Gastrointestinal Pathology Society Newsletter
Volume 9, Number 2
Fall 1991

Contents

1991-1992 OFFICERS AND COMMITTEE MEMBERS

Position	Term Ends
President (1-year term):	
Frank Mitros	1992
Vice-President/President-Elect (1-year term):	
David Keren	1992
Secretary-Treasurer (3-year term):	
Robert Petras	1993
Education Committee (3-year term):	
Robert Pascal (Chairman)	1994
Alexander Brian West	1993
Klaus Lewin	1993
Ludwig Deppisch	1992
Wilfred Weinstein	1992
Shirin Nash	1994
Membership/Nomination Committee (3-year term):	
James K. Kelly (Chairman)	1993
Katherine DeSchryver	1993
Leslie Sobin	1992
Joseph Tomasulo	1992
Randall Lee	1994
Kim Geisinger	1994
Training Programs Committee (3-year term):	
Marcia Gottfried (Chairman)	1993
Ellen Kahn	1993
Yogeshwar Dayal	1992
Paul Manley	1992
Robert Wolber	1994
Linda Ferrell	1994

Publications Committee (Standing):
Henry Appelman (Chairman)
Robert Riddell
Stephen Sternberg (Ex-officio: Editor, Amer J Surg Path)
Frank Mitros (Ex-officio: President of GIPS)
Robert Pascal (Ex-officio: Chairman of Education Committee)
David Keren (Ex-officio: President-Elect of GIPS)

Microgrants Committee (Standing):
John Yardley (Chairman)
Frank Mitros (Ex-officio: President of GIPS)
Robert Petras (Ex-officio: Secretary-Treasurer of GIPS)
Marcia Gottfried (Ex-officio: Chairman of Training Programs)
Robert Pascal (Ex-officio: Chairman of Education Committee)
David Keren (Ex-officio: President-Elect of GIPS)

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

International Liaison:
Harvey Goldman

From Surgical Pathology 3:341, 1990, Field & Wood Publishers - with the publisher's permission.

Tales of the Ampulla of Vater. V

By the shores of Duodenum
where the Villi ply the chyle
Heed Ampulla's tale of Carcinoid
beside the River Bile.

There had come three Pious Patches
from the distant ileal bowel
Much concerned with submucosal growths
were they fair or foul.

Oh do tell us Great Ampulla
savants say they're Carcinoid
Does it mean we're doomed or is it
something that we can avoid?

So upon the slopes of Oddi
Pious Patches harkened well
To the teachings of Ampulla
as diurnal acid fell.

Now genetically they're endocrine
a tribe diffuse spread wide
From well north of the Pylorus
to the colon's distal side.

They're derived from the Kulchitsky clan
for silver they've attractions
Filled with amines hormones peptides
a rich source of gut reactions.

Tell us why they turn malignant
and a course aimed at aggression
Is it overstimulation
or perhaps gene derepression?

Can they ever be benign
and alike an adenoma
Or are all potential dragons
and akin to carcinoma?

They're most frequent in appendix
where behavior's largely mellow
Filled with serotonin granules
on cut surface brightly yellow.

If they compromise the lumen
the result is suppuration
It's a blessing in disguise
leads to early extirpation.

Woe the Carcinoids of Ileum
present when more advanced
Can be into mesenteric fat
their distant spread's enhanced.

Nodules those within the rectum
by palpation are detected
They are typically well localized
and easily resected.

Often having acid phosphatase
and nesting in the wall
Masquerading as prostatic
do avoid this overcall.

In the duodenum there exists
Somatostatinoma
It's a lesion quite distinctive
with small bodies of psammoma.

When anemia is pernicious
then in gastric wall are grown
Tiny carcinoid-like foci
their potential is unknown.

Gastrinoma lies in pancreas
as far as near the spleen
Causing many peptic ulcers
on the shores of Duode'en.

An appendiceal variety
has goblet cells and mucin
Can be dangerous aggressive
more metastases producing.

Note the Carcinoid's growth patterns
they're of diagnostic use
You'll find insular trabecular
gland-like and diffuse.

Almost all argyrophilic
about half argentaffin
With an enolase they're positive
dense granules by EM.

Periodically their name is changed
for instance APUDoma
Neuroendocrinic tumor
or Kulchitsky carcinoma.

Although changing names is stylish
it adds little but confusion
Stick to what is widely understood
yes that is my conclusion.

So the Pious Patches back they sailed
to Ileum's far shore
To the enigmatic Carcinoid
and what fate had in store.

L. H. Sobin

Department of Gastrointestinal Pathology
Armed Forces Institute of Pathology
Washington, DC 20306

Illustrated by

Amy Llewellyn, M.D.
Resident in Pathology
Veterans Medical Center
Albuquerque, NM.

PRESIDENTS MESSAGE

Although it seems as though it were only a year or two ago, a number of years have elapsed since March of 1979 when a relatively small group of individuals sat in a small room in San Francisco. While no one paced expectantly in the hallways, and the pain involved was minimal (nonexistent), a new child was born. The name Gastrointestinal Pathology Club seemed quite appropriate for this young child which strode forth upon the seen at the International Academy of Pathology. As is true of most children not afflicted with some dread disease (such as gluten sensitive enteropathy) we grew, thriving and contributing to the intense activity around us. As we matured, the growth process led to a number of changes. The Gastrointestinal Pathology Club gave way to the more formal sounding Gastrointestinal Pathology Society. However, the spirit of exuberance has remained. While several have noticed the changes of aging (those gray hairs staring out at me from the mirror were not there in 1979) there has been a nice blend of the veterans and the newcomers. This growth has resulted in a rather striking increase in our membership totals. The latest roster shows 145 active members; this is a far cry from the initial period when one sheet would contain the names of all the members.

As the graying of the gut continues, several things have happened. Our relationship with the American Gastroenterological Association has become increasingly stronger. We now have a distinct role in their programs during the time of Digestive Disease Week. We now play a very active role at the ASCP Meetings as well. In addition, our presence at the IAP (oops!, USCAP) has become even stronger. The meeting this spring in Chicago saw our Society put forth an excellent program on colorectal neoplasia. We must thank Dr. Sheahan for his excellent work with the Education Committee. Plans for the spring meeting in Atlanta presently call for a discussion of colitis (with an all star cast of colonophiles); this meeting is being put together under the leadership of Dr. Pascal.

Those of us who have been with the Society for a number of years remember some spirited discussions in the early days as to whether or not we should take on the liver. There were strong opinions on both sides. The natural evolution of time seems to have resolved the issue, for there has been the formation of the Hans Popper Hepato-pathology Society in recent years. Many (most?) of us who do gastrointestinal pathology also do some liver pathology. Certainly there can be nothing but good to come from participation in both Societies, although we may have to seek help from our molecular labs and clone ourselves (so that we can simultaneously attend these two meetings, as well as the Arthur Purdy Stout Society, etc!).

Although things seem to be going along quite well with our organization, there is always room for change and growth. I invite any of you out there to write to me if you have any ideas concerning areas for future growth or change within our Society. I look forward to a banner year for our Society.

Frank

Frank A. Mitros, M.D.
Department of Pathology
University of Iowa
Iowa City, Iowa 52242

EDITOR'S ADDRESS

In the Sunday Philadelphia Inquirer's Magazine section there is a section on What's Hot and What's Not. Usually this talks about movie stars, musician's, singers, politicians, clothing styles, etc. I thought that in this Editorial, I would copy this format and let people know What's Hot and What's Not in Gastrointestinal Pathology (including the journals that are Hot or Not for publication of GI articles). My approach is <u>not</u> by personal bias, but a semi-scientific study of the years 1989, 1990, and 1991 (through June). I looked at Am. J. Surg. Pathol, Human Pathol, Modern Pathol, and Am. J. Clin Pathol. which would be the major Pathology journals publishing articles on Gastrointestinal Pathology as it relates to diagnostic Anatomic Pathology. I purposely excluded journals which publish articles which are of a basic science nature. I also looked at the subject matter presented at the USCAP in 1989, 1990, and 1991. After getting the data together, I thought it would be more judicious to report on what's hot and leave out what's not (so as not to offend workers in the field). During this study, I may have missed some articles, and the subject headings that I chose are arbitrarily broad.

GI Pathology Articles (% of all published articles)

Journals	1989	1990	1991
Am. J. Surg. Pathol	12.6%	11.4%	8.0%
Human Pathology	7.0%	10%	12.8%
Modern Pathology	11.5%	16%	8.0%
Am J Clin Pathol	7.1%	7%	4.8%

(Anatomic Pathology Articles Only)

Human Pathology appears "hot" for GI pathology - going from 7.0% of articles of GI topics in 1989 to 12.8% in 1991. It would appear that since 1989 to present, the Am J Surg. Pathol., Modern Pathology, and Am. J. Clin Pathol. have "cooled off" (not so hot) for GI Pathology article.

