immunohistochemically tissue from patient's with Barrett's esophagus and associated adenocarcinoma. The antibody used was a panel against blood group antigens ABH and Lewis a,b,x, and y. Loss of blood group H was recorded in 4 adenocarcinomas and 1 adjacent Barrett's esophagus mucosa. Incompatible blood group antigens A and B were recognized in O-Rh positive patient and one A-Rh positive patient respectively. Anomalous expression of Lewis a was seen in 7 adenocarcinomas and the adjacent Barrett's esophagus, parallel with loss of Lewis b. Deletion of Lewis x expression was noted in 7 adenocarcinomas and adjacent Barrett's esophagus. There appears to be significant alterations of blood group antigens occurring in Barrett's esophagus and adenocarcinoma associated with Barrett's esophagus. Antigenic modification seen in the different subtypes of Barrett's esophagus with or without dysplasia are similar to those in Barrett's with adenocarcinoma.

HER-2/NEU ONCOGENE EXPRESSION AND PROGNOSIS IN GASTRIC CARCINOMA. EY Lee, ML Cibull, WE Strodel, and J Haley, University of Kentucky, Lexington, KY.

The authors examined the expression of Her-2/NEU oncoprotein in 56 gastric carcinomas using a polyclonal antibody on paraffin-embedded material. Cases that by quantitative image analysis that exhibited more than 10% of the SKBR3 neu content were considered to be positive for neu expression according to the method by Bacus et al (Arch Pathol Lab Med, 1990:114;164). Membrane staining was only noted in those of the intestinal type of cancer. Cytoplasmic staining was noted in both intestinal and diffuse types. Cases which were positive for membrane and/or cytoplasmic staining had a shorter mean survival (308 days) than cases that failed to stain (763 days) ($p<0.05$). There was no statistically significant association between neu immunoreactivity and other clinicopathological parameters, including age, sex, smoking history, blood type, tumor location, gross type, and grade. Seventy-four percent of Stage IV tumors were neu positive compared to 22.2% of Stage I-III tumors ($p<0.05$). This study supports the hypothesis that the expression of neu may be a significant predictor of prognosis in patients with gastric carcinoma. Moreover, contrary to other reports, the present findings suggest that not only membrane staining but also cytoplasmic staining is significant in evaluating neu expression in gastric carcinomas.

INDEPENDENT EXPRESSION OF HER-2/NEU ONCOPROTEIN AND EPIDERMAL GROWTH FACTOR RECEPTOR IN GASTRIC CARCINOMA. EY Lee, ML Cibull, WE Strodel, and J Haley, University of Kentucky, Lexington, KY.

HER-2/neu oncogene shares an extensive homology with the c-erbB-1 oncogene which encodes the epidermal growth factor receptor (EGFR). The authors immunohistochemically studied the localization of neu and EGFR in benign and malignant gastric tissues from 56 specimens with gastric carcinoma (22 diffuse and 34 intestinal) by using polyclonal antibodies in paraffin-embedded material. Both cytoplasmic and membrane staining were noted for the neu oncogene. Similarly, cytoplasmic staining was also noted for EGFR. No significant staining for neu was noted in benign gastric tissues from the same specimens, whereas significant staining for EGFR was noted in benign tissues. Patchy staining was common for neu, while EGFR immunoreactivity was always diffuse. Twenty cases (35.7%) showed positive staining for both, 15 cases (26.8%) for neu only, 4 cases (7.1%) for EGFR only, and 17 cases (30.4%) for neither. The presence of immunoreactivity showed a poorer prognosis, which was statistically significant, however, postivity for EGFR showed shorter survival but not to statistical significance. EGFR positivity did not further reduce survival in neu positive

cases. These findings suggest that the expression of these two closely related proto-oncogenes in malignant and benign gastric tissues is independent of each other and that EGFR does not potentiate the oncogenic effect of neu.

IMMUNOHISTOCHEMICAL DETECTION OF TRANSFERRIN RECEPTOR IN COLORECTAL CARCINOMAS AND PRECURSOR LESIONS. KO Leslie, DL Weaver, and TW Griffin. University of Vermont, Burlington, VT, University of Massachusetts Medical School, Worcester MA.

The authors immunohistochemically studied the distribution and incidence of transferrin receptor (TFr) in human colorectal carcinoma, adenomas, and normal colonic epithelium. All carcinomas examined were moderate to strongly immunoreactive with this antibody. The most intense staining usually tending to be at the leading edge of the invasive growth. Normal colonic epithelium did not show appreciable staining, however, when staining was present in the normal epithelium, it was usually limited to the surface epithelium. Tubular adenomas and tubulovillous adenomas showed consistent immunoreactivity, but more focally less intense than did the carcinomas. These studies suggested that transferrin receptor may be a reasonable cytoplasmic membrane marker for colorectal carcinoma. The presence of the transferrin receptor in potential precursor lesions in the colon, and absence in the highly proliferative basal crypt cells suggests that TFr may be related to neoplastic transformation in this organ.

COMPARISON OF TUMOR PROLIFERATIVE ACTIVITY BY FLOW CYTOMETRY AND KI-67 AND PCNA IMMUNOSTAINING IN HUMAN DIPLOID COLON CARCINOMAS: CORRELATION WITH HISTOPATHOLOGIC PARAMETERS. M.D. Linden, C.K. Ma, J. Kubus, R.D. Brown, R.J. Zarbo, Henry Ford Hospital, Detroit, Michigan.

The object of this study was to examine colon cancers with diploid DNA characteristics to: 1. compare Ki-67 and PCNA tumor proliferation indexes (TPI) to FCM S-Phase fraction (SPF) and proliferative fraction defined by S+G2/M (PF) calculated by both ungated and cytokeratin gated histograms, and 2. to determine if there was a relationship between tumor proliferative activity and histopathological parameters. The authors found no significant correlation coefficient between individual values of Ki-67 or PCNA TPI and FCM-derived SPF or PF among gated or cytokeratin gated DNA histograms. However, when categorized above and below the median FCM, tumor proliferative activity values mean Ki-67 TPI but not PCNA was significantly higher in tumors above median FCM-SPF and FCM-PF. There was no correlation of histopathological factors and FCM tumor proliferative activity or TPI by Ki-67 or PCNA. The authors conclude that for a subset of diploid colon cancers evaluation of tumor

proliferative activity values by immunohistochemistry and flow cytometry do not correlate with histopathological parameters of known prognostic significance.

