THE GASTROINTESTINAL PATHOLOGY CLUB NEWSLETTER

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CONTENTS

EDITORIAL

THE G.I. PATHOLOGY CLUB - FUTURE DIRECTIONS

Our Club (or as it may eventually be called, Society) has been in existence for several years now. Although we were not formally constituted at the time, the first meeting could rightly be said to have taken place in 1979 at San Francisco. Since that date, the Club has prospered and established its credentials as a bona fide scientific society. This has been done mainly at the IAP where our meetings have been more popular with the rank and file than any other subspecialty group. More recently, the Club has also sponsored sessions at the Digestive Disease Week AGA Meeting. In addition to this scientific activity, the Club has been busy in stricking appropriate committees and electing appropriate officers. There is even a NEWSLETTER which appears from time to time. As well as promoting G.I. pathology as a major subspecialty, the Club has also provided a forum for similarly interested individuals to get to know each other.

This early enthusiasm continues unabated and the original Club founders are still active in all areas. However, the GIPC is now moving from infancy to maturity and it is a pertinent time for all Club members to ask themselves what lies ahead. What new directions, if any, should we be moving towards? In this regard it is essential that all members should be ready and willing to contribute either their services or their ideas. All officers of the Club actively encourage you to approach them, either at one of the meetings or later by mail or phone. Your editors are firmly of the opinion that all Club members are potential contributors to the NEWSLETTER. Since there seems an undue modesty about your journalistic prowess we intend to actively solicit contributions. Be warned therefore, we will be on the lookout for you in New Orleans.

As you will see from elsewhere in the NEWSLETTER, one area of expansion of club activities is the international scene, where Harvey Goldman is blazing the trail. Initially, this took the form of personal contacts, but now something more concrete (don't interpret this too literally) is emerging.

Those that will attend the bussiness meeting at the New Orleans IAP Meeting will, I'm told, hear that the Club membership is no longer dramatically expanding as it has been doing in the last few years. This too is a sign that our Club's growth spurt is over and adulthood is approaching. In a few years, it is even possible that an arranged marriage with an European spouse may be considered. Ideas and contributions from as many Club members as possible are the way to ensuring our continued development.

David A. Owen, M.D.

GIPC PROGRAM FOR THE IAP MEETING IN NEW ORLEANS

The GIPC will hold its annual Scientific Session on Sunday, March 9, 1986 at 1:30 p.m. in the Grand Ballroom D, New Orleans Hilton Hotel, New Orleans, Louisiana. This is the program:

Scientific Session A: Gastrointestinal Endocrine Pathology

1:30-2:00 p.m. Endocrine Cells of the Digestive Tract: An Overview. Dr. Juan Lechago
Harbor-UCLA Medical Center, Torrance, California

2:00-2:30 p.m. Carcinoid Tumors and the Carcinoma-carcinoid Spectrum. Dr. Klauss Lewin,
UCLA School of Medicine, Los Angeles, California

2:30-3:00 p.m. Hyperplastic Lesions of the Gut Endocrine Cells. Dr. Yogeshwar Dayal,
Tufts Medical School, Boston, Massachusetts

3:00-3:30 p.m. Recess

Scientific Session B: Research Topics in Gastrointestinal Pathology

3:30-4:00 p.m. Structure and Function of a Major Intestinal Epithelial Barrier: The Occluding Junction
Dr. James Madara, Brigham and Women's Hospital,
Harvard Medical School, Boston, Massachusetts

4:00-4:30 p.m. Pathologic Aspects of Experimental Colonic Carcinogenesis. Dr. Stanley Hamilton,
Johns Hopkins Medical School, Baltimore, Maryland

4:30-5:00 p.m. Summary of Proposed Studies Seeking Multi-institutional Material

a) Malignant Colonic Polyps
Dr. Harry Cooper, Jefferson Medical School,
Philadelphia, Pennsylvania

b) Barrett's Esophagus: Dysplasia-Carcinoma Sequence. Dr. John V. Frei,
University of Western Ontario, London, Ontario

GASTROINTESTINAL PATHOLOGY CLUB

ANNUAL BUSINESS MEETING

The ballots are in! The majority of those responding to the Questioinnaire about the time of the Annual Business Meeting favored maintaining the current format. Therefore:

The Annual Bussines Meeting of the Gastrointestinal Pathology Club will be held immediately following the Scientific Session, at 5:00 pm, in the Grand Ballroom D, New Orleans Hilton, Sunday, March 9, 1986.