In the above journals in the 1989-1990 period GI subjects published (and their numbers) are:

Stomach polyps - 1
Lymphocytic colitis - 2
Nervous system related - 3
UC/Crohn's - 5
Lymphoma/Lymphoid - 7
Endocrine (incl. tumors) - 8
Colorectal cancer - 8
Colon Polyps - 3
AIDS - 2
Transplant - 1
GI - Stromal - 1
Misc - 10
Lymphoctyic gastritis - 1
Barrett's - 3
Esoph. Cancer - 5
Gastric Cancer - 5
Pancreatic Neoplasm - 5
H. Pylori - 3
Colitis (NOS) - 4
Anal CA/Dyspl. - 3
Collagen Colitis - 2

I will let the membership decide for themselves what is hot!!

GI Pathology Subjects Presented at USCAP (1989-1991)*

UC/Dysplasia			Pouchitis			Diversion Colitis			H. Pylori		
89	90	91	89	90	91	89	90	91	89	90	91
0	0	3	0	0	1	0	0	1	2	0	3

Lymphoid			HIV/AIDS			Enterocolitis			Mast Cell/Eosin.		
89	90	91	89	90	91	89	90	91	89	90	91
0	0	3	2	0	3	7	3	7	2	1	2

Barrett's			Esophagitis			Gastritis			Colorectal Cancer		
89	90	91	89	90	91	89	90	91	89	90	91
1	3	1	2	3	1	3	2	4	11	7	11

Gastric Cancer			Nervous System			Pancreatic CA			Esophageal Cancer		
89	90	91	89	90	91	89	90	91	89	90	91
3	4	3	4	1	0	1	1	0	0	1	0

Transplantation			Stromal Lesions			Small Int. Cancer		
89	90	91	89	90	91	89	90	91
0	2	0	4	0	0	1	0	0

Collag/Micro Colitis		
89	90	91
0	1	1

*Excluding liver pathology. Please excuse me if some subjects or presentations have indavertently been excluded. It was not done intentionally.

It appears that through 1989-1991 colorectal cancer, enterocolitis, mast cell/eosinophil disorders, gastritis, and gastric cancer remain constant.

I hope the readers find this editorial of interest, however, I'll not editorialize and allow the membership to decide what is hot (and conversely what is not) in the area of GI pathology. I would enjoy hearing from the membership regarding what they think is Hot and what is Not.

Harry

Harry S. Cooper, M.D.
Department of Pathology
Hahnemann University Hospital
Broad & Vine Sts.
Mail Stop 435
Philadelphia, PA 19102

COLONIC PSEUDOSARCOMATOUS MYOFIBROBLASTIC PROLIFERATION. A Anand et al. Southwestern Medical Center at Dallas, and University of Miami.

This group presented three cases of what they called myofibroblastic proliferations of the large intestine. Clinically they manifested as a mass, obstruction, or an incidental discovery. Grossly the lesions measured 4-8 cms. and had the appearance of a malignant tumor showing infiltration of the intestinal muscle wall and surrounding fat. Histologically there were dense cellular spindle cell proliferations in a storiform pattern and fascicles. These cells were infiltrated by lymphocytes and plasma cells, and myxoid areas with ganglion-like cells similar to that of proliferative fasciitis were noted. Mitoses were sparse and there was no cellular atypia. Immunohistochemical studies and electron microscopy indicated that these spindle cells were of myofibroblastic origin. One may erroneously diagnose these lesions as sarcoma. The authors comment that these lesions are probably reactive and not a true neoplasm and that complete excision appears to be adequate therapy, however, we are not given the length of follow-up as to know the biology of these lesions.

SUCRASE-ISOMALTASE EXPRESSION IN CHRONIC ULCERATIVE COLITIS AND DYSPLASIA. C. Andrews et al. New England Deaconess Hospital, Boston, MA.

The authors used a polyclonal antibody to Sucrase-Isomaltase to investigate its presence and utility in detecting dysplastic changes in chronic ulcerative colitis. The authors studied 76 sections of 33 cases describing immunostaining and whether it was membrane and/or cytoplasmic, superficial, or in the deep crypt epithelium, and the percentage positivity. Surface membrane staining was noted in all 28 dysplastic cases, however, 29 of 48 cases without dysplasia showed similar staining patterns. In contrast, cytoplasmic positivity was present in 25 of 28 dysplastic cases, and only 2 of the 48 cases without dysplasia ($p<0.001$). The presence of cytoplasmic staining of

Sucrase-Isomaltase in the superficial cells revealed a sensitivity of 89%, specificity of 96%, negative predictive value of 94%, and a positive predictive value of 93%. It appears that cytoplasmic staining correlates strongly with the presence of dysplastic changes and may help in its detection.

CLINICOPATHOLOGIC EVALUATION OF POUCHITIS FOLLOWING ILEAL POUCH-ANAL ANASTOMOSIS (IPAA). M.J. Becich and collaborators from Washington University School of Medicine, St. Louis, MO and Harvard Medical School, MO and Boston, MA.

The authors prospectively examined the ileal-anal pouches of 20 patients with chronic ulcerative colitis. They described those pouches in which there is adaptation to the new environment and those pouches in which there is none. In those pouches in which there is relatively normal villous architecture and minimal inflammation, there was a positive adaptation. On the other hand, in those cases in which there was inflammation with erosions and an increased acute inflammation and loss of villi, there was poor adaptation. The authors comment that the severity of changes in the original resection specimens correlated with subsequent pouchitis. Intraepithelial neutrophils and lymphocytes were the best early histologic predictors of the development of pouchitis.

HELICOBACTER PYLORI AFFECTS THE QUALITY OF EXPERIMENTAL GASTRIC ULCER HEALING: A QUALITATIVE AND QUANTITATIVE HISTOLOGIC ANALYSIS IN A NEW ANIMAL MODEL. H.X. Bui, et al. Albany Medical College and VA Medical Center, Albany, NY.

The authors created experimental gastric ulcers in Sprague-Dawley rats by the focal serosal application of acetic acid. One group was fed normal saline as a control, while an experimental group was given an oral 2 ml suspension of H. pylori twice a day for seven days. After this period ulcer size was measured grossly and examined microscopically. Ninety percent of the control group showed gross and microscopic healing. One hundred precent of the experimental group given H. pylori showed the persistence of chronic active ulcers. Histologically the ulcer bed showed

acute and chronic inflammation with fibroblasts and capillaries. The authors concluded that H. pylori delayed healing in experimental gastric ulcers. This model may be extremely useful for studying the role of H. pylori in the healing of experimental peptic ulcers.

p53 GENE DELETIONS AND GENE PRODUCT EXPRESSION IN COLON CARCINOMAS. A. Cardesa et al. Hospital Clinico Provincial, Barcelona, Spain.

The authors studied the expression of mutant p53 oncogene in colonic carcinoma and adenomas using monoclonal antibody PAB 1801. They also used restriction fragment length polymorphism to study allelic deletions. By means of RFLP, 12 of 64 carcinomas showed heterozygosity for the p53 gene, and 10 of these (83%) had deletion of one allele in the tumor sample when compared to the normal mucosa. Expression of mutant p53 was found in 67% of the carcinomas and in 11% of adenomas. The authors found no correlation between expression of p53 staining and the degree of tumor differentiation, stage of the tumor, or Ki-67 proliferative index. However, the authors noted that mucinous and right-sided colon cancers tended to be less positive for p53 than nonmucinous adenocarcinomas and distal carcinomas.

COLONIC MUCOSAL INJURY AND INFLAMMATION ASSOCIATED WITH HUMAN IMMUNODEFICIENCY VIRUS TYPE-1 (HIV) INFECTION. F. Clayton, et al. St. Luke's Hospital, New York, NY.

The authors examined 75 rectal biopsies from 54 HIV-infected patients with and without opportunistic infections. The finding of HIV P24 correlated with lamina propria lymphocyte densities, however, lymphocyte densities correlated inversely with the diagnosis of AIDS and with the presence of opportunistic infections. A spectrum of histologic findings was seen in the presence or absence of opportunistic infections. The most common findings were focal epithelial degeneration (apoptosis) in 62%, subepithelial histiocytic aggregates in 85%, and lymphocytic depletion in 89%. The authors conclude that HIV expression in the gut is related to disease stage and independent of opportunistic infections, and there are characteristic histopathologic

features in rectal mucosa of HIV-infected patients that may be related directly to the HIV expression.

MONOCLONALITY IN GASTRIC LYMPHOMA - IN-SITU HYBRIDIZATION FOR IMMUNOGLOBULIN LIGHT CHAIN mRNA COMPARED TO IMMUNOHISTOCHEMICAL DETECTION OF LIGHT CHAIN. P. Close et al. University of Cape Town, South Africa.

The authors performed both in situ hybridization and immunohistochemistry for light chains in formalin-fixed paraffin-embedded tissues from 16 cases of B cell gastric lymphoma. In situ hybridization was used to detect mRNA sequences using a pretreated technique to unmask the mRNA. A four stage streptavidin-biotinylated alkaline phosphatase method was used with biotinylated DNA nucleotides as probes. In situ hybridization was able to detect monoclonality in 50% of the cases. Immunohistochemical technique was able to detect immunoglobulin light chain monoclonality in 68.8% of the cases. Combining both techniques the rate of detection of light chain monoclonality was 81.3%. The authors concluded that the light chain mRNA in situ hybridization is a useful adjunct to the detection of monoclonality in gastric lymphomas.

p53 PROTEIN EXPRESSION IN THE TRANSITIONAL MUCOSA AND ADENOCARCINOMAS OF THE COLORECTUM. J. Connolly et al. M.D. Anderson Cancer, Houston, TX, and University of South Dakota.