DISTRIBUTION OF COLON-OVARIAN TUMOR ANTIGEN IN ADENOCARCINOMAS: AN IMMUNOHISTOCHEMICAL STUDY OF 490 CASES. T. Loy and V. Darkow, University of Missouri School of Medicine and Harry S. Truman Veterans Administration Hospital, Columbia, MO.

To determine the distribution of colon ovarian tumor antigen (COTA) and adenocarcinomas, the authors studied formalin-fixed, paraffin-embedded tissues from 490 cases of adenocarcinoma from a variety of primary sites using the commercially available monoclonal antibody to COTA (BioGenex Laboratory). COTA was present in a high percentage of colonic ovarian, endometrial, endocervical, lung, prostatic, pancreatic, esophageal, and stomach carcinomas. COTA was absent in both kidney and thyroid cancers. The authors conclude that COTA is present in a wide variety of adenocarcinomas. Immunostaining for COTA may be helpful in ruling out renal cell carcinoma and thyroid carcinomas in certain clinical settings.

EXPRESSION OF THE 70-KD HEAT SHOCK PROTEIN (HSP70) IN ISCHEMIC BOWEL DISEASE. X-P Lu, R. Omar and W.W.L. Chang, Department of Pathology, West Virginia School of Medicine, Morgantown WV.

Heat shock proteins are a family of polypeptides which are induced in response to various forms of cell injury. These proteins presumably have some sort of protective function. The authors used anti-HSP70 monoclonal antibody and standard immunocytochemistry to study the expression of HSP70 in surgical specimens of the small and large intestines from patiens with ischemic bowel disease and non-ischemic controls. Strong HSP70 immunoreactivity was observed in viable and regenerating epithelial cells of both the surface and crypt epithelium within or adjacent to necrotic foci in all ischemic specimens. No immunoreactivity was detected in necrotic tissue. The normal-appearing epithelial cells distant from the infarcted areas were negative in the small intestine, but weakly positive in the large intestines. Smooth muscle cells of ischemic areas also showed diffuse staining. Control specimens showed no detectable staining. The findings suggest a possible role of HSP70 in intestinal epithelial and muscle cell response to ischemic injury, especially in the recovery phase.

IMMMUNOHISTOLOGIC CHARACTERIZATION OF GASTROINTESTINAL STROMAL TUMORS. C.K. Ma, M.B. Amin, E. Kintanar, M.D. Linden, R.J. Zarbo, Henry Ford Hospital, Detroit Michigan.

There is much controversy regarding the cell origin or the issue of differentiation of mesenchymal tumors of the gastrointestinal tract. In order to further clarify this matter, the authors studied 128 gastroinestinal stromal tumors from their institution. Small intramural lesions and typical esophageal and rectal leiomyomas were excluded. The tumors were classified as typical leiomyoma and spindle or epithelial type GI stromal tumors based on the predominant pattern. The tumors were divided into benign (<5 cm and <5 mitoses per 50 HPF), malignant (>5 mitoses per 50 HPF), and borderline (>5 cm and <5 mitoses per 50 HPF) lesions. A panel of antibodies was used to differentiate towards myogenic (muscle actin HHF-35, alpha smooth muscle actin, and desmin), Schwann cells, S-100 protein, cells of Auerbach's plexus (neurofilament), and enteric glia (GFAP). All typical leiomyomas were strongly positive for the three muscle markers. The gastrointestinal stromal tumors were positive for smooth muscle actin and HHF-35, while a very small percentage (6%) were positive for desmin. The authors conclude that a high percentage of gastrointestinal stromal tumors either benign or malignant, express smooth muscle actin and muscle specific actin suggesting smooth muscle differentiation. Desmin is not detectable in most gastrointestinal stromal tumors, paraffin-embedded sections, and very few gastrointestinal stromal tumors show evidence towards Schwann cell or Auerbach's plexus or enteric glial cell differentiation.

PROSPECTIVE EVALUATION OF T-LYMPHOCYTES IN ESOPHAGEAL MUCOSAL BIOPSIES. M.M. Mangano, M.D., H.H. Wang, M.D., and D.A. Antonioli, M.D. Departments of Pathology, Beth Israel Hospital and Harvard Medical School, Boston, MA.

The authors have previously shown that in the esophagus intraepithelial cells with irregular nuclear contours (CINC) as well as mononuclear cells (MN) with round nuclei are T-lymphocytes and may be an independent marker of esophagitis. Such a marker would be very helpful because a fair number of biopsies in patients with clinical symptoms and endoscopic findings of esophagitis lack traditional histological features of esophagitis in biopsy specimens. The authors prospectively evaluated biopsy specimens from 201 consecutive patients for the presence of CINC and MN and also in selective cases stained for T-cell and B-cell markers. Immunohistochemical results show that the majority of CINC and MN were T lymphocytes. Among clinical symptoms, only dysphagia was associated with an increased number of T lymphocytes, however, there was no significant difference in t he number of T lymphocytes in patients with or without endoscopic or histological features of esophagitis. The authors conclude that T lymphocytes are a normal

component of esophageal epithelium. T lymphocyte number does not appear to be a independent marker of reflux esophagitis.

SUPERFICIAL ANTRAL VASCULAR ECTASIA IN BONE MARROW TRANSPLANT PATIENTS. D. Marmaduke, J. Greenson, I. Cunningham, E. Herderick, F. Cornhill, The Ohio State University Hospitals, Columbus, Ohio.