AGENDA

I. Approval of Minutes of 1985 Meeting - Dr. Rickert

II. Financial Report - Dr. Rickert

III. Committee Reports

- A. Announcement of new committee assignments - Dr. Lewin
- B. Education - Drs. Madara and Haggitt
- C. Membership/Nomination - Dr. Kahn - to follow New Business
- D. Publications - Dr. Appelman
- E. Training Programs - Dr. Yardley
- F. International Liaison - Dr. Goldman
- G. Newsletter - Drs. Lechago and Owen

IV. Old Business

- A. Response to questionnaire about time of Annual Business Meeting - Dr. Rickert
- B. Response to questionnaire about change in name of the Gastrointestinal Pathology Club - Dr. Rickert

V. New Business

VI. Report of Membership/Nomination Committee - Dr. Kahn

- A. Announcement of New Members
- B. Nomination of Vice President

VII. Election of Officers

VIII. Induction of New President

IX. Adjournment

REVIEW OF POSTER PRESENTATIONS AT THE 1985 TORONTO IAP MEETING

Traditionally, it has been the policy of the GIPC NEWSLETTER to review only the proferred papers from the IAP Meetings. Recently, however, poster presentations have become equally important and are attracting considerable scientific interest. Therefore, starting with this issue, we will also be reviewing posters.

A large number of interesting and important posters were on view in Toronto. One of these concerned a topic that few people have at their fingertips, namely cricopharyngeal dysphagia. This was presented by Dr. Reyes and coworkers from Mount Sinai Hospital, Chicago. They examined cricopharyngeal muscle biopsies from four patients with abnormal function and showed interstitial fibrosis with necrosis, vacuolar change and atrophy of the voluntary muscle. Secondary axonal degeneration was noted. There was also paucity of intramuscular capillaries, although it was not clear if this was primary or secondary. The histologic features were similar in all four patients who had a variety of clinical diagnoses such as Parkinson's disease, oculopharyngeal muscular dystrophy, gastroesophageal hernia, and Zenker's diverticulum.

Drs. Smith and Hamilton from Johns Hopkins, Baltimore, presented the results of a retrospective immunohistochemical study of CEA in Barrett's esophagus. Using the PAP technique with a polyclonal anti-CEA antibody, they looked at adenocarcinomas, dysplastic mucosa, and non-dysplastic mucosa. They found that carcinomas were often CEA-positive and that high grade dysplasia was more frequently and more intensely CEA-positive than low grade dysplasia and non-dysplastic mucosa. However, the patchyness of the staining reduced its value as a diagnostic tool for esophageal biopsies. It would appear that CEA immunohistochemistry is unlikely to replace a careful evaluation of dysplasia in H&E-stained sections in the appraisal of premalignant change.

From Case Western Reserve, Cleveland, and Johns Hopkins, Baltimore, Dr. Mendelsohn and colleagues made a presentation of gastric carcinoid tumors and intestinal metaplasia. This was most interesting to both your editors and produced a number of conclusions. The authors examined 10 cases of gastric carcinoid, three of which had or were suspected of having PA (along with type A gastritis), and seven cases which did not have PA but had severe type B gastritis. All cases had endocrine cell hyperplasia, particularly of G cells and serotonin-containing cells, although in only one of the cases (with PA) was the hyperplasia sufficiently severe to produce multiple carcinoid "tumorlets". Thus, there appears to be an established link between intestinal metaplasia of the stomach and the development of gastric carcinoids in some cases.

Dr. Payne and coworkers from the University of Arizona, Tucson, had the considerable fortitude to examine stool specimens from 788 patients with gastroenteritis! They looked for viral particles by direct ultrastructural examination. Forty five per cent of specimens were positive, with corona virus-like particles (CVLP) and rotavirus

being the most common findings. Less common viruses included adenovirus, astrovirus, pico/parvovirus, Norwalk agent and calicivirus. In 20 cases, more than one virus type was identified.

From Queen's University, Kingston, Canada, Drs. Manley and Partington reported five familial cases of severe neonatal colitis. This unusual condition, which presents with severe bloody diarrhea and shows marked destruction of the surface epithelium and concurrent inflammation, resulted either in death or failure to thrive. The etiology is unknown; allergy to maternal colostrum or transplacental passage of antibodies to colonic mucosa have been postulated as possibilities.