The authors studied expression of p53 oncogene protein in frozen tissue from both the transitional mucosa adjacent to colorectal carcinomas and the actual colorectal carcinomas themselves. In all cases the transitional mucosa and normal mucosa failed to express p53 activity, while 9 of 17 adenocarcinomas showed positivity. The immunoreactivity was nuclear in location. The authors conclude that the absence of staining for p53 protein in transitional mucosa does not support the theory that transitional mucosa is a preneoplastic change.

LAMININ IN GASTRIC CARCINOMA. P. Crotty and C. Limas. University of Minnesota, Minneapolis, MN.

The authors examined the expression and distribution of laminin in gastric carcinomas of varying degrees of differentiation. The authors found an association between the ability of tumor cells to form glands and the deposition of linear extracellular laminin. Tumor cells that grew in cohesive groups showed intracytoplasmic laminin, while signet ring cells were consistently negative both intracellularly and extracellularly. This pattern of expression showed no correlation with other markers for differentiation. The authors conclude that laminin deposition is an expression of cellular differentiation relevant to the ability for cohesive group and arrangement of tumor cells into defined structures.

MAST CELL - EOSINOPHIL ENTEROCOLITIS. K. DeSchryver-Kecskemeti and R.E. Clouse, Departments of Pathology, CWRU, Cleveland, OH, Washington University, St. Louis, MO.

The authors blindly examined biopsies from patients with irritable bowel syndrome, follow-up for polypectomy, lymphocytic colitis, collagenous colitis, and mast cell-eosinophilic enterocolitis. The authors compared the intensity of mast cells and eosinophils in these entities and the location of the infiltrate within the mucosa. There was a significant difference in the total inflammatory scores between irritable bowel syndrome and follow-up polypectomy versus lymphocytic collagenous and mast cell eosinophilic enterocolitis. However, the infiltrate in mast cell enterocolitis was distinctive in that the inflammatory infiltrate was predominately in the deep portion of the mucosa in the space between the crypts and the muscularis mucosa. In contradistinction, the inflammatory infiltrates in lymphocytic colitis and collagenous colitis tend to involve the superficial mucosa.

LECTIN HISTOCHEMISTRY IN BARRETT'S ESOPHAGUS (BE). M. Doria et al. Hines VA Medical Center and Loyola University Medical Center.

The authors studied lectin binding in Barrett's epithelium, dysplastic epithelium, and in adenocarcinoma. There was increased staining of the epithelium by the lectin ConA in Barrett's esophagus with adenocarcinoma and dysplasia in comparison to regular metaplastic epithelium. There were decreased scores for lectin binding for UEA, SBA, and PNA in adenocarcinoma compared to metaplastic epithelium. The authors conclude that lectins, especially ConA, illustrate the altered glycoconjugate expression seen with aberrant glandular differentiaton of Barrett's epithelium. It should be noted, however, that the authors failed to compare the binding of lectins in the normal stomach and duodenum with that seen in Barrett's esophagus.

LACK OF CORRELATION BETWEEN $rasp^{21}$ AND THE METASTATIC POTENTIAL OF HUMAN GASTRIC CARCINOMA. K. Fan. John L. McClellan Memorial VA Hospital, Little Rock, AR.

In this study the author used quantitative radio immunopercipitation and qualitative immunohistochemistry to study the expression of p^{21} protein in gastric carcinomas. The author found that well differentiated intestinal-type adenocarcinomas expressed the highest level of p^{21}, whereas poorly differentiated carcinomas of the signet ring type expressed the lowest levels of p^{21}. The author also note that p^{21} was expressed in the normal mucosa, however, carcinomas expressed a higher level of p^{21}. The author found no correlation between the expression of levels of p^{21} and the incidence of lymph node metastasis.

LASER-INDUCED FLUORESCENCE MICROSCOPY IN MUCOSAL ULCERATIVE COLITIS: IMPLICATIONS FOR SPECTROSCOPIC DIAGNOSIS. M. Fitzmaurice et al. Henry Ford Hospital, Detroit, MI and Cleveland Clinic Foundation, Cleveland, OH.

The authors examined unstained frozen sections from colons with ulcerative colitis for the presence of laser-induced fluorescence using 370 nm Argon laser excitation light. Neither normal colonic epithelial cells or epithelial cells in

repair fluoresced significantly. This is in contrast to the authors' previous studies which showed that neoplastic epithelium has a significant laser-induced fluorescence. While their study failed to include cases of dysplasia, the authors concluded that the intensity of laser-induced fluorescence in the colon and mucosal ulcerative colitis without dysplasia is low, even in the presence of epithelial repair. They suggested that laser-induced fluorescence spectroscopy may be useful in detecting dysplasia during colonoscopic surveillance with patients with mucosal ulcerative colitis.

DNA ANALYSIS OF VILLOUS ADENOMAS AND ADENOCARCINOMAS OF THE APPENDIX. J.A. Gates et al. Yale University, New Haven, CT and The West Haven VA Medical Center, West Haven, CT.

The authors performed flow cytometric analysis on 9 cases of appendiceal villous adenomas, five of which were associated with invasive adenocarcinomas. All the villous adenomas and carcinomas of the appendix were diploid with low S-phase fractions except for one patient with an S-phase fraction of 23% who clinically had pseudomyxoma peritonei and subsequently died 4 years posoperatively. The authors conclude that all villous adenomas and carcinomas of the appendix were diploid, and only one had a high S-phase fraction.

THE NEW SIDNEY SYSTEM CLASSIFICATION OF GASTRITIS: APPLICABILITY TO GASTRIC BIOPSIES. R.M. Genta and L.K. Green, VAMC, Baylor College of Medicine, Houston, TX.

The Sidney working system on gastritis was derived by one microbiologist and two pathologists to devise a new classification of gastritis. Essentially this system looks at an etiology, a topography, and a morphology. An example of a diagnosis would be H. pylori associated chronic antral gastritis with moderate activity, no atrophy, and no intestinal metaplasai. It is important for this system to have two biopsies from the antrum and two biopsies from the fundus. The etiological division is H. pylori, autoimmune, drug, idiopathic. Topograph is antrum, corpus, pan gastritis. Morphology is normal, acute, and chronic inflammation, intestinal metaplasia, etc.

This system also requires close interaction with the endoscopist and pathologist.

GASTROINTESTINAL (GI) LESIONS IN LEWIS RATS AFTER EXPOSURE TO IMPLICATED L-TRYPTOPHAN (L-TRP). T. Gramlich, L.J. Crawford, J.I. Rader, E.M. Sternberg, K. DeSchryver-Kecskemeti, Institute of Pathology, CWRU, Cleveland, OH and NIMH, Bethesda, MD, FDA, Washington, DC.

The authors examined rats given L-Tryptophan and compared the light and electron microscopic findings on colonic and small intestinal mucosal blood vessels and lamina propria inflammatory infiltrate compared to controls. There was a statistically signifcant increase in the number of eosinophils, mast cells and monocytes with evidence for activation and degranulation. The L-Tryptophan eosinophilic myalagia syndrome has many features of idiopathic scleroderma/eosinophilic fasciitis, including similar changes in the gastrointestinal tract. The authors feel that this Lewis rat model with exposure to L-Tryptophan may be a suitable model to further study the pathogenesis of gastrointestinal involvement in idiopathic connective tissue diseases.

MORPHOLOGIC COMPARISON OF PRE - AND POST-TREATMENT BIOPSIES OF INFLAMMATORY BOWEL DISEASE (IBD) IN AN EICOSAPENTANOIC ACIDE (EPA) MULTICENTER THERAPEUTIC TRIAL: IMPLEMENTATION OF A SCORING SYSTEM EVALUATING DISEASE ACTIVITY INDEX (DAI). T.L. Gramlich, W.F. Stenson, K. DeSchryver-Kecskemeti. Departments of Pathology, CWRU, Cleveland, OH, and Medicine, Washington University School of Medicine, St. Louis, MO.

The authors examined pre and post treatment biopsies in 72 patients with inflammatory bowel disease. The patients were treated with a diet supplemented by eicosapentanoic acid and placebo. The biopsies were semi-quantitatively evaluated by scoring acute and chronic inflammatory changes (0-3), including erosion, architectural distortion, mucin depletion, crypt destruction, endothelial cell changes, presence and kinds of inflammatory cells and degree of fibrosis. A 7:1 improvement was seen in the overall disease activity index in eicosapentanoic treated patients compared to placebo. Epithelial changes accompanying inflammation as reflected by epithelial

polarity, mucin content of surface and crypt epithelial cells and inflammatory cells, cryptitis exhibited the greatest degree of improvement. Systemic evaluation of disease activity index may be important in inflammatory bowel treatment protocols. The authors suggest that routine surgical pathology reports in these patients should also include the disease activity index which is easily reproducible and convenient to use.