The authors reviewed all gastric biopsies from bone marrow transplant patients between 1986 and 1991 and identified 10/29 patients with makedly enlarged vessels within their superficial antral mucosa. Clinicopathological features of these 10 patients were studied to determine the etiology of this superficial antral vascular ectasia (SAVE). The cross-sectional area of SAVE was measured by digital morphometry and compared to match controls of chemical gastritis and normal antral biopsies. All the 10 SAVE patients received standard bone marrow transplant regime of Busulfan and Cytoxan. No patients received total body irradiation. Most endoscopies were performed on the average of 166 days post bone marrow transplant in order to evaluate gastrointestinal bleeding or abdominal pain. Endoscopically the authors found erythematous and granular mucosa. All SAVE patients had elevated hepatic enzymes, four patients had hepatic veno-inclusive disease, and 8 patients had GHVD. The authors' indicates that the vessel size in biopsies in SAVE was significantly larger than vessels in chemical gastritis and normal antral controls. SAVE was a significant cause of gastrointestinal bleeding in these patients. Superficial antral vascular ectasia was associated with hepatic dysfunction with or without graft vs. host disease, suggesting portal gastropathy as a possible underlying mechanism.

HISTOLOGIC FEATURES GUIDING THE APPROPRIATE USE OF CYTOMEGALOVIRUS IMMUNOHISTOCHEMISTRY. C.T. Masada, J.R. Dobson, J.W. Wisecarver, R.S. Markin, J.Linder, Univ. Nebr. Medical Center, Omaha, NE.

Specimens which are suspected for infection with cytomegalovirus not uncommonly fail to show the routine characteristic intranuclear inclusions. The authors undertook this study to see which if any histological features can reliably guide the selection of gastrointestinal biopsies for diagnostic cytomegalovirus immunohistochemistry. The authors studied 34 orthoptic liver transplant patients with symptoms suspicious of CMV enteritis. The biopsies were allocated for: 1) H&E stain, 2) CMV immunostain, 3) determination of CMV early antigen by spin amplification methods, and 4) lung fibroblast cell culture innoculation. Acute inflammation was a sensitive (100%) and relatively specific (90.4%) feature of CMV enteritis in this patient population. The classic viral inclusions were absent in 9 of 22 (40.9%) of the biopsies with positive immunostaining. Acute inflammation was present in all 22 biopsies. The authors found that in the lack of acute inflammation immunostaining for CMV was

negative in all cases and was positive in no cases. This should help direct the clinician in the use of these immunohistochemical stains.

SYMPTOMATIC PRIMARY GASTRIC AMYLOIDOSIS. DM Menke, JT Wolfe, CT Flemming, WA Oldenburg, PJ Kurtin, RM Kyle, Mayo Clinic, Jacksonville, FL, and Rochester, MN.

Among 779 cases of primary systemic amyloidosis seen at the Mayo Clinic, 59 patients (8%) had gastrointestinal amyloidosis, and 8 (1%) had biopsy-established gastric amyloidosis. All these patients had symptomatic gastric amyloidosis presenting with gastric hemorrhage, gastric tumor, gastric outlet obstruction, gastroparesis, nausea, vomiting, and weight loss. All patients developed heart failure, nephrotic syndrome, peripheral neuropathy, or carpal tunnel syndrome. Weight loss was a very significant clinical finding in these patients. Gastric amyloid was identified by Congo red stain in perivascular and submucosal tissue in all cases. All cases stained selectively for lambda or kappa light chains. Six of the eight patients died with a median survival of only 107 days. Cause of death was usually cardiac failure or renal failure.

THE RELATIONSHIP OF QUANTITATIVE NUCLEAR MORPHOLOGY TO MOLECULAR GENETIC ALTERATIONS IN THE ADENOMA-CARCINOMA SEQUENCE OF THE LARGE BOWEL. J.W.R. Mulder, G.J.A. Offerhaus, E.P. deFeyter, J.F. Floyd, S.E. Kern, B. Vogelstein, and S.R. Hamilton, The Johns Hopkins University School of Medicine and Hospital, Baltimore, MD.

Fuelgen-stained isolated nuclei from 22 adenomas and 42 carcinomas which had been analyzed for ras-gene mutations and allelic deletions on chromosomes 5q, 18q, and 17p were characterized by image analysis. Both nuclear area and nuclear shape factor representing irregularity correlated with tumor progression ($r=.57$ and $r=52$, $p<.0001$), while standard nuclear texture, a parameter of chromatin homogeneity was adversely correlated ($r= -.80$, $p<0.0001$). The nuclear parameters were strongly inter-related ($p<0.0005$). In multivariate analysis the nuclear parameters were associated with the adenoma-carcinoma sequence ($p<0.0001$) were not influenced significantly by individual genetic alterations. Nuclear texture was inversely correlated with fractional allelic loss, a global measure of genetic changes in carcinomas ($r= -.39$, $p= -0.011$). These findings indicate that nuclear morphology in colorectal neoplasms is strongly related to tumor progression and cannot be explained by the individual genetic changes studied. Nuclear morphology and biological behavior are complex phenomena influenced by a variety of factors including accumulation of alterations in cancer-associated genes.

RELATIONSHIP OF CELL PROLIFERATION TO EVOLUTION OF MALIGNANCTY IN ADENOMAS REVEALED BY MAPPING OF PROLIFERATION ZONES. J.C. O'Keane, Shi Yang, P. Schroy, L.S. Gottlieb, M.J. O'Brien, Mallory Institute of Pathology, Boston Univ. School of Medicine, Boston, MA.

The authors used tritiated thymidine uptake, Ki-67, and proliferative cell nuclear antigen (PCNA) to study cell proliferation in colorectal adenomas. Using PCNA, the authors constructed detailed maps of proliferation patterns using digitalized images. Proliferation zones were classified as high (>66% cell cycling), intermediate (33-66% cell cycling), and low (<33% of cell cycling). These were then outlined in red, black, and green respectively using a digitizing tablet. High proliferating zones were present in a range of 5-70% of the total outline per adenoma (median 10%). Such zones expanded to greater than 10% were found in 5/6 adenomas with high grade dysplasia and 2/7 adenomas with low grade dysplasia and consistently mapped to complex glands but not to simple tubulvillous structures. Conclusion: Preliminary analysis of proliferation maps suggests that expansion of high proliferation zones is associated with adenoma progression to malignancy.