Dr. Foucar et al., from the University of Iowa, Iowa City, presented a 110 member extended kindred, some of whose members show a curious association fo visceral myopathy with dysplastic cutaneous nevi and multiple basal cell carcinomas. The visceral myopathy is not clearly defined but, in several cases, resulted in megaduodenum and urinary bladder dysfunction. The genetic association between visceral myopathy and cutaneous pathology in these patients has not been elucidated.

Some names from Harvard, Boston, headed by Antonioli presented the rectal biopsy findings in allergic proctitis. These were from infants with milk protein allergy. Controls were provided by biopsies from Hirschprung's disease (normal mucosa) and from other forms of childhood proctitis. They found that although some of the allergic proctitis patients had numerous eosinophils in the lamina propria and epithelium, lesser amounts of these cells were also present in both controls. Other features examined, including neutrophils, mucosal edema, and architecture were similar in all groups.

The term microscopic colitis has been used to describe a group of patients who have diarrhea of unknown origin, with an abnormal rectal biopsy but a negative barium enema and negative endoscopic findings. Dr. Lee and colleagues from U. of Texas and Baylor, Dallas, investigated a group of these patients and found the histologic features to be: a) expansion of the lamina propria by edema and inflammatory cells, b) cryptitis and crypt abscess formation, and c) reactive epithelial changes. What is not clear is whether these patients have an early mild form of ulcerative colitis, which may regress, remain unchanged, or develop into full-blown ulcerative colitis.

A poster by Drs. Banner and Gould from Rush Medical College, Chicago, described the distribution of neuroendocrine cells in Crohn's disease. Serotonin and somatostatin-containing cells were found, concentrated at the edge of ulcers. In intact but atropic mucosa which presumably represented areas of healed inflammation, the neuroendocrine cell population was normal. It is interesting that in one case containing malignancy, the surrounding gastric metaplasia showed the presence of gastrin-containing cells.

Dr. Kelly from the University of Calgary, Canada, presented two posters. The first of these dealt with inflammatory polyps of the colon in inflammatory bowel disease. He pointed out that this is

rather a rag bag term and that it is possible to histologically subdivide the polyps into three types: a) the pure epithelial regeneration type, b) the pure granulation tissue type, and c) mixed types. The pure epithelial type could show either active or healed ulceration at the base. Ulceration appeared to be a prerequisite for all types of inflammatory polyps. The second poster dealt with the sinuses and fissuring ulcers of Crohn's disease. One hundred and fifty-five gross specimens were examined and mapped. The sinuses were closely associated with strictures and penetrated to the serosa often alongside blood vessels. The fissuers were not so closely related to strictures and were of two types: a) fissuring ulcers and b) acute fissures. It was suggested that both forms may be the result of increased intraluminal pressure.

A poster from Dr. Hull and coworkers from Indiana University, Indianapolis, showed the findings of their transmission and scanning electron microscopy studies of colonic basement membrane in malignancies. Normally, the basement membrane of the surface epithelium and upper crypt contains fenestrations through which epithelial cell processes protrude. Absence of fenestrations was also a feature of the basement membrane underlying the non-invasive portion of adenocarcinomas present at the edge of tumors. The significance of this finding is not elaborated upon by the authors.

An analysis of 104 (or 106, according to the title) Dukes stage B colonic adenocarcinomas was carried out by Drs. Neil and Idikio from Memorial University of Newfoundland, St John's. After subdividing these patients into B1 and B2, these authors found out that 31.8% of B1 cases were dead 5 years after diagnosis while 40.2% of B2 cases died within 5 years. They consider these findings significant enough to warrant separation between Dukes B1 and B2 stages when attempting prognostic pronouncements in these patients.

An interesting flow cytometry study of synchronous colonic adenocarcinomas was presented by Dr. Schwartz and coworkers from Rush Medical College, Chicago. They examined 23 tumors from 10 patients, and found a variety of ploidy patterns. In many, although not all were synchronous tumors, there was a substantial similarity of ploidy, even though the neoplasms were histologically dissimilar. The authors conclude that this provides some evidence that synchronous colonic tumors have a common origin and are spread through intraluminal seeding.

Dr. Schinella and colleagues from Cornell University, New York, and Laval University, Quebec, examined two cases of anorectal condyloma with malignant transformation. In one of these cases, a molecular hybridization application revealed HPV genome material in both malignant tumor and condyloma. This provides further evidence of the viral etiology of these conditions.

