THE GASTROINTESTINAL PATHOLOGY CLUB NEWSLETTER
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PRESIDENT'S NOTE

Robert H. Riddell

The time since the last Newsletter has flown rapidly, but two major concerns are worthy of discussion. The first concerns the possibility of Club Members co-operating on projects, the second the possibility of a Journal of Gastrointestinal Pathology.

The response to the questionaire on club projects was encouraging, about half of the membership responding. Let me say that I was pleased to see so many replies to my questionaire. This proves that at least half of the members at least read the journal and are willing to respond, something that the Editors of this Newsletter have also been trying to encourage. (A lively correspondence section would add considerably to its contents).

Two subjects, namely Barrett's esophagus (especially its association with dysplasia and cancer) and 'early' invasive carcinomas in colorectal adenomas, prompted so much interest that we may be able to develop outstanding retrospective and prospective studies on both subjects. However, instituting these studies will not be without inherent difficulties. I would exemplify potential problems by pointing out that at the University of Chicago we have about 25 adenocarcinomas in Barrett's esophagus that have been resected and have biopsies on about 40 other patients with this disease, some of whom have undergone antireflux operations or resection or both. A small cohort of these have been investigated in depth and several papers are in the works regarding these. I have full slide files in my office on these patients. A convincing argument would be required to get this material from our Department and we would need assurances that even a retrospective study would be completed fairly quickly and all slides returned intact. I will assume that other large centers have similar quantities of slides. Should only 6 other centers agree to co-operate, this will likely provide well over 100 resections. It is likely that pathologists from at least 3 and possibly 6 participating centers would like to see all of the slides and perhaps be involved in the writing of manuscripts. How is all of this to be arranged? Currently it would be easy for me to appoint a primary investigator as one outline received was far superior to the others. But would the remaining interested parties be willing to support such a study? The same is also true of malignant adenomas. I suspect that the only way out is to get all those interested in participating in these projects into a room (or bar) at the time of the IAP and see if we can work out a suitable arrangement. In the time between now and the San Francisco meeting I would ask the Executive Committee and any interested members to put on paper their ideas on how we can ensure that these relatively large-scale plans regarding both Barrett's esophagus and invasive carcinoma in adenomas can be put into action. Hopefully, we will have given the matter enough thought to sort out some good methods of implementing them. In the meantime, I have selected two projects, one largely prospective and one largely retrospective, for clubmembers to get their teeth into.

1) Prospective: Are G.I. lymphomas lymphoid or histiocytic or both? Designated investigator - Dr. Leonard Kahn - Long Island Jewish Hospital, New York. It is very hard to get fresh material from these tumors, the

chance of getting surface and cytoplasmic markers using fresh cells, the FACS or frozen sections for histochemistry thereby being lost, and with it the chance to really come to grips with a problem about which there is not only considerable controversy but one which will also take up much of our educational session at the IAP. Most large centers are now sufficiently aware of the problem to save material from these tumors to carry out these studies. In future, could you also freeze some and take an extra couple of blocks for Len. Should such a tumor come your way in the fresh state please call him at 212-470-2461 to obtain instructions on how to transport this material and where to send it. Remember to send all relevant clinical data.

2) Largely retrospective. Menetrier's disease and gastric polyposis - how many diseases are really in this group? When does one stop and another start? Designated investigator - Dr. David Owen - (University of British - Columbia) at the Dept. of Pathology, Vancouver General Hospital, 855 West 12th Avenue, Vancouver B.C. V5Z1M9, Canada.

All who have had to look up the literature on this disease realize what an incredible mess it is. Here is our opportunity to help sort it out in double quick time. Please send David anything that you have in your files that might be confused clinically, macroscopically, or microscopically with your idea of Menetrier's. This includes all cases of numerous gastric polyposis, He will require a set of slides, a kodachrome or two if possible, and an appropriate potted history, particularly regarding evidence of protein loss. This is a real test of whether these combined projects will work or not. My guess is that we ought to easily be able to turn up at least 25 and possibly as many as 50 or more cases between us with a minimum of time involvement from each member. Before continuing to read this Newsletter please make a physical note to get to files today and see how many cases you have there. If you can spare your file slides, I am sure that they will be returned, but a new set would of course be preferable.