DECAY-ACCELERATING FACTOR (DAF) EXPRESSION ON HUMAN SMALL (SI) AND LARGE INTESTINAL (LI) EPITHELIAL CELLS. T.L. Gramlich et al. Department of Pathology, CWRU, Cleveland, OH.

The authors immunohistochemically examined the expression of DAF an important down regulating protein of complement acitivation in 31 histologically unremarkable paraffin-embedded sections of large intestine and small intestine. There was an increasing crypt to surface gradient in cytoplasmic immunoactivity and variability in intensity and distribution of staining between mucosal areas, as were differences among patients consistent with possible physiological regulation and expression of this protein. There was a concordance between the Golgi-type staining and blood group A and AB compared to blood groups O and B. Concordance of blood group antigens is similar to that reported for other immunologically important proteins since DAF activities are essential physiologically in protecting cells from autologus complement attack, identification of DAF in small and large intestine suggested this mechanism of control. Complement activation is also important in these locations.

MORPHOLOGY OF DIVERSION COLITIS IN PATIENTS FREE OF OTHER MUCOSAL INTESTINAL DISEASE. S. Haque et al. Yale University Department of Pathology, New Haven, CT.

The authors attempt to to define the histopathological features in diversion colitis using patients without previous underlying IBD. Thirty-two consecutive patients with Hirschsprung's disease who had undergone defunctioning colostomy, subsequent distal bowel resection, and reanastomosis were studied. These patients had

no other causefor colitis. Two of the patients had symptomatic coloproctitis. Twenty-one patients had histological evidence of diversion colitis, the most striking feature was diffuse nodular lymphoid hyperplasia with reactive germinal centers. There was increased cellularity in the lamina propia most severe in the upper third consisting mainly of plasma cells and lymphocytes, with few neutrophils and eosinophils. Also noted was mucin depletion reactive changes in the crypt epithelium, cryptitis, and surface exudate. The more severe florid cases also had apthous ulcers, crypt abscess, and slight architectural distortion. Marked distortion of architecture and fibrosis were absent. The authors conclude that diversion colitis develops in a significant portion of infants with colonic diversion in the absence of other inflammatory mucosal disease.

PROGNOSTIC INDICATORS IN RECTAL CANCER: RESULTS OF MULTIVARIATE ANALYSIS. J. Harrison, P. Dean, R. Vander Zwaag and F. El-Zeky, Univ. Tennessee - Baptist Memorial Hospital, Memphis, TN.

The authors studied 348 resected rectal cancers by using the pathological staging system of Jass et al. (peritumoral lymphocytic infiltration, tumor growth pattern, depth of tumor invasion, and number of lymph node metastasis) Using univariate analysis significant variables affecting five year survivals were: 1. depth of tumor invasion, 2. lymph node metastasis, 3. extramural venous invasion, 4. tumor grade, 5. tumor growth pattern, 6. peritumoral lymphocytic infiltration, 7. tubular configuration, 8. nuclear polarity, and 9. tumor type. A Cox stepwise proportional hazard analysis revealed that only the depth of tumor invasion, lymph node metastasis, extramural venous invasion, and tumor grade proved to be of significance. The authors failed to confirm that host lymphocytic response and tumor growth pattern were significant variables in this system. It appears that other well done studies like this are necessary in order to further assess the Jass system and to evaluate its reproducability and clinical significance.

APPLICATION OF COMPUTERIZED MORPHOMETRY TO DETECTION OF LOW-GRADE DYSPLASIA IN CHRONIC ULCERATIVE COLITIS. P. Hytiroglou et al. The Mount Sinai Medical Center, New York, NY.

The authors investigated whether computerized morphometric evaluation of nuclear features were of help in detecting mild forms of dysplasia. The authors looked at nuclear size and shape (area, perimeter, maximum and minimum chords, circularity). They also looked at descriptors pertaining to argyrophilic nucleolar organizer regions (number, area, perimeter). By multivariate analysis the authors found that the value of the mean nuclear area was the most important discriminating feature being 20-40% higher in dysplastic than in non-dysplastic mucosa. The argyrophilic nuclear organizing region number was also important, being higher in dysplasia. The authors

feel that computerized morphometry may be useful in detecting subtle forms of colorectal dysplasia.

THE APPENDIX IN INFLAMMATORY BOWEL DISEASE (IBD) IN CHILDREN. E. Kahn et al. North Shore University Hospital, Manhasset, New York.

The authors histologically examined the appendices from 41 children with IBD (24 with Crohn's disease and 17 with ulcerative colitis) who required colonic resection. All the appendices were abnormal. Granuloma formation and mesoappendiceal involvment were only noted in Crohn's disease patients. The authors noted that specific changes of Crohn's disease or ulcerative colitis in 50% and 58% of the appendices respectively. Parameters such as the characteristic of the mucosal infiltrate (diffuse vs. patchy) and mononuclear infiltrates of the muscularis propria did not discriminate between ulcerative colitis and Crohn's disease.

HISTOPATHOLOGICAL STUDY OF RIGHT VS. LEFT SIDED COLONIC ADENOCARCINOMA. E.B. Kintanar, M.W. Lee, C.K. Ma, Henry Ford Hospital, Detroit, MI.

The authors histologically examined Duke's Stage B and Stage C carcinomas from the right side and the left side of the colon and compared findings between each site. They assessed the following features: Microglandular cribiform pattern, neuroendocrine differentiation, mucin production, squamous differentiation, Paneth cell metaplasia, and cytoplasmic acidophilia resembling apocrine cells. The authors noted that a microglandular cribiform pattern was observed more frequently in right-sided cancers (42%) compared with left-sided cancers (35%). Neuroendocrine-like features and Paneth cell metaplasia were non-discriminant from right and left sided tumors. The authors conclude that some of the morphological changes may be attributable to the different embryological origins of the mid and hind gut.

Ki-67 IMMUNOSTAINING AND SURVIVAL IN COLORECTAL CARCINOMA. Y. Kubota et al. Cleveland Clinic Foundation, Cleveland, OH.

The authors, using a cell image analyzer, analyzed the proliferative activity in 100 cases of colorectal carcinoma with a minimum three year follow up using Ki-67 immunostaining. The authors calculated a Ki-67 score (% positive X 100). The Ki-67 scores were higher in Dukes' A cases vs. Dukes' B, C, and D, but did not correlate with survival. The Dukes' stage, lymph node metastasis, infiltrative growth pattern, lymphocytic infiltration, fibrosis, extramural venous spread, and tumor grade were significantly associated with survival in a univariate model. In a multivariate analysis, only the Dukes' stage, infiltrative growth pattern and lymphocytic infiltration were features which were independently significant regarding survival. The authors concluded that proliferative activity in colorectal carcinoma as measured by Ki-67 immunostaining is not a prognostic indicator.

IMMUNOCHEMICAL ANALYSIS OF p53 EXPRESSION IN COLON CANCER. M.B. Lindstrom and C.M. Fenoglio-Preiser, V.A.M.C. and Department of Pathology, U. of New Mexico, SOM, Albuquerque, NM and Department of Pathology, U. Cincinnati Medical Center, Cincinnati OH.

The authors used the monoclonal antibody vs. p53 antigen (PAb-421) to study 22 human colon cancers and non-neoplastic adjacent tissue. Sixty percent of the cancers expressed positivity for p53 and no staining was noted in the normal mucosa. When the authors divided the groups into those tumors which had greater than 70% positive nuclei and those which had less than 20% positive nuclei, they failed to find any correlation between grade and stage. Three year follow-up information revealed no correlation between prognosis and expression of p53.

NONSPECIFICITY OF "COLON SPECIFIC ANTIGEN" IN ADENOCARCINOMAS: AN IMMUNOHISTOCHEMICAL STUDY OF 401 CASES. T. Loy et al. University of Missouri School of Medicine, Columbia, MO.

The authors studied 401 cases of adenocarcinomas from various primary sites immunohistochemically using the commercially-available antibody to Colonic Specific Antigen. Formalin-fixed, paraffin-embedded tissue was used. The authors found that this antibody was not specific for colonic adenocarcinomas. Ninety-two to 100% of ovarian, endocervical, endometrial, gastric, and pancreatic cancers stained for this antigen. However, this antigen failed to stain kidney and hepatocellular carcinomas. While this tumor is not specific for colon, its negativity may be helpful in the differential diagnosis of renal cell and hepatocellular carcinoma.

NATURE AND SIGNIFICANCE OF CELLS WITH IRREGULAR NUCLEAR CONTOURS (CINC) IN ESOPHAGEAL MUCOSAL BIOPSIES. M. Mangano et al. Beth Israel Hospital and Harvard Medical School, Boston, MA.