From Drs. Holburt and Freedman, UCLA School of Medicine, Los Angeles, emanated a study of gastric carcinomas in 19 young adults. They confirmed the known poor prognosis and delay in diagnosis generally encountered in this group of patients, with no inidividual surviving longer than 36 months. Ten cases were classified as diffuse

carcinoma, four as intestinal carcinoma, and the remainder were unclassifiable.

Studies on a related topic were presented by Dr. Radi and coworkers from University of New Mexico, Albuquerque, who investigated the prognostic implications of endocrine differentiation in gastric cancers occurring in young persons. This study included 17 patients with 9 diffuse carcinomas, 3 intestinal carcinomas, 4 mixed carcinomas and 2 carcinomas that were unclassifiable. By immunocytochemical methods, they were able to demonstrate focal positivity for GI hormones: somatostatin in 7 cases, serotonin in 5 cases, gastrin in 3 cases, and HCG in one case. The mean survival of the patients was 25.2 months, but 31% were alive and well 2 to 5 years after diagnosis. There was a strong positive correlation between survival and endocrine differentiation of the primary tumors.

Drs. Blackman and Vimadalal from Cedars-Sinai, Los Angeles, presented their experience with endoscopic biopsies of 19 duodenal and 16 ampullary neoplasms. They found 11 benign and 24 malignant tumors. Immunostaining for CEA was not of appreciable diagnostic value. Accurate diagnosis by endoscopy alone was difficult in many cases because of the frequent association of adenomas with carcinomas. Correlation of the histologic with the endoscopic apperance, on the other hand, can result in a more accurate evaluation of these relatively unusual lesions.

From the University of Michigan, Ann Arbor, Dr. Kern and colleagues presented an elegant study of the Paneth cell population in the isolated ileal loops of rabbits. Fourteen rabbits had two ileal loops fashioned: one was flushed daily with saline and the other was flushed daily with a solution containing an insoluble antibiotic. The loops were cultured daily and at the end of two weeks were examined histologically. The antibiotic treated loop had significantly less bacterial flora and significantly less Paneth cells. The implications of these findings are that bacterial growth is a stimulus for Paneth cell proliferation.

Dr. Swerdloff and coworkers, from the Michael Reese Hospital in Chicago presented a poster summarizing the findings of an experimental model in which they studied the effects of alcoholic injury an IgA-producing cells in the rabbit gastrointestinal tract. The found that four months after starting alcoholic administration there is a significant increase in the numbers of IgA-producing cells in the lamina propria of the duodenal and jejunal mucosa of the experimental animals. No data were presented about the histology of the mucosa in the same animals.

Macrophage populations in the stroma of colonic adenocarcinomas were studied by Dr. Luebbers and colleagues from Case Western Reserve, Cleveland. Using the markers acid phosphatase, alpha naphthyl butyrate esterase and peroxidase, they showed different populations at the edge and in the center of the tumors. They also showed a difference in the macrophage populations of primary tumors with and without metastases. This finding may be useful in assessing the metastatic potential and prognosis of these malignancies.

Dr. Thor and colleagues from the National Cancer Institute, Bethesda, used monoclonal antibodies against a synthetic peptide reflecting sequences of the human oncogene Ha-ras T24 product, to investigate the presence of such oncogene in breast ductal carcinomas and colonic adenocarcinomas. They found that 63% of ductal carcinomas and 49% of colonic adenocarcinomas express this oncogene, as opposed to 9.5% of benign breast lesions and 0% of benign colonic lesions. The authors also suggest that, in some colonic adenocarcinomas, enhanced ras p21 expression may be related to the invasive potential of the neoplasm.

From the City of Hope National Medical Center, Duarte, came a study conducted by Dr. Burke and coworkers on the immunocytochemical characterization of 35 cases of gastrointestinal lymphoma. Twenty-six cases were classified as immunoblastic lymphoma, but other patterns, including follicular formation, were also observed. All cases but one were phenotyped as B cell lymphomas whereas no true histiocytic lymphomas were encountered.

There were also a number of posters devoted to the liver which presented various works, both experimental and clinical. Dr. Axe and coworkers from Johns Hopkins, Baltimore, compared the efficacy of smear versus rinse preparations in the diagnosis of primary or metastatic cancer, following fine needle aspiration of the liver. Cell blocks provided the greatest diagnostic yield while 17% of the cases were positive with rinse preparations only, thus justifying their use in a significant number of cases.