Both of the above projects should be considered as primary objectives for club members. The response to these projects will ultimately determine whether it is worth considering other studies in which the resources of club members can be used. The membership should also be aware that the following interests were also expressed:

Esophagus:	Smooth muscle tumors - Wirman
Stomach:	Hyperplastic polyps with malignant change - Ming
Stomach/ Intestines:	Smooth muscle tumors - Barr
Small Intestines:	Refractory sprue - Madara, Whipples-Dobbins
Intestines:	Protozoal/Metazoal infections - Gourley.
	All infections - Lee.
	Psuedo-obstruction - Schuffler.
	Heavy metal diseases - Sommers.
	Iatrogenic/drug induced disease-Riddel
Appendix:	Neoplasms - Appelman
Colorectum:	CMV colitis - Rotterdam.
	Collagenous colitis - Hamilton/Surawicz
	Colitis cystica Profunda - Surawicz
	Hirschsprungs/gangliocytic dysplasias - Riddel

Anal tumors: All-Nassar.
Anal duct carcinomas - Appelman
Liver/biliary
tract: Bilary tract dysplasia - Appelman.
All hepatic bile duct hypoplasias - Ellen Kahn.

I am sure that attempts to support these interests would be appreciated by the parties concerned. Please feel free to use these interested parties as consultants. Full names and addresses can be obtained from the list of Club members.

The second part of this epistle concerns the possibility of a Club Journal. As Henry Appelman pointed out in his last 'column' there is now an incredible choice of journals to which papers may be proffered. This is of course a two-edged sword. On one hand it allows us to address whatever we believe to be the best forum, whether general medicine, general surgery, gastroenterology, pathology or other specialized journals. This is an incredible luxury. The problem is that it makes life awfully difficult to try to stay abreast with it all and most have stopped trying, particularly with literature searches being so fast and relatively cheap to obtain.

Could "The Club" support a journal? Probably it could and one large publisher has already expressed an interest in such a journal. Whether it could attract and sustain sufficient quality publications is a different question. The "review articles" that might fill some of its pages initially will be made at least partly irrelevant by the wealth of GI pathology books that are about to, or have just come onto the market, most edited and written largely by club members. Would there be any point in asking Henry Appelman to plagiarize himself by rewriting his lifes work on appendiceal neoplasms, as he has in Tom Norris's book on Pathology of the Colon, Small Intestines, and Anus, or to ask Bill Dobbins to republish his beautiful chapter on small intestinal biopsy in the same book? A further counter-argument is that some 'new' journals are off to a very shaky start and ultimately some may go under.

In considering the survival potential of such a journal a brief comparison with our counterparts in Ob/Gyne pathology is probably germane. Charlie (Sheldon) Sommers reminded me of "Diagnostic Gyn and Obst" which, despite an excellent editorial board attracted few papers, and these mostly case reports. It had 200 subscription in its first year, rising to 600 subscriptions after 4 years. This was still insufficient to cover costs, causing the publisher to fold the publications. I think that we should note this experience carefully and learn from it. If a Journal of GI Path obtained this number of subscriptions either initially or in 4 years, I would personally be elated. However, this is still less than the break even point and might therefore prove both embarrasing and demoralizing to those who had put in the incredible amount of work required to get the journal off the ground. The IAP-backed 'successor' to Diag. Gyn & Obst. (The International Journal of Gynecologic Pathology) seems to be fairing a little better with a circulation of about 1100 (of whom 300 are members) within 2 years. This is enough for the journal to be financially viable, at least for the time being. One is also bound to consider whether, if a Journal of GI Pathology were started, even club members would use the journal other than for articles that they did not mind being read almost exclusively by a small number of GI pathologists. Many libraries just do not have the financial health to keep ordering new journals indefinitely, and it would be difficult

to envisage our journal being made an exception, I for one would certainly think twice before submitting what I considered to be an outstanding article to such a journal.