ESOPHAGEAL SQUAMOUS PAPILLOMAS: CLINICAL-PATHOLOGIC EVALUATION AND ANALYSIS FOR HUMAN PAPILLOMA VIRUS (HPV) BY IMMUNOPEROXIDASE (IP), DNA IN-SITU HYBRIDIZATION (ISH), AND POLYMERASE CHAIN REACTIONS (PC) TECHNIQUES. R. Odze, M. Upton, D. Shocket, H. Goldman, and D. Antonioli, Mount Sinai Hospital, Toronto, Ont. Canada, New England Deaconess, Beth Israel, the Children's Hospital, and Veterans Affairs Medical Center, Boston, MA.

The pathogenesis of esophageal squamous papillomas (ESP) is unknown. Chronic irritation and human papilloma virus are two proposed etiologies. To investigate these hypotheses, the authors analyzed clinical data and histological features from 38 ESP from 33 patients. They also performed immunohistochemistry and in-situ hybridization and PCR for the detection of HPV. Esophagitis was documented histologically in 14/23 patients, and another 7 patients had gastritis. Two patients had history of neck irradiation.Eighty percent of the ESPs were located in the distal esophagus, while 18% were in the mid-esophagus. Histologically 19/38 ESPs had focal areas of koilocytes. Immunohistochemistry and in-situ hybridization studies were negative, except for a single HPV type 6 and 11 positive immunohistochemistry specimen froma patient with respiratory tract papillomatosis. PCR detected HPV type 16 in 4/6 cases of mid esophageal ESPs, but none of the 12 lower ESPs. The authors conclude that the pathogenesis of ESPs is

multifactorial. Many are associated with chronic mucosal irritation (esophagitis), but those in the middle and upper esophagus may be more closely linked with HPV infection.

IMMUNOHISTOLOGIC CHARACTERIZATION OF GOLD TYPES 1-5 ANTI-CEA MONOCLONAL ANTIBODIES IN COLON CANCER. R. Paxton, J.M. Esteban, H. Battifora, P. Metha and J. Shively. Divisions of Pathology and Immunology, City of Hope, Duarte, CA.

The authors studied 100 colorectal cancers immunohistochemically with various CEAs against types 1-5 of the Gold classification. The authors found that specificity and sensitivity for CEA varied signficantly among monoclonal antibodies tested. The anti-CEAmonoclonal antibodies from Gold epitope groups 1 and 2 had superior specificity and sensitivy. Monoclonal antibodies from Group 5 had extensive cross-reactivity, with CEA-like molecules present in normal tissues. The authors conclude that anti-CEA antibodies should be optimally characterized prior to their use for clinical or diagnositic purposes in order to avoid false results due to prior sensitivity or cross-reactivity. Monoclonal antibodies from Gold group 1 are highly recommended for clinical use.

SOLITARY RECTAL ULCER SYNDROME (SRUS): CLINICAL AND PATHOLOGIC FACTORS ASSOCIATED WITH DELAYED DIAGNOSIS. R. Petras, J. Tjandra, V. Fazio, Cleveland Clinic Foundation, Cleveland, OH.

The authors analyzed 25 patients with SRUS in whom erroneous clinical/pathological diagnoses had been made. The mean duration of incorrect clinical/pathological diagnosis was 5 years. The diagnostic changes of SRUS (fibromuscular obliteration of the lamina propria) were misinterpreted in 23 cases. The various misinterpreted diagnoses were: non-specific ulcer, inflammatory bowel disease, adenoma, hyperplastic polyp, Peutz-Jegher polyp, angiodysplasia, pseudomembranous colitis, collagenous colitis, and mucinous carcinoma. The authors conclude that the failure to diagnose SRUS was often due to inadequate biopsy material. Diagnostic errors associated with adequate biopsy material resulted from the failure to properly recognize fibromuscular obliteration as a key pathological finding in this disorder.

ESOPHAGEAL PATHOLOGY FOLLOWING MORRHUATE SCLEROTHERAPY. E.S. Pizer, S.R. Hamilton, G.M. Hutchins, The Johns Hopkins Medical Institutions, Baltimore, MD.

Sodium morrhuate is an alkaline cod liver oil derivative, and is injected at endoscopy for sclerosis of esophageal varices. The authors reviewed the clinical and pathological features of 13 patients who had morrhuate sclerotherapy for control of varices, and who were autopsied at the Johns Hopkins Hospital. Patients who died from 2-22 days after morrhuate injection had esophageal ulceration, intramural hemorrhage, and severe

necrosis and inflammation with abscess formation. Blood vessels at the site of injection were necrotic and thrombosed, while others nearby appeared unaffected. Candida was found in the inflamed esophagus wall in 3 cases and bacteria in 2. In contrast, the patients who had sclerotherapy from 45-185 days prior to death showed organized thrombosed varices, abundant small intramural varices, and only slightly focal fibrosis. The observations suggest that patient who died shortly after morrhuate sclerotherapy have a high prevalence of severe esophageal injury and intramural infection, but in those who survived longer the esophagus demonstrates excellent repair of injury.

"THE TORKELSON SYNDROME." L. Puttagunta, C. Foulston, L.J. Smith, W. Syzmanski, L.D. Jewell, and H. Pabst., University of Alberta, Edmonton, Alberta, Canada.

The authors report a distinct morphological entity of autosomal dominant inheritance in which the clinical symptoms are vomiting and severe secretory diarrhea rapidly causing life-threatening dehydration and hypovolemia. The small biopsies are quite characteristic and are present during the asymptomatic phase. They consist of massive edema of the lamina propria with resultant club-like deformities of the villi and patchy areas of acute enteritis. There are scattered foamy histiocytes containing imbued edema fluid. The epithelium is intact and unremarkable and organisms are not present. Immunohistochemistry revealed normal immunoglobulin-bearing cells, and the enterocytes show a normal HLA-DR expression. By electron microscopy, enterocytes are normal with preservation of microvillous borders and cell junctions. This entity has a characteristic morphology which the authors present in this presentation.