A poster by Dr. Groben and colleagues from the University of North Carolina, Chapel Hill, presented a study of 22 children between 3 and 18 years of age with chronic active liver disease (CALD). The authors found a variety of histopathologic features which included focal panlobular involvement and early prominent fibrosis, as compared to adults with CALD. For reasons that are not clear to the editors, they conclude that children may have mechanisms to deal with CALD different from those present in adults.

Dr. Markin and coworkers from the University of Nebraska, Omaha, presented the case of a newborn with multiple congenital abnormalities and a mixed hamartoma of the liver. This is a benign congenital lesion that presents as a liver mass. Histologically this lesion is characterized by cords of immature hepatocytes, separated by vascular channels and fibroconnective cords which blend with proliferated bile ducts at the periphery of portal areas. The authors interpret the multiple congenital malformations in this patient as suggestive of <u>in utero</u> vascular disruption of the omphalomesenteric duct.

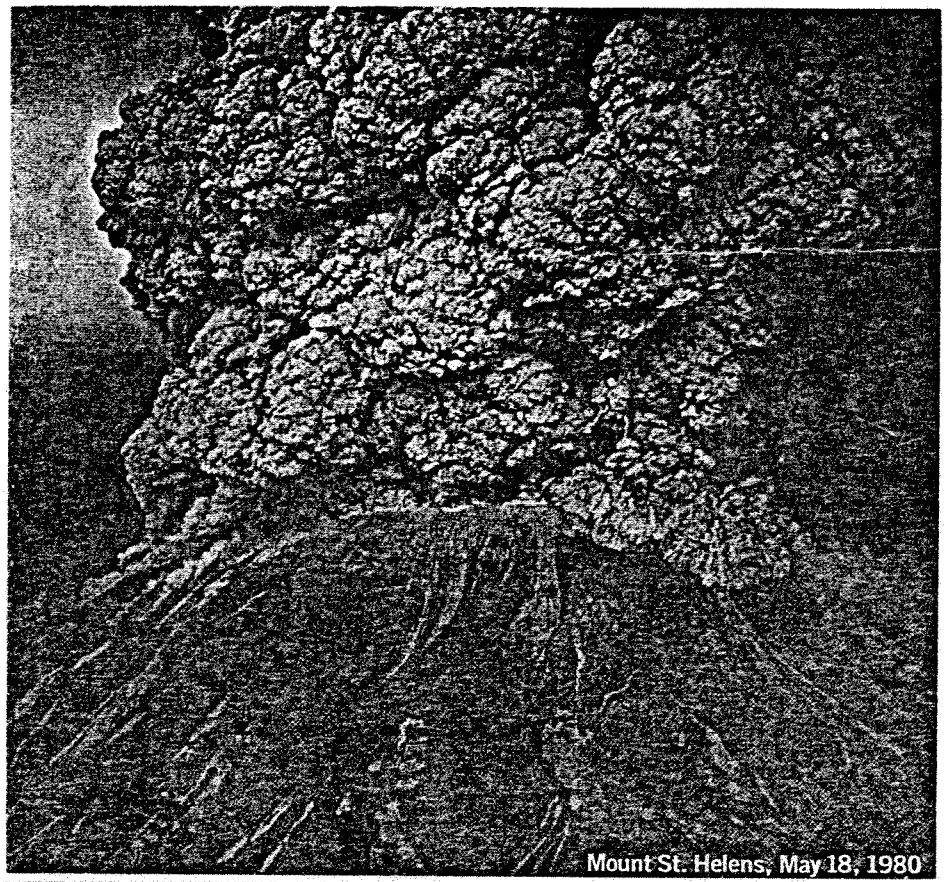
A poster by Drs. Shulman and Gown from the Fred Hutchinson Cancer Research Center and the University of Washington, Seattle, presented the results of a study on the postmortem liver specimens of 21 patients after bone marrow transplantation. They found veno-occlusive disease (VOD) in 10 cases and graft-versus-host disease (GVHD) in 13 patients. Immunocytochemical studies done in these livers revealed intense staining of collagenous wall around veno-occlusive areas with Factor VIII antibodies, in spite of the fact that the vascular

endothelium has been destroyed. A similar finding was encountered in areas of centrilobular perisinusoidal fibrosis. No comments were offered by the authors as to the meaning of thes findings.