Finally, it should be pointed out that there are two fairly recent pathology journals that seem to have been accepted, have thrived and have attracted high quality articles. These are Histopathology (which comes from the British Division of the IAP) and the American Journal of Surgical Pathology. The latter has grown steadily with a circulation that is now around 5000; it also has a good content of GI oriented articles, the current issue (October 1983) having no less than 3 of its 7 original articles on GI pathology. Its editor (Steve Sternberg) is a Club member. The AJSP has already adopted the Arthur Purdy Stout Society, whose name appears on the front cover of each issue, and also publishes its Proceedings. While I would not like to see the invited speakers to our annual IAP educational session saddled with the additional burden of preparing a manuscript for publication, nevertheless perhaps the club should consider whether the AJSP and GIPC might adopt one another.

This mutual adoption/marriage would give club members an established journal as an outlet which many of us already take and many have contributed to. We could also use the journal for club announcements and possibly receive prominence on the cover as does the Arthur Purdy Stout Society. I would, however, welcome all alternative thoughts from the membership, particularly any other viable propositions for a Journal of GI Pathology. The issue of a journal or outlet for club members needs settling now that it has been raised. I believe the Club and AJSP would mutually benefit from this association. Unless a good alternative is suggested from the membership, I will explore this issue further with the Executive Committee of the Club, and with Steve Sternberg. (I have of course, ensured that Dr. Sternberg would not read this letter and be startled by its contents). If a mutually agreeable arrangement can be made, I will bring it before the membership at our next meeting in San Francisco.

Before I am accused of nepotism, the question of "Why not Human Pathology "? must be addressed. It certainly has a much larger circulation, I believe over 11,000, but already seems to have more articles than it can handle; indeed the "Dysplasia in IBD" paper, originally scheduled for publication in the March 1983 issue, was delayed until the November issue, this despite a very high priority rating. Given the current very long waiting period and the obvious editorial support of the AJSP, the argument for the latter seems overwhelming. I will be interested in your responses.

Finally, I think that the Executive Committee of the Club should reconsider how our rather meagre, although quite adequate, funds might be utilized. Although not 'flush' with loot, it is apparent that we are accumulating the stuff at a faster rate than we can spend it. While I am in favor of the Executive Committee perhaps having their meeting just before the IAP meeting in Tahiti, it might be a little difficult to justify to the membership except for our obvious interest in how the GIT might be better served in this location. If we cannot find better causes for our funds, it might be reasonable to consider cutting our membership fees so that it

roughly covers our annual expenditure. I personally feel that it is difficult to justify the current annual fee. While Drs. Antonioli and Appelman may at this moment be making a big dent in our funds to support our Newsletter, perhaps our Secretary/Treasurer, Bob Rickert and the rest of the Executive Committee would give this thought.

Unless there is a further Newsletter before the San Francisco meeting, this will be my "Swan Song". I would like to take this opportunity to thank all members actively involved in the administration of Club activities for their splendid service over the last year, the members for their support, and wish Jack Yardley every success as the Club's fifth president. Although reminiscences are obviously premature, it has been fascinating watching the activities of the Club grow and blossom. There is still considerable room for further growth, but we have come a long way in a relatively short period of time. I would remind you that the Club has educational sessions in 1984 not only at the IAP meeting in San Francisco, but also at Digestive Diseases Week in New Orleans in May and at the IAP Congress in Miami. This coming year will be crucial in developing a solid foundation both nationally and internationally. It promises to be an exciting year.

Editorial

With this issue, the GI Club Newsletter enters its second year. Stan Hamilton has contributed a report of his En Face Histopathologic Technique for the Technical Section, one of the regular features of the Newsletter. This issue also contains the inauguration of what we hope will become another regular item, critical reviews of current publications in gastrointestinal pathology. Our first venture in this area includes excellent critiques by Rodger Haggitt of the paper by Thompson et al on Barrett's esophagus and by David Keren in the current Whipples literature.