EXPRESSION OF OA519 (HAPTOGLOBIN-RELATED PROTEIN EPITOPES) IN CLORECTAL CARCINOMAS: COMPARISON WITH MOLECULAR GENETIC ALTERATIONS AND METASTASIS. M.S. Redston, S.E. Kern, B. Vogelstein, and S.R. Hamilton, The Johns Hopkins University School of Medicine and Hospital, Baltimore, MD.

The authors analyzed the immunohistochemical expression of OA519 (Haptoglobin- related protein epitopes) with monoclonal antibody in 27 colorectal carcinomas which had also been analyzed for ras gene mutations and allelic deletions of chromosomes 5q, 18q, and 17p. All tumors expressed OA519. The degree was quantitated, and was found to be low in 6/27 (22%), intermediate in 12/27 (45%), and high in 9/27 (33%). Allelic deletion of 17p containing the p53 gene was associated with high or intermediate expression of OA519. The increased OA519 expression was associated with development of distant metastasis, and that 11/21 (57%) of patients with intermediate or high expression later developed metastasis as compared to 0/6 of those with low expression. The findings

support a relationship between OA519 expression, molecular genetic alterations, and the development of metastatic phenotype in colorectal carcinomas.

PROLIFERATING CELL NUCLEAR ANTIGEN (PCNA) IN COLONIC POLYPS AND IN ADENOCARCINOMAS OF THE COLON. P. Robinson, W. Wu, and M. Nadji, University of Miami, Miamia FL.

Using a monoclonal antibody to PCNA, the authors immunohistochemically investigated the presence and pattern staining of PCNA in formalin-fixed, paraffin-embedded tissues of 10 hyperplastic polyps, 9 tubular adenomas, 9 villous adenomas, and 8 colonic adenocarcinomas. PCNA is a nuclear antigen that is associated with S-phase of the cell cycle. The nuclei of the lesions were semiquantitated as to the extent of nuclear staining and graded 1 to 4 (1 = 25% or less, 2= 26-50%, 3= 51-75%, and 4=>75%). In the normal colon, PCNA labeling was limited to the nuclei of the cells at the base of the crypts. The highest labeling for PCNA was found in villous adenomas (average grade 3.7). Colonic adenocarcinomas, tubular adenomas, and hyperplastic polyps had grades of 3.1, 2.7, and 2.1, respectively. This villous adenoma seemed to show the highest nuclear proliferative activity. The clinical significance of this is presently unknown, and the authors suggest investigations in a larger series should be undertaken.

BACTERIA-FREE GASTROTOXIC HELICOBACTER PYLORI FILTRATES: AN EXPERIMENTAL STUDY. J. Ross, H. Bui, A. delRosario, M. Abdulla, M. Khan, M. George, J.Schrader, Albany Medical College, Albany, NY.

The pathogenesis of Helicobacter pylori associated gastritis and peptic ulcer disease remains unknown. Cell free filtrates of H. pylori are known to injure epithelial cells in culture, and a cytotoxin has been described capable of injuring gastric mucosa. To study this problem, the authors studied the effects of cell-free filtrates of H. pylori in Sprague-Dawley male rats in whom acetic acid ulceration had been created. Seventy-two hours after the ulceration, one group of rats was given 2 ml. of bacteria free filtrate twice a day for seven days. The control group was treated with intragastric normal saline. Ninety percent of control rats showed grossly healing and entire re-epithelialization of the ulcers at sacrifice on day 11. Greater than 80% of the H. pylori filtrate-exposed rats showed persistence of active ulcers, and intense chronic inflammation. No gastric H. pylori organisms were identified microscopically or by culture in either group. The authors conclude that H. pylori bacteria-free filtrates may delay healing and promote persistence of chronic inflammation. The cytotoxic effect of H. pylori may play a major pathogenesis in human gastric injury.

FLAT MUCOSA OF FAMILIAL POLYPOSIS AND SPORADIC COLON CARCINOMA EXPRESS a2,6-LINKED SIALIAC ACID NOT FOUND IN NORMAL COLONIC MUCOSA. J. Roth, T. Sata, B. Stamm, and P.U. Heinz, Department of Pathology, University of Zurich Medical School, Zurich, Switzerland.

The authors have used colloid gold-labelled reagents for the histochemical detection of Sialic acid in different linkages in paraffin-embedded human colon specimens. Sialic acid in an alpha 2,6 linkage to galactose was visualized with the Sambucus nigra I lectin. The epithelium in normal and transitional mucosa, as well as that showing mild dysplasia exhibited no staining, however, there was staining in adenomas with severe dysplasia, sporadic carcinoma, and the surface epithelium of flat mucosa in patients with familial polyposis. In contrast, Sialic linkage in an alpha 2,6 to N-acetylgalactosamine and Sialiac acid in an alpha 2,3 linkage to galactose beta 1,4 N-acetylglucosamine or to galactose beta 1,3 N-acetylgalactosamine were detetable in normal as well as neoplastic colonic mucosa and flat mucosa in familial polyposis. The authors conclude that the neoplastic transformation of human colonic epithelium is accompanied by the de novo expression of a specific sialyltransferase. These findings provide the basis for studies of the possible role of cell surface alpha 2,6 linked sialic acid in growth behavior of human colonic epithelial cells and as presymptomatic marker in familial polyposis.

DNA TUMOR CONTENT IN COLORECTAL CARCINOMA PREDICTOR OF PATIENT'S OUTCOME? A PROSPECTIVE FLOWCYTOMETRIC (FCM) STUDY OF 129 PATIENTS. WA Sakr, C Suchowski, DW Visscher, D Wever, D Bouwman, and JD Crissman, Wayne State University and Harper Hospital, Detroit, MI.

Prognostic significance of tumor ploidy studies in colorectal cancers is controversial. Many previous studies that utilized paraffin-embedded tissues failed to correlate ploidy with stage and/or survival. In the present study, the authors examined 129 colorectal carcinomas using fresh tissue which was analyzed by two color flow cytometry and evaluated by Dukes' stage and disease status. The authors concluded that: 1) the outcome of patients with colorectal carcinoma is best predicted by tumor stage, 2) a portion of aneuploid tumors and of higher S-phase fraction values increased with higher Dukes' stage, but the trend was not statistically significant, 3) ploidy and S-phase fraction were not significant in predicting tumor recurrence and/or final patient outcome (survival).