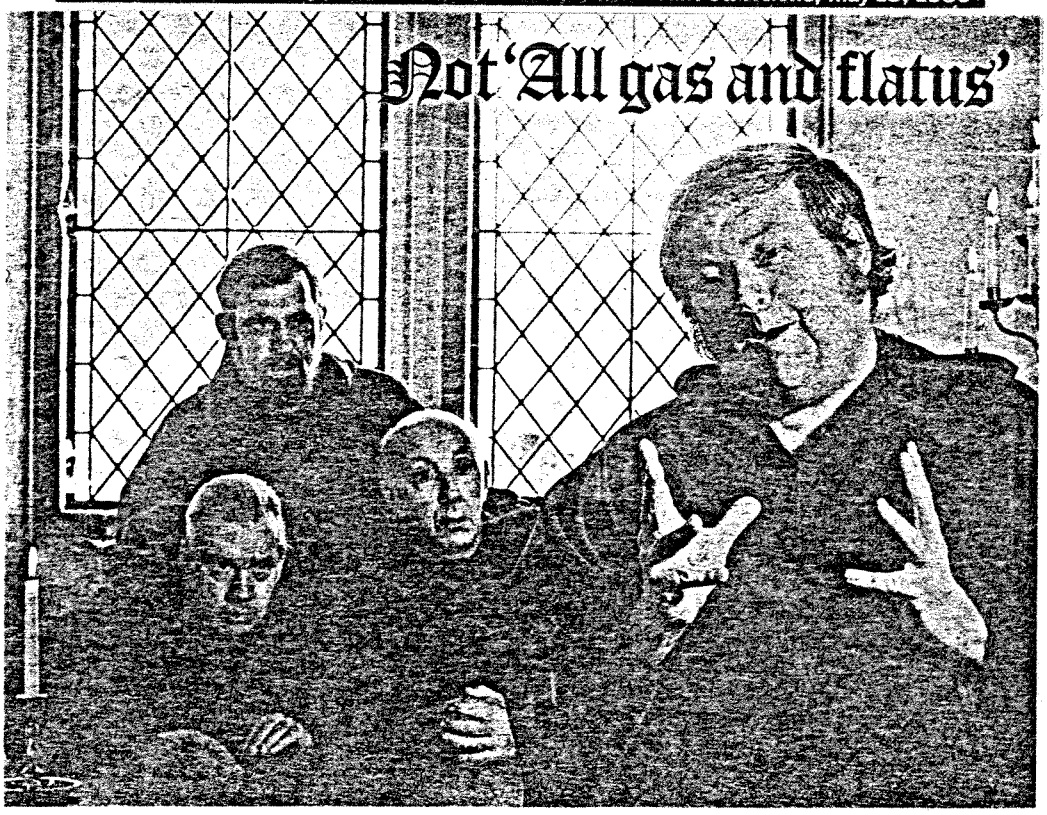
Finally, Dr. Suen from the University of British Columbia, Vancouver, examined 24 cases of hepatocellular carcinoma and determined that 23 of them had been correctly diagnosed by fine needle aspiration biopsy. He found out that a combination of histoarchitectural and cytologic features was essential in arriving at an accurate cytologic diagnosis.

THE CENTERFOLD IS BACK!

BY HENRY APPELMAN



Mount St. Helens, May 18, 1980



REPORT FROM THE PUBLICATIONS COMMITTEE

This committee, under the chairmanship of Dr. Henry Appelman, has acted on two issues during the past year. First, as was discussed at the annual meeting in March of 1985, there was a request by a publisher for assistance in producing an Atlas of Gastrointestinal Pathology. The possibility of a Club-sponsored atlas was discussed at length, both among the membership in the annual meeting, later among the members of the Publications Committee and, finally, with the publisher. It was uniformly agreed that such a venture was logistically almost impossible. Club members might contribute to such an undertaking, but the actual development of the book would still require shepherding by one individual or, at most, by a small group. This could be accomplished more effectively by individual Club members, rather than by the Club as a whole. Therefore, the entire issue of Club sponsoring of an atlas was dropped and there were not further discussions with the publisher.