Also included in this issue are the programs for the GI Club's contributions to the AGA meeting in May, 1984 and to the XV International Congress of the IAP next September. These programs are evidence of the recognition of the Club's role in gastrointestinal pathology education by two prestigious external organizations.

As we have mentioned before, the contents of the Newsletter reflect the desires of the membership. We, the Editors, have been distressed by the lack of spontaneous participation in the Newsletter by the Club's members. During the past year, we have received only one letter from a member, and that was laudatory. Where are the whining, nagging complaints that surface continuously in every other organization? Is there no one in the membership to complain, cajole, or simply whimper over our inadequacies, our "old boy network", our narcissism? We depend upon you, the members of the GIPC to take us into your confidences (in print, of course) and fuel our editorial fires. Wake up, out there, you complacent so-and-so's. COMPLAIN!

Notice

Request for Collaboration on Cases of Collagenous Colitis

We are currently studying tissue from a patient with collagenous colitis. We would like to have access to additional case material in order to verify our findings in this one case. If you have access to tissue from cases of collagenous colitis and would be willing to collaborate, please call or write to:

Stanley R. Hamilton, M.D.
Department of Pathology
The Johns Hopkins Hospital
600 N. Wolfe Street
Baltimore, MD 21205
Tel.: (301) 955-8377

THE GIPC GOES TO THE AGA IN NEW ORLEANS:

GASTROINTESTINAL PATHOLOGY CLUB SYMPOSIUM
MORPHOLOGIC STUDY OF INTESTINAL DISORDERS
May 22, 1984, 8:00-10:00 PM

MODERATORS:
Dr. John H. Yardley, Professor of Pathology, Johns Hopkins University, Baltimore
Dr. Cyrus E. Rubin, Professor of Medicine, University of Washington, Seattle

TOPICS:
1. Freeze fracture analysis of small intestinal epithelium - functional implications in patients with celiac sprue.
   Dr. James L. Madara, Assistant Professor of Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston

2. Structure and function of the intestinal intraepithelial lymphocyte.
   Dr. William O. Dobbins, III, Professor of Internal Medicine, VA Medical Center and University of Michigan, Ann Arbor

3. The gut as a target organ in acquired immunodeficiency syndrome.
   Dr. Wilfred M. Weinstein, Professor of Medicine, UCLA Medical School, Los Angeles.

FELLOWSHIPS IN GI PATHOLOGY

A one year subspecialty training in gastrointestinal surgical pathology beginning July 1, 1984 is available through the Division of Surgical Pathology, Washington University, Barnes Hospital, St. Louis, Missouri. The goal of the program is to provide expertise in both clinical and experimental aspects of gastrointestinal pathology in preparation for an academic environment. Candidates will have the opportunity to develop basic skills in diagnostic pathology, electron microscopy, freeze fracture, immunocytochemistry, and tissue culture as their clinical and experimental projects would require. Very active adult and pediatric clinical gastroenterology units provide a unique opportunity for clinicopathologic correlation, including teaching responsibilities. Salaries would depend on level of training.

Inquiries regarding this program should be sent to:

Dr. K. DeSchryver
Associate Professor
Division of Surgical Pathology
Washington University
Box 8118
St. Louis, MO 63110

Notice

Questionnaires on GI Training Fellowships

Jack Yardley tells us that although he has had a good response to his earlier mailing, there are still some outstanding questionnaires. He would appreciate receiving the completed forms as soon as possible because he will be collating the data for his report to the Club membership very soon.

GIPC GOES TO THE XV INTERNATIONAL CONGRESS OF THE IAP - 1984
SEPTEMBER 2-7, MIAMI BEACH

Presented to the Gastrointestinal Pathology Club (USA), in conjunction with the Club d'histopathologie digestive (France) and the British Society of Gastroenterology Pathologists' Group (Britain).