The authors investigated esophageal mucosal biopsies for the presence of CINC. They studied biopsies of normal mucosa, reflux esophagitis, infectious processes, Barrett's esophagus, adenocarcinoma, and squamous cancer. The sections were stained for S-100 protein, leukocyte common antigen, L-26 (B-cell marker), and T cell markers (UCHL-1 and Leu 22). The CINC had the immunohistochemical profile of T lymphocytes (LCA positive, Leu-22 positive, UCHL-1 positive, L-26 negative, and S-100 protein negative. The average number of CINC was higher in normal, infectious, and Barrett's esophagus compared to areas adjacent to tumors. Of eleven patients with normal biopsies, five had endoscopic evidence of esophagitis and the average number of CINC was 6.4 compared to 3.5 in 6 patients with normal endoscopy ($p=0.015$). CINC are T lymphocytes present in a variety of esophageal diseases. Preliminary correlation with endoscopic findings suggests that they may be another, possibly independent, indicator of esophagitis.

HER-2/NEU ONCOGENE PROTEIN AND PROGNOSIS IN GASTRIC ADENOCARCINOMA. S. Masood, E.A. Barker, R.E. Barnes. University of Florida Health Science Center, Jackonsville, and Molecular Oncology, Inc., Gaithersburg, MD.

The Her-2/neu oncogene is a transmembrane glycoprotein which as tyrosine-kinase activity. It is similar to but distinct from epidermal growth factor receptor. As the Her-2/neu oncogene expression has been shown to be associated with prognosis in breast cancer, the authors studied 57 gastric adenocarcinomas for the expression of Her-2/neu oncoproteins by means of immunohistochemical staining (Triton Biosciences, Alameda, CA) on formalin-fixed tissue. Her-2/neu oncogene protein whas seen with strong membrane staining in 23% of the cases, cytoplasmic staining in 46% of the cases, and 42% of normal gastric mucosa. There was no association between the expression of Her-2/neu oncoprotein in other parameters such as age, size, site, type of tumor, differentiation, nodal status, and survival. The authors feel that the Her-2/neu oncoprotein may be not be a significant predictor of prognosis in patients with gastric adenocarcinoma.

FLOW CYTOMETRIC AND IMMUNOHISTOCHEMICAL EVALUATION OF c-erb-B-2 ONCOGENE EXPRESSION IN FAMILIAL POLYPOSIS COLI: A POSSIBLE ROLE IN NEOPLASTIC PROGRESSION. S.J. Melnick et al. Mount Sinai Medical Center, Miami Beach, FL.

The authors studied a single case of familial polyposis associated with carcinoma. Quantification of c-erbB-2 expression was performed by flow cytometry on selected polyps and the cancer. Immunoperoxidase methods were used to assess the distribution and abundance of the oncogene product. The antibody used in this study was a murine monoclonal antibody against a 185 kD membrane glycoprotein (Triton Bioscience). The authors noted that the c-erb-B-2 expression was elevated in polyps but diminished in the cancer. Heterogeneity of the immunoperoxidase staining was observed with decreased c-erbB-2 expression in the more atypical cells. The authors feel that this provides evidence for a role of c-erbB-2 expression in the early stages

of colonic carcinogenesis.

SMALL INTESTINAL STROMAL TUMORS (SIST) WITH SKEINOID FIBERS. REPORT OF EIGHT CASES. Kyung-Whan Min, M.D. University of Oklahoma, College of Medicine.

The author reported eight cases of SIST with eosinophilic stromal globs composed of tangles of curved fibers with crossbands simulating an appearance of skeins and are designated as skeinoid fibers. Light microscopic and immunohistochemical studies were typical for SIST, except the skeinoid fibers. They were strongly PAS positive and stained blue on Trichrome stain. In previously reported tumors, these skeinoid fibers were found only in acoustic neuromas, neurofibroma, and plexosarcoma of the mesentery, which suggest that skeinoid fibers arepossibly an ultrastructural marker for neurogenic tumors and SIST with skeinoid are neurogenic in origin.

C-JUN AND C-FOS FRACTIONAL ANALYSIS COLONIC CARCINOMA EMPLOYS A G_0-G_1 TRANSITION PHASE IN VIVO. H. Momose, K.L. Chang, J.Jones, S. Lee, M.J. Dyaico, J.C. Braman, J.A. Sorge, and W.S. Nichols: From Molecular Pathology Section, Cedars-Sinai Medical Center, Los Angeles, Stratagene, La Jolla, Ca.

C-jun and C-fos expression characterize the G_0 and G_1 transition phase, while c-myc and B-actin are identified during later phases of the cell cycle. In this study, the authors examined colon cancers and adjacent mucosa. RNA blots were performed to determine the ratios of jun/myc, jun/B-actin, fos/myc, and fos/B-actin gene expression. Normal values of these fractions would be expected in a cell cycle employing normal G_0-G_1 transitional events, and a decrease in jun and fos fractions would occur in G_0-G_1 bypass. The results show that for colon carcinoma, jun and fos expression fractions are statistically equivalent to those of corresponding normal mucosa. The authors conclude that proliferating colonic carcinoma cells typically employ the G_0-G_1 trabsition phase, and do not appear to bypass early cell regulatory events.

CARRAGEENAN-INDUCED INTESTINAL INJURY: A SCANNING AND TRANSMISSION ELECTRON MICROSCOPIC STUDY. T. Moyana and T. Lalonde. Univ. of Saskatchewan, Canada.

The authors used transmission and scanning electron microscopy to study the early changes in carrageenan-induced intestinal inflammation. The authors studied three groups of rats. Group A was parenterally sensitized to carrageenan followed by oral administration of a 1.5% solution of carrageenan. Group B was sensitized parenterally to carrageenan and giving only water by mouth, and Group C was the control. Scanning EM from Group A showed changes ranging from minute defects involving individual villi to button-like ulcers. Transmission EM confirmed that focal ulcers were associated with fibrinous exudate. Also noted were subtle epithelial changes such as mitochondrial swelling, dilatation of the rough endoplasmic reticulum, increased numbers of cytolysosomes, and myelin figures. The changes seen in Groups B and C were minor. While the authors do not delineate the pathogenesis of gut injury in the carrageenan model, the findings suggest that one of the early events in epithelial cells is damage to organelle cytomembranes.

CARRAGEENAN-INDUCED INTESTINAL INJURY: A COMPARATIVE STUDY OF THE EFFICACY OF CORTICOSTEROIDS AND OXYRADICAL SCAVENGERS. T. Moyana et al. University of Saskatchewan, Saskatoon, Saskatchewan.

The authors studied the effect of corticosteroids and oxyradical scavengers in inhibiting carrageenan-induced intestinal injury. The authors studies four groups of Sprague-Dawley rats. Groups A, B, and C were parenterally sensitized and given oral carrageenan for thirty days. Group A received no drugs, whereas group B was given superoxide dismutase, and Group C received steroids. Group D was a control. In Group A small pinpoint ulcers were noted. Superoxide dismutase did not completely abrogate these abnormalities, but significantly lessened them. With steroids mucosal ulcers were still present and were larger, and, there was hardly any inflammatory repair reaction. The authors conclude that superoxide dismutase are efficacious in

experimental IBD, and that their effect differs from that of steroids. Oxyradical scavengers may be useful in the future and therapy of IBD.

THE RELATIONSHIP OF MOLECULAR GENETIC ALTERATIONS AND ABNORMAL TOTAL DNA CONTENT IN COLORECTAL CARCINOMA. G.J.A. Offerhaus et al. The Johns Hopkins Medical Institutions, Baltimore, MD.

Alterations including ras gene mutations, allelic deletions on chromosome 17p, 18q, and 5q, and proportion of nonacrocentric chromosomal arms with allelic deletions termed fractional allelic loss (FAL) have been described in colorectal cancer. The authors looked at the total DNA content of colorectal cancers by flow cytometry and compared them to genetic chromosomal abnormalities. Aneuploid tumors had significantly more frequent loss on chromosome 17p and 18q than the diploid tumors. The mean FAL and aneuploid tumors was significantly greater than the diploid tumors. The DNA index was statistically significantly correlated with FAL. Ras gene mutations were not associated with altered DNA content. There was also a trend toward less frequent loss of 17p and/or 18q and lower FAL and lower DNA index on right sided than left sided tumors, but the differences were not statistically significant. The results suggest that abnormal DNA content in colorectal cancers usually reflects specific allelic deletion and general molecular genetic alterations. The differences between tumors on the right and left side favor a different pathobiology at these sites.

A NEW SPECIES OF MICROSPORIDIA CAUSING DIARRHEA IN AN AIDS PATIENT. J.M. Orenstein, M.D., M. Tenner, B.A., A. Cali, Ph.D., and D.P. Kotler, M.D., George Washington University Medical Center, Washington, D.C., Rutgers University, Newark, NJ, St. Luke's-Roosevelt Hospital Center, N.Y., NY.

The microsporidia enterocytozoon bienusi (EB) has been associated with many cases of diarrhea in AIDS patients. In this study, the authors used light microscopy and transmission electron microscopy to study small and large intestinal tissues from an

AIDS patients with chronic diarrhea. The authors found that on the basis of finding spores with characteristic injection apparatus, this organism was different than that of EB. In this case histiocytes were also infected along with enterocytes. This microsporidia resembles that of the genus Encephalitozoon. The authors note that the organisms were visible by light microscopy in semi-thin plastic sections and retrospective in gram-stained paraffin sections. The authors conclude there is now evidence for at least two species of microsporidia associated with diarrhea in AIDS patients.