EXPRESSION OF p53 IN HUMAN ESOPHAGEAL CARCINOMA. AN IMMUNOHISTOCHEMICAL STUDY WITH CORRELATION TO PCNA EXPRESSION.

H. Sasano, S. Miyazaki, Y. Goukin, T. Nishihra, T. Sawai, H. Nagura. Departments of Pathology and Surgery, Tohoku University School of Medicine, Sendai, Japan.

The authors studied p53 immunohistochemically by using the monoclonal antibody pAb1801 in 15 cases with esophageal squamous carcinoma. Immunoreactivity was detected in the nuclei of tumor cells in 4% paraformaldehyde-fixed frozen (12/15) and paraformaldehyde paraffin-fixed embedded sections (11/15), but not in routinely processed (10% formaldehyde fixed specimens). p53 expression was correlated with malignant phenotype. p53 was not observed in histologically normal mucosa, except in three cases in which immunoreactivity was observed in parabasal and basal cells. Immunostaining of Ki-67 and PCNA correlated strongly with p53 expression in carcinoma in dysplastic cells, but not in normal mucosa. Immunohistochemical patterns of p53 were not related to clinicopathological parameters in the cases studied. Therefore, p53 expression was strongly associated with the proliferation of carcinoma cells but not that of normal cells in esophageal carcinoma.

PROGNOSTIC VALUE OF PLOIDY ANALYSIS OF SMALL BOWEL MALIGNANCIES.

M. Troster, J.V. Frei, V.V. Martinez. University and Victoria Hospitals and the University of Western Ontario, London, Ontario, Canada.

The authors studied 36 primary, non-endocrine small intestinal carcinomas with flow cytometry using the modified Hedley technique on paraffin-embedded tissues. Twenty tumors (56%) had an abnormal DNA content. There was no correlation between ploidy, sex, age, pathological grade or stage. There was no significant increase in survival with diploid tumors. Survival increased with lower grade tumors and with lower stage tumors. Multivariate analysis showed that pathological stage and grade are independent prognostic indicators, but ploidy is not. The influence of pathological stage was greater than that of grade in predicting survival. Conclusion: 56% of small bowel carcinomas were aneuploid. Diploid tumors did not significantly have specifically a better survival. Aneuploidy is not an independent variable of surivival, as are grade and stage and tumor.

QUANTITATIVE DNA STUDIES BY IMAGE ANALYSIS IN LONG-STANDING ULCERATIVE COLITIS. F.E. Venco, S.C. Nahas, N.S. Mismeti, and R.E. Ibrahim, University of Sao Paulo Medical Center and MCom Informatics, Sao Paulo, Brazil.

The authors looked at quantitative DNA studies on Fuelgen-stained tissue sections by image analysis performed on 22 patients with ulcerative colitis of more than seven years duration. The areas selected for analysis were those with: dysplasia (1 patient, 2 biopsies), adenomatous change (1 patient), and adenocarcinoma (1 patient), atypical regenerative epithelium, probably negative for neoplasia (2 patients), and regenerative atrophic or metaplastic mucosa free of atypical changes (all patients). Aneuploidy was identified exclusively in specimens with dyspalsia, and adenocarcinoma and adenomatous change. The non-atypical mucosa from these patients was diploid. All the specimens of non-atypical mucosa from the remaining patients and those with atypical regeneration were also DNA diploid. The assessment of dysplasia and cancer risk in UC using current techniques is highly subjective. Image analysis is a subtle means for ploidy analysis and simultaneous histological evaluation. In disagreement with previous articles, the authors did not identify ploidy alterations in the non-atypical mucosa. Aneuploidy was present only in areas of definite dysplastic/neoplastic changes. The authors believed that the finding of aneuploidy should be regarded as highly indicative of dysplasia/malignancy.

EVALUATION OF CELIAC DISEASE BIOPSIES FOR ADENOVIRUS 12 DNA USING A MULTIPLEX POLYMERASE CHAIN REACTION (PCR). C.J. Vesy, J.K. Greenson, T.W. Prior, A.C. Papp, P.J. Snyder, S.J. Qualman, The Ohio State University Hospitals and Children's Hospital, Columbus, Ohio.

It has been postulated that Celiac disease (CD) is initiated by adenovirus. To test this hypothesis, the authors used PCR-based strategy to screen for adenovirus-12 (Ad12), cytomegalovirus (CMV), and Herpes Simplex Virus I/II (HSV) in formalin-fixed, paraffin-embedded small bowel biopsies from adults and children with celiac disease. Controls consisted of small bowel biopsies from normal adults and children, and adults and children with active duodenitis. Ad12 DNA was found in 2/208 adult CD biopsies, 0/19 child CD biopsies, 0/28 adult normal biopsies, 1/12 child normal biopsies, 0/13 adult active peptic duodenitis biopsies, and 0/9 child active peptic duodenitis biopsies. HSV DNA was present in 2/28 adult and 2/19 child CD biopsies. CMV DNA was present in 1/28 adult CD biopsies. HSV and CMV DNA was not found in any of the control patients. The authors conclude that Ad12, CMV, and HSV DNA was not identified in significant numbers in any patient group. The absence of Ad12 DNA in CD patients argues against persistent

adenovirus infection, but does not preclude remote infection with AD v irus prior to the onset of CD. The absence of CMV and HSV DNA in CD, active peptic disease, and active duodenitis suggest that neither virus is involved in the persistence of these inflammatory conditions.

CATHEPSIN-B IMMUNOSTAINING VS. CLINICOPATHOLOGIC PARAMETERS IN COLORECTAL ADENOCARCINOMA. D. Visscher, W. Sakr, C. Suchowski, B. Sloane, D. Weaver, D. Bouman, and F. Sarkar, Wayne State University School of Medicine and Harper Hospital, Detroit, MI.