MODERATOR: Dr. Harvey Goldman

TOPICS:

1. Mucosal biopsy of acute and chronic reflux esophagitis
   Dr. Harvey Goldman, Professor of Pathology, Beth Israel Hospital and Harvard Medical School, Boston, USA

2. Biopsy diagnosis of gastric lymphomas and pseudolymphomas
   Dr. Francois G. Potet, Professor of Pathology, Hopital Beujon and Paris University, Clichy, France

3. Liver involvement in lymphoma and related diseases
   Dr. Kristin Henry, Professor of Pathology, Westminster Hospital and Medical School, London, England

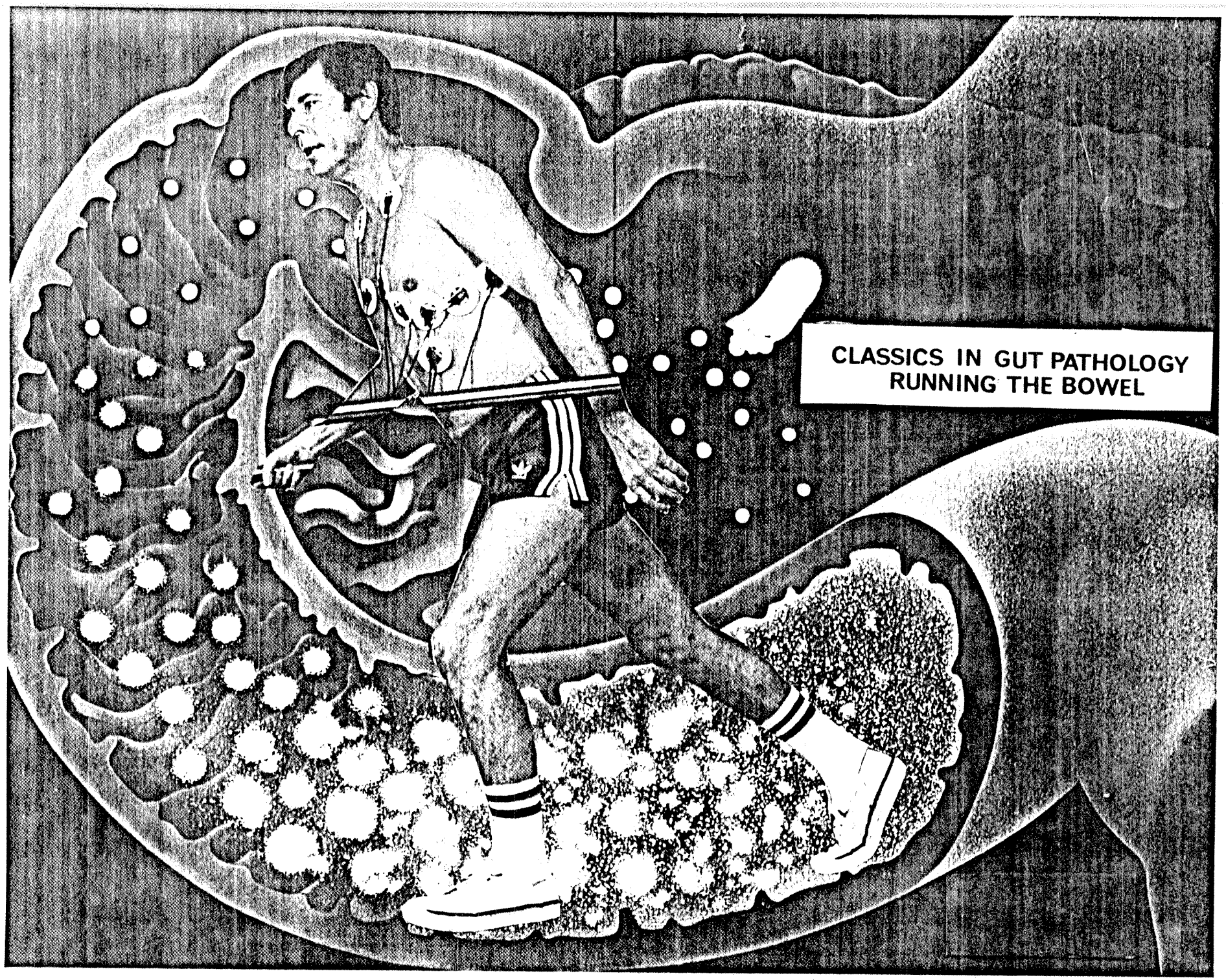
Discussion period

4. Problems in rectal biopsy diagnosis
   Dr. David Ansell, Consultant at City Hospital and University of Nottingham Medical School, Nottingham, England

5. Giant condyloma accuminata and related squamous lesions of the anus. A continuous "precancerous" spectrum?
   Dr. Wladimir V. Bogomoletz, Director of Pathology, Institut Jean-Godinot, Reims, France

6. Gastrointestinal manifestations of acquired immunodeficiency syndrome.
   Dr. Klaus Lewin, Professor of Pathology, University of California, Los Angeles, USA

Discussion period


CLASSICS IN GUT PATHOLOGY
RUNNING THE BOWEL

TECHNICAL SECTION

En Face Histopathologic Technique for Examining Colonic Mucosa

Important information related to the pathogenesis of various colonic mucosal diseases can be obtained by histopathologic study of grossly normal mucosa which is most likely to contain early lesions. For example, in Crohn's disease, active inflammation and granulomas are not infrequently identified in rectal biopsies of grossly normal mucosa. In addition, microscopic dysplastic foci have been demonstrated in grossly normal mucosa of patients with large bowel carcinoma and particularly adenomatous polyposis of the GI tract (familial polyposis coli). Such studies of early lesions in grossly normal mucosa are hampered by the problem of sampling. With routine histopathologic sections taken perpendicular to the mucosal surface, large numbers of step or serial sections are usually required to visualize focal lesions. As a solution, Dr. H.J.R. Bussey of St. Mark's Hospital in London originated the technique of intentionally embedding and sectioning colonic mucosa in the plane of the luminal surface, i.e., en face. With this technique, large surface areas of mucosa can be studies in relatively few histologic sections.