THE SPECTRUM OF COLONIC HISTOPATHOLOGY IN ALLOGENEIC BONE MARROW TRANSPLANT PATIENTS. S. Robey-Cafferty, J. Connelly, J. Bruner. University of South Dakota School of Medicine, Vermillion, SD and UT M.D. Anderson Cancer Center, Houston, TX.

The authors reviewed all colonic biopsies obtained from allogeneic bone marrow transplant patients (ABMT) from the M.D. Anderson Cancer Center between 1976 and 1989. Biopsies were performed on patients who had diarrhea, and were performed between 12-172 days post ABMT (mean 56.4 days). Seven of the biopsies showed a pattern which was reminiscent of chronic ulcerative colitis. These biopsies were taken 18-153 days post ABMT (mean 64.3). Severity of chronicity did not correlate with the severity of GVH. In four patients four biopsies taken 35-135 days post ABMT (mean 79.2), the authors found acute GVH changes plus evidence of chronicity. Twenty-one of the biopsies obtained 17-172 days post ABMT (mean 52.1) showed only changes of acute GVH. Six biopsies were normal or showed infectious colitis. Immunoperoxidase stains for CMV were negative in all patients. The authors conclude that the most frequent colonic lesion in ABMT patients is acute GVH, however, features of chronic colitis are common in these patients, and should not be interpreted as evidence of idiopathic inflammatory bowel disease.

Ki-1 (CD30)-POSITIVE ANAPLASTIC LARGE CELL LYMPHOMA (ALCL) MIMICKING GASTROINTESTINAL CARCINOMA. C. Ross et al. University of Michigan, Ann Arbor, MI.

The authors report two cases in which clinical and morphological features mimicked gastrointestinal carcinoma. One case was a sigmoid colon lesion, the other a gastro-esophageal lesion. The sigmoid colon lesion was negative for CD45 in formalin-fixed tissue, but positive in B5 post-fixed material. This tumor was negative for cytokeratin, CD15, muramidase, LN1, L26, CD45RO, S-100, HMB45, PAS, and Alcian blue. The gastro-esophageal lesion was CD45 positive. The tumor cells expressed CD30, CD4, CD43, CD45RO, CD45, and EMA. The authors conclude that clinical, morphological, and some immunological features of ALCL may mimick gastrointestinal carcinoma.

HELICOBACTER-PYLORI - IT'S ROLE IN THE PATHOGENESIS OF PEPTIC ULCER DISEASE IN A NEW ANIMAL MODEL. J.S. Ross et al. Albany Medical College and VA Medical Center, Albany New York.

The authors studied the effects of daily intra-gastric administration of H. pylori in 65 Sprague-Dawley rats with intact gastric mucosa and rats with experimental-induced gastric ulcers. In Group 1, rats with ulcers received H. pylori suspension, in Group 2, rats with ulcers received normal saline, and in Group 3 sham operated rats received H. pylori suspension. The authors grossly measured ucler size and histological findings. The presence of H. pylori in the stomach of rats with pre-existing gastric ulcers resulted in delayed healing of the ucler and persistent chronic active inflammation. Daily administration of H. pylori in rats with intact gastric mucosa resulted in no significant histological changes. The authors concluded that H. pylori causes little or no effect on intact gastric mucosa, and the presence of predisposing factors (pre-existing gastric ulcer) is required for H. pylori enhancement of inflammation and tissue damage.

ASSESEMENT OF PROLIFERATIVE ACTIVITY (PA) IN COLORECTAL CARCINOMA BY Ki-67 IMMUNOSTAINING: COMPARISON WITH CLINICOPATHOLOGIC FEATURES AND RESULTS OF FLOW CYTOMETRY (FCM). A. Sahin et al. M.D. Anderson Cancer Center, Houston, TX.

The authors studied the PA in fresh tissues from 74 surgically resected colorectal cancers by FCM and immunostaining using the Ki-67 monoclonal antibody. They also studied colonic mucosal samples adjacent to and at least 5 centimeters away from the tumor. The colorectal cancers were Stage I (2), Stage II (38), Stage III (27), and Stage IV (7). The mean range of Ki-67 and S-Phase values was 17.1% (0-60%) and 17.5% (0-39%), respectively. The authors found that the mean Ki-67 percentage positivity in tumor samples from women was significantly lower than that of men. There was poor correlation between immunostaining and FCM-derived PA values. The Ki-67 derived PA values did not correlate with patient age, nodal status, tumor size, site, stage, degree of differentiation, or DNA ploidy. The adjacent normal colonic mucosa section showed Ki-67 positivity confined to the lower portion of the crypt. It appears that the Ki-67 PA data is not an independent prognosticator for colorectal cancer.

TUNGSTEN-ENRICHED MOLYBDENUM-DEFICIENT DIET PROTECTS AGAINST ISCHEMICA REPERFUSION INJURY IN WEANLING RATS. J. Seanger et al. University of South Alabama, Mobile, AL.

In adult animal models, dietary tungsten sufficiently protects against Ischemia-reperusion (I/R) injury by decreasing the activity of xanthine oxidase. In this study, the authors investigated pregnant rats who were randomized to diets of either standard rat chow or tungsten-rich molybdenum-deficient chow and were maintained on these diets postpartum during breast feeding of their pups. The pups were then subjected to I/R injury by occlusion of the superior mesenteric artery for 30 minutes. Gross and microscopic morphometric studies of the small intestine of these pups following injury revealed less significant villous necrosis and fibrosis in the treatment group than in the controls. These findings support the protective role of tungsten against I/R-induced injuries and support transfer of protection from mother to neonate.

CATHEPSINS B&L IN COLORECTAL CANCER: CORRELATION WITH MULTIPLE PATHOLOGIC PARAMETERS. K. Sheahan et al. Mallory Insititue of Pathology, Boston, MA.

Cathepsins B and L are lysosomal enzymes which have been recently linked to tumor stage in breast and colorectal cancers. The authors investigated the relationship of levels of cathepsins B and L to multiple pathologic parameters. Fresh tissue was analyzed using enzyme assays and slot and Northern blots. There was a significant increase in cathepsins B and L in colorectal cancers compared to normal mucosa. Cathepsins B and L and cathepsin B mRNA levels showed a significant inverse correlation with Dukes' stage. Non-metastatic tumors showed significantly higher values than metastatic tumors. This pattern was observed for both enzymes in rectal cancers, but only for cathepsin L in colon cancer. Both enzymes also showed a significant correlation with the character of invasive margin (expansile > infiltrative) and the presence or absence of peritumoral lymphocytic infiltrate (present > absent). The authors conclude that the cathepsins B and L are more

abundantly produced by tumors in early stages and in tumors with favorable histologic features.

POLYMERASE CHAIN REACTION DEMONSTRATES HUMAN PAPILLOMAVIRUS (HPV) DNA IN SQUAMOUS AND BASALOID CARCINOMA OF THE ANUS, BUT NOT IN ADENOCARCINOMA OF THE COLON. K.R. Shroyer, J.G. Kim, N.W. Pearlman, and W.A. Franklin, Univ. of Colo. Health Sci. Center, Denver, CO and Catholic Univ. Med. College, Seoul, Korea.

Thirty one archival tissue blocks from 28 patients with adenocarcinoma of the colon and 6 blocks from patients with basaloid or squamous cell carcinomas of the anus were studied by in-situ hybridization and PCR. HPV DNA was was detected in 100% of the cases of anal basaloid or squamous cell carcinoma and 0% of the cases of colon adenocarcinoma. The positive cases included two cases of type 16, one case each of type 11, 18, and 33 HPV. By in-situ hybridization the HPV DNA was found in tumor cell nuclei. The authors conclude that HPV DNA is found in anal basaloid and squamous cell carcinoma but is not found in colonic adenocarcinomas.

IDENTIFICATION OF GASTROINTESTINAL T CELL LYMPHOMAS USING ROUTINELY PROCESSED TISSUE. G. Tallini et al. Yale University School of Medicine, New Haven, CT.

The authors studied formalin-fixed, paraffin-embedded tissue from gastrointestinal lymphomas with various monoclonal antibodies. The markers for T cells were UCHL-1 (CD45ro), MT-1, and Leu 22 (CD43). B cell markers were: L26 (CD20), LN-1 (CDw75), and LN-2 (CD74). Antibodies Leu M1 (CD15), MAC 387, and HAM 56 were used as markers of myelocytic/monocytic/macrophage lineage. Tumors were also studied with leukocyte common antigen (CD45), Ki-1 (CD30), and HLA-DR (LN3). Five diffuse large cell lymphomas of T cell origin were detected (5/5 MT-1+, 5/5 leu 22+, 4/5 UCHL-1+). Interestingly, the LN-2 antibody (B cell) was expressed by neoplastic T cells in two of five patients. All tumors were negative for Ki-1 and histiocytic markers. Evaluation of different fixatives showed better histologic resolution and greater immunoreactivity with B5 compared to formalin or Bouin's fixation.