Acetone fixed frozen sections of 46 colorectal tumors were immunostained for Cathepsin-B (CB) and type IV collagen (TIVC) using the avidin biotin technique. Intensity of neoplastic staining was compared to disease parameters and outcome. Stage B patients (n=18) showed no correlation between CB staining and outcome. Among Stage C patients, however, 7/12 (58%) with less than 1+ staining remained disease free compared to 0/5 with greater than 1+ staining. The authors data supports a role for Cathepsin-B in the progression of colorectal adenocarcinoma. Immunostaining correlates with poor differentiation (infiltrating growth) and was often accentuated at the invasive front on the tumor masses. These observations suggest that invading neoplastic cells elaborate Cathepsin-B in order to autolyze extracellular matrix proteins. There was intratumoral staining heterogeneity which implied active infiltrating growth may be focal within a given neoplasm. Cathepsin-B expression may be related to aggressive behavior in colorectal neoplasia, however, its clinical value as a prognostic marker is probably limited to specific patient subsets.

PRIMARY GASTRIC LYMPHOMA AND HELICOBACTER PYLORI. A. Wotherspoon, C. Ortiz-Hidalgo, T. Diss, M. Falzon, P. Isaacson. University College & Middlesex School of Medicine, London, UK.

Primary gastric lymphoma has features in common with mucosa associated lymphoid tissue (MALT) from which it is thought to arise. The normal gastric mucosa is devoid of lymphoma tissue, and its presence in gastric mucosa is almost invariably secondary to infection by Helicobacter pylori. The authors examined the acquired lymphoid tissue in 420 cases of H. pylori-associated gastritis and 40 cases of primary gastric lymphoma. The lymphoid tissue which accumulates in response to H. pylori infection demonstrated features of MALT. On analysis, Helicobacter-associated lymphoid tissue was found in 95% of gastric lymphomas, suggesting that the acquisition of MALT by the stomach as a result of infection with H. pylori is a necessary precursor for the eventual development of gastric lymphoma which may arise following the action of secondary factors.

HAM56 ANTIBODIES IN THE DIFFERENTIAL DIAGNOSIS BETWEEN COLORECTAL AND GYNECOLOGICAL MALIGNANCY. M. Younes, P.R. Katikaneni, L.V. Lechago, and J. Lechago. Department of Pathology, Baylor College of Medicine, and the Methodist Hospital, Houston, TX.

Ham56, a monoclonal antibody first utilized to identify macrophages and endothelial cells, will also stain many carcinomas, except in the digestive tract. The authors attempted to use this antibody in the differentiation between ovarian and colonic metastases, or between primary ovarian and metastatic colonic carcinoma in the ovary. The authors studied 24 formalin-fixed and paraffin-embedded ovarian carcinomas (16 primary, 4 colonic metastatic), and 14 peritoneal implants (10 ovarian and 4 colonic). These were immunostained with the Ham56 antibody using and ABC immunoperoxidase technique. Positive staining was considered only when a linear membranous pattern was noted. Using these parameters, 15/16 ovarian primaries and 9/10 ovarian implants were positive. Colonic ovarian metastastases and peritoneal implants were all negative. It would appear that the Ham56 antibody, especially when used together with CEA antibodies, may be useful in the distinction between colorectal and ovarian malignancies.

HAM56 EXPRESSION IN CARCINOMAS: DIAGNOSTIC UTILITIES. M. Younes, L. True. Baylor College of Medicine, Houston, TX, and University of Washington Medical Center, Seattle, WA.

The authors studied the expression of Ham56 immunoreactivity in a range of formalin-fixed, paraffin-embedded adenocarcinomas. The authors demonstrated that this marker is expressed by a wide range of adenocarcinomas. However, this antibody did not react with colonic carcinomas, suggesting that it could be used in a panel of antibodies in the differential diagnosis of metastatic adenocarcinoma of unknown primary site.

TOTAL COLONIC AGANGLIONOSIS (TCA): PATHOLOGIC DIAGNOSIS AND EMBYROLOGIC CONTROVERSIES. C.M. Zahn and E.J. Perlman. The Johns Hopkins Hospital, Baltimore, MD.

The authors report 4 cases of TCA who presented with presumed small bowel obstruction leading to laparatomy. TCA was not diagnosed at initial surgery, and 3/4 patients were subsequently diagnosed at 6 months, 21, 12, and 8 days of age. Three of the four patients died. All specimens showed absent ganglion cells with a transition zone at 2,12, and 40 centimeters proximal to the ileocecal valve and 25 centimeters distal to the ligament of Trietz. All showed a florid neuronal proliferation within the submucosal plexus extending from the rectum up the sigmoid colon, but not beyond. The more proximal colon and small bowel showed virtually absence of neuronal tissue in both plexus extending to the transitional zone. The pathological findings of TCA in the distal colon

are identical to these seen in classic Hirschsprung's disease. However, a more proximal lack of neuronal proliferation with a "empty" plexus seen at the time of frozen section in a patient with presumed Hirschsprung's disease should raise the possibility of TCA. Lack of proximal nerve proliferation and TCA suggest that the distal neuronal proliferation in TCA and Hirschsprung's disease is sacral, rather than vagal in origin. Thus, the possibility exists that Hirschsprung's disease represents a failure of neuronal migration along the sacral fibers, rather than incomplete migration along the vagal fibers.

April 13, 1992

Review "Viral Hepatitis: Biological and Clinical Features, Specific Diagnosis, and prophylaxis".

Second Edition by F. Blaine Hollinger et al. published by Raven Press February, 1991. Price $78.00 Number of pages 204.

This is the second edition of a book which has become a favorite reference source for individuals interested in viral hepatitis. The second edition has been expanded with newer molecular biology information about hepatitis A and B, as well as a discussion of recent serologic findings for hepatitis C.

This thoroughly referenced book gives a complete review of the history, pathogenesis and pathology, clinical features, serology and epidemiology of hepatitis A virus and hepatitis B virus. The clearly written text provides the reader with both a complete background of these diseases as well as practical suggestions for interpreting the laboratory evaluation of these patients.