The second major consideration by the Publications Committee during the past year was the relationship between the Club, its scientific session, and the American Journal of Surgical Pathology. The committee debated whether to publish the entire proceedings of the Scientific Session, selected papers, or simply abstracts. Inherent in these discussions was consideration of the purposes of the sessions and, consequently, whether any interaction with the Journal would satisfy these purposes. A final set of recommendations by the Publications Committee will be presented to the Executive Committee and, afterwards, to the membership at te New Orleans Meeting.

NOTICE OF INTERNATIONAL MEETINGS

Dr. Harvey Goldman

Let us hope for some rebound of the dollar values, as Europe beckons in August and September of 1986. The main event is the XVI International Congress of the IAP in Vienna from August 31 through September 5. G.I. attractions will include a Symposium on G.I. Diseases in Childhood and Infancy on September 2, a Symposium on G.I. Pathology featuring 6 talks (see Program in NEWSLETTER) on September 3, a WHO Classification of Precancerous Lesions of the GI Tract on September 4, and a Slide Seminar on GI Pathology on September 5. There has also been a call for porferred papers and posters. In case you missed the earlier announcements and want further information and registration forms, contract Dr. J. H. Holzner, President of XVI International Congress of IAP, Department of Pathology, 4 Spitalgasse, A-1090 Vienna, Austria. Given the competition of the city of Vienna, I doubt that you'll have trouble finding a sear at any of the scientific sessions.

Who goes to Europe for just a week? So, one week earlier from August 21 - 27, and just a trip on the Danube River away, there will be an International Congress of Cancer in Budapest. For information on this event, contact 14th International Cancer Congress, Congress Bureau MOTESZ-UICC Congress, Budapest POB 32, J-1361, Hungary. Finally, if you really don't want to rush home, the British and French GI Pathology Clubs are planning a combined session in Cardiff, Wales later in September (? the week of September 22). This is an informal event, and you can get information from Dr. Geraint T. Williams, Department of Pathology, Heath Park, Cardiff CF4 4XN, United Kingdom.

For those who like to dream of the future, the next meeting of the European Congress of Pathology will be in Prague in September 1987 and the next International Congress of the IAP will take place in Dublin in September 1988.

SYMPOSIUM OF GASTROINTESTINAL PATHOLOGY

Organized by the International Gastrointestinal Pathology Group
IAP Congress Symposium B8 - Wednesday, September 3, 1986

PROGRAM

Moderator:	Dr. Harvey Goldman, Boston, USA
0830:	Tumor Markers in Gastric Carcinomas and during Gut Development. Dr. F. Borchard, Düsseldorf, FRG
0850:	Pathological Features and Significance of Gastric Dysplasia. Dr. J. P. Camilleri, Paris, France
0910:	Histological Diagnosis of Wilson's Disease Dr. D. G. D. Wight, Cambridge, U.K.
0930:	Discussion
0950:	Intermission
1010:	Recent Advances in Ischemic Bowel Disease Dr. H. T. Norris, Greenville, U.S.A.
1030:	Premalignant Lesions in Colorectal Cancer Dr. M. F. Dixon, Leeds, U.K.
1050:	Endocrine Cell Component of Gastrointestinal Adenocarcinomas, Dr. C. M. Fenoglio-Preiser, Albuquerque, U.S.A.
1110:	Discussion
1130:	Adjournement

The two previous GIPC NEWSLETTERS have contained a lively discussion between our colleagues J. Yardley and S. C. Ming regarding the interpretation and nomenclature of precancerous gastric dysplasias. We have the distinct pleasure of introducing in the present issue a new character in the cast of what could become a classic of the stature of "Dallas" with a bit of luck. We think the readers will enjoy the light-hearted but truly insightful discussion that P. Correa has been kind enough to share with us.

THE NOMENCLATURE OF GASTRIC CANCER PRECURSORS

A GUIDED TOUR TO THE TOWER OF BABEL

Pelayo Correa, M.D.
Professor of Pathology
L.S.U. Medical Center
New Orleans, Louisiana

It all started more than a century ago when Kupffer (1883) wondered what those islands of intestinal epithelium were doing in the middle of the gastric mucosa (1). Only after the Second World War were we able, through the eyes of Jarvi (1951) and Morson (1955), to link those islands with cancer development (2,3). Twenty years later, our Japanese friends, led by Abe, decided that since there were two types of intestine (small and large), they both should be represented in the stomach (4). Sure enough, they found that normal enzymes of the small intestine (leucine aminopeptidase and alkaline phosphatase) were present in certain cases of intestinal metaplasia which they appropriately named "small intestinal type" but yet in other cases were not detectable with the techniques then available. Since the latter was the normal situation of the large intestine, they called this metaplasia "colonic type".