GASTRIC HELICOBACTER PYLORI: HISTOLOGICAL CRITERIA DISTINGUISHING POSITIVE FROM NEGATIVE BIOPSIES - A DISCRIMINANT FUNCTION ANALYSIS. M. Tanaka et al. McMaster University Medical Centre, Hamilton, ON.

The authors examined 98 slides from biopsies of patients who were positive for H. pylori and 168 from patients who were negative for H. pylori. By analysis of covariance; severity of chronic inflammaton, plasma cells in the lamina propria, neutrophils in the pits and lamina propria, and lympoid follicles showed statistically significant F values for the presence of H. pylori. H. pylori may be missed when using H&E alone. Special stains are time and cost-consuming and should not be done on all biopsies. Special stains for H. pylori need not be done in H. pylori negative (H&E) biopsies in the absence of the above histological findings.

DISTRIBUTION OF COLLAGENOUS COLITIS IN SYMPTOMATIC PATIENTS. M. Tanaka et al. McMaster University Medical Centre, Hamilton, ON.

The authors investigated the distribution of the subepithelial collagen band and inflammatory infiltrate in 17 patients with collagenous colitis. All patients underwent full colonscopy with mutiple biopsies. The thickened collagen band (TCB) frequently had a patchy distribution, even though overall it was equally distributed through the colon. Positive biopsies were significantly less in the rectum (27%) than in other sites (60 to 83%). In five of the patients only one biopsy was positive. Mucosal inflammation was diffuse and usually present in biopsies with a TCB, but was variable in biopsies without a TCB. Three of 8 rectal biopsies without a TCB lacked chronic inflammation. In the sigmoid and descending colon all biopsies without a TCB except one were inflamed. The authors concluded that the rectum was least frequently involved. If multiple flexible sigmoidoscopic biopsies are entirely normal quantitatively regarding inflammation, then collagenous colitis is very unlikely to be found elsewhere.

MITOMYCIN-INDUCED COLITIS IN RATS: SIMILARITY TO HUMAN ULCERATIVE COLITIS. H. Wang et al. Hines VA Hospital, Hines, IL and Loyola University Medical Center, Maywood, IL.

Adult rats were given single intraperitoneal injections of Mitomycin-C (MC), sacrificed at varying time intervals, and the entire GI tract was histologically examined. There was diffuse inflammation (neutrophils and eosinophils) limited to the mucosa. Also noted were crypt loss, ulceration, and crypt abscesses. Regenerative colonic epithelium was noted in areas distant from the inflammation and areas of possible dysplasia were noted. Histological changes were first seen 24 hours post injection and maximal at 7 days, however, the changes subsided after 14 days. These changes were found to be dose-dependent. The authors feel that MC induced colitis is a reliable model with many histological similarities to human ulcerative colitis including changes of glandular dysplasia.

DNA PLOIDY AND S-PHASE FRACTION IN RECTAL CANCER. S. Warner, J. Harrison, R. Vander Zwaag, F. El-Zeky, P. Rabinovitch, and P. Denn, Univ. of Tennessee-Baptist Memorial Hospital, Memphis, TN and Univ. of Washington, Seattle, WA.

Using flow cytometry, the authors retrospectively analyzed DNA ploidy and S phase fraction (Spf) in 309 paraffin-embedded rectal cancers. Seventy two percent of the tumors were diploid range, and 28% were aneuploid, however, there was no statistically significant difference in survival. A significant stage to aneuploid relationship was observed. Five year survivals for tumors greater than and less than 5% Spf were 44% and 45% respectively. When neoplasms were stratified as diploid Spf less than 4%, diploid Spf greater than 4%, and aneuploid Spf less than 10%, and aneuploid Spf greater than 10%, there was no difference in five-year survivals. Compared with conventional histopathological parameters, the DNA ploidy and S phase fraction analysis offer no improvement over routine histopathology in predicting prognosis of rectal cancers when using archival tissue.

GASTROINTESTINAL CRYPTOCOCCOSIS. K. Washington et al. Duke University Medical Center, Durham, NC.

The authors report a case of gastric cryptococcal infection diagnosed endoscopically as the initial presentation of AIDS. This patient subsequently died revealing widespread cryptococcal infection. The authors found six other cases out of 24 autopsy cases with disseminated or pulmonary cryptococcal infection. The gastrointestinal sites in these six cases were esophagus, stomach, terminal ileum, and colon. Prediposing factors were AIDS (2), hematologic malignancy (3), and steroid therapy (1). The authors conclude that cryptcoccal infection involves the GI tract more frequently than previously reported.

MULTIDRUG RESISTANCE GENE PRODUCT (P-GLYCOPROTEIN) EXPRESSION AS A MARKER FOR AGGRESSIVE COLON CARCINOMAS. R.S. Weinstein, T.M. Grogan, J.S. Coon, and I.B. Roninson. Departments of Pathology, University of Arizona, Tucson, AZ, and Rush-Presbyterian St. Luke's Medical Center, Chicago, IL and the Department of Medical Genetics, University of Illinois in Chicago, IL.

The authors immunohistochemically studied the presence of p-glycoprotein by the use of monoclonal antibodies C219 and JSB-1 in primary colon cancers stage B1 or greater. Sixty five of 95 tumors were found to be positive for p-glycoprotein. The authors found solitary invading cells at the edge of the tumors expressed p-glycoprotein in 47 cases. There was a significantly greater incidence of lymph node metastasis and vessel invasion in cases with p-glycoprotein positive invasive cells. A multivariate analysis showed that the presence of p-glycoprotein positive invasive cells is an independent predictor of vessel invasion and that p-glycoprotein may be useful as a new tumor marker.

THE VALUE OF THE PREOPERATIVE MUCOSAL BIOPSY IN THE DIAGNOSIS OF COLORECTAL MUCIN-PRODUCING ADENOCARCINOMAS (MPAC). M. Younes et al. Baylor College of Medicine and the Methodist Hospital, Houston, TX.

The authors assessed the value of the pre-operative biopsy in predicting the type of colorectal tumor present on resection. They studied the pre-operative mucosal biopsy and colectomy specimens in 193 patients with colorectal adenocarcinoma. Eighty two percent of the biopsies showing MPAC had greater than 50% mucinous component in the resection specimen, while only 8% of those biopsies showing non-MPAC had greater than 50% mucinous component. Forty five percent of the MPAC biopsies were stage C2, compared to only 17% of non-MPAC biopsies. Similarly, 13% of MPAC and 32% of non-MPAC biopsies were stage B1. The authors conclude that colorectal adenocarcinomas revealing MPAC on preoperative biopsies are more likely to show a high mucin content and to be at a more advanced stage upon resection.

ASSOCIATION BETWEEN MUCOSAL HYPERPLASIA OF THE APPENDIX AND ILEOCECAL REGION MALIGNANCY. M. Younes et al. Baylor College of Medicine, and the Methodist Hospital, Houston, TX.

The authors studied hyperplastic changes of the appendiceal mucosa and their association with other disease processes in the colon. They examined 41 consecutive ileocolectomy specimens in which the appendix was present. Six (14%) appendices showed mucosal hyperplasia (defined as significant when it involved more than 50% of the circumference in at least one section sampled) and 5 of these 6 cases were associated with an adenocarcinoma always within 8 centimeters of ileocecal valve. The association between hyperplasia of the appendiceal mucosa and adenocarcinoma of the ileocecal region was found to be statistically significan ($P<0.05$). This data suggested that further investigation to exclude associated malignancy may be warranted in the presence of significant mucosal hyperplasia in appendectomy specimens.

GASTRIC MUCOSA WITH LYMPHOID STROMA. G. Zamboni et al. Instituto di Anatomia Patologica Universita di Verona, Italy.

Gastric carcinoma with lymphoid stroma (GCLF) is defined as gastric carcinoma infiltrated uniformly with an abundance of lymphocytes and plasma cells through the entire tumor. It is a distinct pathological entity with favorable prognosis. The authors report features of 12 cases of GCLF (2.8% of 420 gastric carcinomas surgically resected). Two of 12 tumors were of the early type, and 10 of 12 cases were advanced cancers. All patients were alive 1-18 years (mean 6) (one died after 7.5 years). The tumor cells were frequently arranged in a trabecular pattern with dense infiltrates of intraepithelial lymphocytes present within cancer cell nests. The tumor cells diffusely expressed HLA-DR. The intraepithelial like lymphoid cells and the majority of the stroma lymphocytes were UCHL-1 positive (T cells). The authors hypothesize that the lymphoepithelial interactions between the prominent lymphoid infiltration, including intraepithelial T lymphocytes, and the HLA-DR positive neoplastic cells may represent an immune mechanism against the tumor and be responsible for the favorable prognosis of this peculiar type of gastric carcinoma.

CARCINOMA-LIKESIGNET RING CELL EPITHELIAL CLUSTERS IN GASTRIC MALIGNANT LYMPHOMA. G. Zamboni et al. Istituto di Anatomia Patologica Universita di Verona, Italy.