In the chapter on non-A, non-B hepatitis viruses, Hollinger includes a discussion of hepatitis C virus which was current to the actual publication date of this book (November 1990). The laboratory evaluation of hepatitis C is reviewed with regard to both serology and to the need for non-serologic markers due to the imperfections of the hepatitis C testing available at that time. Although there have been recent advances with the second generation hepatitis C virus testing available currently, they are still not at the level of testing for hepatitis B virus. Therefore, although the reader must note that information about the second generation tests will not be available in this book, the chapter on non-A, non-B hepatitis viruses is a very useful summary. Lastly, whereas this is not a heavily illustrated text, the judiciously chosen illustrations are of high quality both at the light microscopic and ultrastructural level. They provide the reader with a clear demonstration of the viruses and the histolopathologic changes.

In summary, this is a very readable, clear, well-referenced textbook which would be a useful addition for any pathologist who deals with either biopsies from patients with viral hepatitis or with the clinical laboratory evaluation of serum from these patients.

ATTENTION

Gastrointestinal Pathology Society
Pathologist - in - Training Awards

Our Society has established an award of $250.00 for the best poster or platform presentation at the USCAP related to gastrointestinal Pathology by a pathologist in training. Please keep this in mind for future years and inform your residents.

The applicant submits his/her abstract to the USCAP, after acceptance, the resident should then submit his/her application for consideration to:

Marcia R. Gottfried, MD
Department of Pathology, Box 3712
Duke University Medical Center
Durham, NC 27710
(919) 684-5084

Applying for the GIPS award does not preclude application for the Stowell-Orbison Award.

The GIPS Pathologist - in - Training award for 1992 was awarded to Mohul B. Amin of Henry Ford Hospital, Detroit Michigan. His paper was "Prognostic Value of PCNA Index in Gastric Stromal Tumors: Correlation with Mitotic Count and Outcome." - The complete abstract follows:

227 PROGNOSTIC VALUE OF PCNA INDEX IN GASTRIC STROMAL TUMORS: CORRELATION WITH MITOTIC COUNT AND OUTCOME

M.B. Amin, C.K. Ma, M.D. Linden, J. Kubus, R.J. Zarbo, Henry Ford Hospital, Detroit, MI.

Histologic diagnosis of benign and malignant gastric stromal tumors (GST), of epithelioid or spindle cell type is often problematic. Morphologic studies of GST indicate that mitotic counts and tumor size are major discriminating factors. The objective of this study was to measure tumor proliferation of GST by immunostaining formalin fixed tissue sections with anti-proliferating cell nuclear antigen (PCNA, clone PC10) for correlation with mitotic counts and clinical outcome. 46 GST were obtained from a 25 year review of our files. Mitotic figures were counted per 50 high power fields (MC). MC and tumor size were used to categorize tumors into 3 groups: 1) Benign (BN) = <5MC, <5cm; 2) Borderline (BL) = <5MC, >5cm; 3) Malignant (MN)>5MC, >5cm. PCNA tumor proliferation index (TPI) was assessed by counting of 200 tumor cells per case and expressed as a % (+). Clinical follow-up was available in 38 cases, none of the 16 BN or 13 BL tumors recurred or metastasized. 6/9 MN metastasized and 1/9 recurred. Mean PCNA TPI values were significantly different (p=.0017, Krusal-Wallis) between BN (9.6), BL (16.6), and MN (30.9). There was a significant correlation (p=.0069) between mean PCNA TPI for BN and BL with MC<5 and for MN with MC>5. Spearman Rank Correlation demonstrated a significant relationship between MC and PCNA TPI (p=.0020, R=.46364). In the MN group, mean TPI for MN with metastases (37.9) was not significantly different (p=.1851) from MN without metastases (21.3). No correlation was found comparing PCNA TPI for epithelioid vs. spindle cell type GST. Based on our experience with GST, we conclude: 1) PCNA derived TPI correlates with MC indicating that this is an additional prognostic parameter in the assessment of GST; 2) in tumors with <5MC, PCNA TPI provides a quantitative parameter to potentially separate BL from BN tumors. This is not possible with MC alone as MC for BL and BN tumors may overlap; and 3) the intermediate PCNA TPI of BL lesions further justifies separation of GST into BN,BL and MN categories.

ATTENTION ALL GI PATHOLOGY SOCIETY MEMBERS!

HAVE YOU CONSIDERED A MICROGRANT RECENTLY?

NOW COULD BE THE PERFECT TIME.

The GIPS Microgrants Committee has received no new requests for some time. Have you forgotten us? Have you run out of ideas? We are ready and eager to work with you.

The range of possible projects that the Committee is prepared to support is limited only by the GIPS members' needs and imagination. We especially want to promote interaction among the members and between members and others who work in GI disease. Examples of proposals that you could submit are:

- Research projects
- Fellowships for junior persons (short or long-term)
- Support for a visiting scholar
- Support for a continuing education program in GI disease
- Help in organizing special or interim meetings involving Society members

Ground Rules and Procedures: These have been kept to a minimum, but a certain amount of bureaucracy is unavoidable. The formal policies and procedures of the Microgrants Committee are as follows:

1) Projects should fit within the broad goals of the Society to promote education and research in diseases of the gastrointestinal tract. All members are eligible.

2) Write a letter to the address shown below giving a brief (hopefully no more than a couple of pages) description of the project. It should have a defined purpose and set of goals. State briefly how these will be achieved and give an idea of your timetable.

3) While some background information such as references is usually desirable, send supporting documents only when they are essential. All collaborators should indicate, in writing, their willingness to participate.

4) The period of award will normally be for 1 year, but can be continued. The Committee is authorized to award up to $1500 per year per project. **(Now you know why they're called microgrants.)** Include an itemized budget using standard NIH budget format. Support can be requested for all types of expenses and activities, but the committee is reluctant to support purchase of equipment.

5) An annual progress report (again, brief and in the form of a letter) should be provided. You may also be asked to make a verbal report at the annual meeting of the Society.

Timetable: Deadlines for submission of application are May 15, September 15, and January 15. In addition, urgent requests will be given early consideration at the discretion of the Chairman.

Send enquiries and application to:

John H, Yardley, MD
Department of Pathology
The Johns Hopkins Hospital
Baltimore, MD 21205

(410) 955-9790

May 15, 1992
MICGT03.MEM