Then came one of our German friends who, in 1976, presented to the pathology society of his country a paper showing that "enterocolic metaplasia" was more frequently associated with cancer than the small intestinal metaplasia (5). They reported the presence of sulfated acid glycoproteins and interpreted this change as a progressive loss of differentiation (de-differentiation). Many other colleagues found the same association, and the subject became a hot issue (6,7).

More Japanese came later with larger and better batteries of enzyme stains. They decided that some of the metaplasias had all the enzymes of the small intestine (8). Since this was a complete set, they labeled that kind of metaplasia "complete". In other cases, they found that some (or most) of the enzymes were not present and, therefore, those metaplasias were labeled "incomplete". This is, again, an indication that the incomplete form was more advanced than the complete form, which did not bother them. But it bothers your tour guide because, in logical thinking, things become more complete when

the process is more advanced, not the otherway around. Some friends of mine thought that those sequences in the nomenclature were assigned not by the authors of the papers but by the secretaries typing them (not a very rare occurrence).

From the "completeness" of the enzymes, some friends of mine crossed the bridge to the completeness of the morphology and called intestinal metaplasia "complete" when small intestinal cells (absorptive enterocytes, Paneth cells, etc.) were present and incomplete when the "colonic" mucin-filled cells were present (9). By this logic, we should all call our small intestine "complete intestine" and our colon "incomplete intestine" (Ref.: Paper to be accepted for publication in next year's edition of Gray's Anatomy). This seems to bother our English friends who in later papers, when they learned to master the mucin stains, dropped the former nomenclature and resorted to the Roman numerals (10). They called the metaplastic patients' stomachs Type I when they showed only sialomucins; Type II when sialomucins and neutral mucins were present; and Type III when sialomucins and sulfomucins could be found. This makes your tour guide dizzy because neutral mucin is the normal "dip" of the stomach, while sulfomucins predominate in the colon. Since we know that we start with the normal stomach and end up (just before we develop cancer) with a stomach looking like a colon, it follows that God located our guts in the right order: first the stomach, then the small intestine in an intermediate position and, lastly, the tail end. Following this logic, the English Type II should become Type I because it retains some of the normal mucins and their Type I should be Type II because of its intermediate position. We all agree that Type III is the most advanced step in this chimeric transformation in which our gastris muscle is lined by colorectal mucosa. The summit of the metaplastic part of the tower seems to have been reached when two types were re-entered into the nomenclature menu: small intestinal type and large intestinal type and then each of them was divided into a "complete" and an "incomplete" variety (11). At this point, everybody in the tour got indigestion and threw up all of the Roman numerals and all of the complete and incomplete residues.

But when you think you are at the summit of the tower, you are lifted into the next floor which contains the colorful hall of the ladies we happily called "dysplasias". They were first called "atypical epithelium", again by our Japanese friends (12). But we, Westerners, wanted a more sexy name and divided them into "hyperplastic" and "adenomatose" dysplasias according to their curves (13). Our more puritanic English friends, however, insisted in the use of Roman numerals and called them Type I and Type II, although we all agree that were are talking about the same "femmes fatales" (14). The main problem at this point is to agree on which girls should be accepted to the club. Some of our friends will accept any girl who volunteers by looking atypical, either because her curves are a little too bumpy or because she has too much chromatin in her eyes. They like to call them by the tune of their dancing: inflammatory or reparative dysplasias.

Many of us want the club to be very snobbish and will reject the above candidates. We will accept only those commited to go "all the

way". Sometimes, however, the host goes out of steam before the dysplasias perform their act, and other times the host finds some mysterious way of keeping them in line. We all suspect that if the dysplastic ladies had their way, the host will no longer be able to breathe.

At this point, another group of our friends are telling us: Let's be honest (15). They claim we can distinguish most innocent girls from most bad girls, but there are those teasers for whom we can only offer an educated guess. And that guess is not good enough for the clinician or for the patient. They are asking that we introduce the category of "indefinite" between the innocent and the wild girls. It is still to be decided if opening a new "indefinite" category is wiser than being very demanding on the admission to the "dysplasias" club. I guess we will be wiser by trying to look honest and admitting that we don't know everything.

This is the end of the tour. You may sign in for next year's tour at the exit door, if you can find it!

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