In 20 of 88 cases of gastric malignant lymphoma the authors noted single or multiple intramucosal clusters of epithelial cells with signet ring-like appearance. In three of these cases these clusters were particularly diffuse in the lamina propria and were histologically indistinguishable from signet-ring cell carcinoma. These epithelial cells were cytokeratin positive and negative for leukocyte common antigen, and failed to express intracytoplasmic immunoglobulin. The regional lymph nodes did not show any carcinomatous metastases in any case. The authors are not certain whether these clusters of cells represent true carcinoma associated with malignant lymphoma, or are merely an aspect of the spectrum of changes occurring in

lymphoepithelial lesions. This histological finding may be particularly worrisome in evaluating forceps biopsy material.

CYTOGENETIC ANALYSIS OF COLORECTAL TUMORS BY INTERPHASE IN-SITU HYBRIDIZATION AND IMAGE ANALYSIS. E. Zampa, K. Min, M. Moyer, R. Bonner, G. Hemstreet, C. O'Hare, and R. Postier, University of Oklahoma, Oklahoma City, OK and University of Texas (San Antonio) Health Sciences Centers.

The authors studied the cytogenetics of supressor p53 oncogene and DCC (Deleted in Colorectal Cancer) chromosome 18 by developing a procedure which allowed rapid identification of chromosomes 17 and 18 status in any given cell. The authors used alpha satellite DNA probes for chromosomes 17 and 18 in identifying FITC labeled chromosomes. The nuclei were counterstained with Hoechst33258. Using an image analysis system the fluorescent intensity of each nucleus and the number of probe stained areas was determined. A tumor was considered either hypo or hyper diploid for a particular chromosome if more than 15% of the cells had less than two or more than two FITC stained areas per cells respectively. In addition, a cell was considered hyperdiploid if the total DNA content exceeded 5C as determined by image analysis. The authors found that all malignant tissue examined showed abnormalities in the number of 17, 18, or both chromosomes. Increase or decrease in 17 or 18 did not necessarily correlate with increase or decrease in total DNA content.

BOOK REVIEW

MUCOSAL BIOPSY OF THE GASTROINTESTINAL TRACT
by Richard Whitehead.
W. B. Saunders Company-4th.edition, 1990.

Mucosal Biopsy of the Gastrointestinal Tract has been the classic text for all of us interested in gastrointestinal pathology since its original publication in 1973 and until recently it was the only available reference source and the gold standard. The readership of this newsletter are all familiar with this work which is now in its 4th. edition and has been updated to over 400 pages and 19 chapters with a new section on the biopsy pathology of HIV infection. A new and useful change in the format is the inclusion of a list of references following each section on individual organs. This is a valuable resource for gastrointestinal pathologists working on any specific topic.

There are useful new additions to the text of the 4th. edition. Special forms of gastritis are described in greater detail with a new section on H. pylori infection. However, I still prefer the format in the 3rd. edition in which gastritis and its subtypes is dealt with in one instead of two rather long chapters. A welcome change is the combination of separate chapters on duodenal/ileal biopsies and jejunal biopsies into one comprehensive section on the small-intestinal biopsy in disease states. This book is also probably the most easily available source of information on the pathology of diarrhea in the pediatric population. The section on infective colitis has been expanded and the pathology of the "gentler colitides" has been added. The final section on biopsy pathology of HIV infection is superficial but a good place to start.

Some problems do arise in relation to terminology, but this seems to be inevitable when author and audience are separated by the oceans! I would also have been most grateful for good diagnostic criteria which based on his own personal experience, Dr.Whitehead finds useful in one of the most problematic areas in g-i pathology, i.e. dysplasia, whether it be in Barrett's esophagus, gastric mucosa or IBD. Also, since gastrointestinal lymphomas is now such a large topic of major interest to all of us in the field, a book such as this one would be serving an important function with an entirely separate section on this topic with a contribution by a hematopathologist, in the 1995 edition. Although there are now texts which are more useful for residents and non subspecialty pathologists such as the two volumes pertaining to gastrointestinal pathology in the Contemporary Issues in Surgical Pathology series and the recent IAP monograph, this work still remains the gastrointestinal pathologists' book of gastrointestinal pathology where one can find valuable information on topics as diverse and rare as acrodermatitis enteropathica and balantidiasis! In the final analysis, Dr.Whitehead must be congratulated for his untiring energy and unceasing efforts on our behalf.

Shirin Nash,
Brigham & Women's Hospital & Harvard Medical School,
Boston, Ma.

BOOK REVIEW

CANCER OF THE BILE DUCTS AND PANCREAS

Edited by Paul E. Preece, Alfred Cuschieri, R.David Rosin
W.B. Saunders Company 1989

This is a new work edited by 3 British surgeons and written by 32 contributors predominantly European, who represent all the medical and surgical disciplines involved in the diagnosis and management of cancer of the bile ducts and pancreas. As such, this book will be of greater use to clinicians who belong to GIPS rather than the practising pathologists in the society. Nevertheless, of the 19 chapters, 3 are particularly appealing to pathologists for purposes of diagnosis and teaching and especially for preparing conferences on this particular topic. Many of the other chapters will be informative for general medical interest and as a source for clinical material which is not readily available in the pathology literature.

The first chapter on the epidemiology, etiology and pathology of bile duct tumors by Dr. P.P. Anthony, is an excellent review of the subject with tables and illustrations; and is not available in this consise yet detailed format in any of the other well-known texts. The references are from clinical and pathology sources and are current upto 1986. The chapter on cancer of the pancreas, morphology and biology, by Dr. Kloppel is also useful, particularly with regard to marker studies in pancreatic carcinoma, precursor lesions, and prognostic factors. The multi-author chapter on the cell biology of pancreatic carcinoma provides details of the fine structure of pancreatic ducts and the neoplasms derived from them and also a characterization of tumor products. Another chapter I particularly appreciated is the one on pancreatic endocrine tumors which includes diagnosis, clinical syndromes, and management. This is an area in which although the pathology is routine, the clinical aspects and differential diagnosis are always stimulating and this is a well-written and informative chapter by Drs. Anderson and Bloom.

This is a small volume which is well-illustrated and easy to read. Although not an absolute must, it certainly will be a useful addition to the libraries of members of the society.

Shirin Nash
Brigham & Women's Hospital & Harvard Medical School,
Boston, Ma.

UNITED STATES AND CANADIAN ACADEMY OF PATHOLOGY, INC.

The United States-Canadian Division of The International Academy of Pathology

NATHAN KAUFMAN, M.D.
Secretary-Treasurer
& Executive Director

April 30, 1991

David A. Owen, M.D.
Department of Pathology
Vancouver General Hospital
855 W. 12th Avenue
Vancouver, BC V5Z 1M9, Canada

RE: Gastrointestinal Pathology Society

Dear ~~Doctor Owen:~~ David

In accordance with our procedures, Companion Meetings co-sponsored by the Academy and scheduled at our meeting are reviewed every 5 years, starting with the 1986 meeting. Your program has been reviewed by a task force established for this purpose for the 5 year period 1986-90 inclusive. By action of Council at its 1991 meeting, your society has been approved for further co-sponsoring by us and scheduling at the time of our meetings for a period of five years (1991-1995 inclusive) at which time you will be subject to re-review.

We are pleased that this review process has resulted in a positive decision to continue co-sponsoring your session at our meeting each spring. We would ask that a special effort be made by your society's program moderator to emphasize to the attendees the need for evaluations to be handed in since they are important for continuing improvements in the program as well as when we ourselves are reviewed by ACCME for continuing accreditation.

We want to draw to your attention that criticisms from the evaluations have noted that handouts are not made available to the registrants. Although not mandatory, some societies prepare excellent handouts for their respective sessions. We would ask you to consider instituting this practice as it enhances the meeting and improves the quality of presentations and the value of the session as perceived by the attendees. They use these handouts as reference material and find them valuable.

We wish to commend your society for the presentation of thematic symposia of high educational and scientific quality; and we are are looking forward to continuing working with you.

Sincerely,

Nathan Kaufman, M.D.

NK:jqj

cc: Dr. Robert Petras

3643 Walton Way Extension / Augusta, Georgia 30909 USA / Telephone (404) 733-7550

~ Gastrointestinal Pathology Society
USCAP Companion Meeting
Sunday, March 15, 1992
Preliminary Program

Colitis

"Many shall run to and fro, and knowledge shall be increased."

Daniel 12:4

Robert R. Pascal, M.D. - Moderator:

1:30	Distinguishing Between Inflammatory Bowel Disease and Other Types of Colitis.	Harvey Goldman
2:00	Acute Versus Chronic Colitis.	Henry Appelman
2:30	Granulomatous Inflammation of the Colon.	Rodger Haggitt
3:00	The Association of Mycobacteria with Inflammatory Bowel Disease.	David Graham
3:30	The Mucosa-associated Immune System and Inflammatory Bowel Disease.	David Keren
4:00	Complications of Inflammatory Bowel Disease (Excluding Carcinoma and Dysplasia)	Robert Petras