Optimal results with the en face technique are most often obtained when the semilunar folds in a fresh specimen are flattened as much as possible during fixation. Thus, after the specimen is opened and gently rinsed of feces, the bowel should be stretched transversely and longitudinally while being pinned on a slab of cork or styrofoam. The slab is then inverted in a pan of fixative. Following overnight fixation and routine pathologic examination of the specimen, the mucosa of interest can

be "filleted" in a sheet from the muscularis propria by dissection in the plane of the submucosa using a scissors or scalpel. This dissection step can be omitted if the bowel wall is thin enough to permit paraffin infiltration, e.g. rat colon, human cecum. The sheet of tissue is then divided into rectangular portions measuring approximately 2.5 x 1.5 cm. The sheets can be marked with India ink for orientation if mapping of lesions is planned. For paraffin infiltration, each rectangle is flattened between two sponge sheets (Lipshaw Mfg. Co., Detroit, MI) in a cassette and processed. The paraffin infiltrated tissue is then placed luminal surface down in an embedding cassette. After the embedding cassette is filled with melted paraffin, a warmed rectangular portion of a glass slide is pressed against the mucosa to hold it flat to the cassette. The embedding cassette is then placed on ice to harden the paraffin around the mucosa. The glass slide is removed as hardening of the paraffin begins. At the time of sectioning, the paraffin block is trimmed so that as much of the mucosa as possible appears on the slide. For detailed studies, step or serial sections can be prepared.

We have used en face technique to demonstrate active inflammatory lesions and granulomas in grossly normal colon from Crohn's disease resection specimens (see Refs. 2 and 3). We have also applied the technique to the demonstration of multifocal colonic dysplasia in the azoxymethane-treated rat model of experimental colonic carcinogenesis (see Ref. 4). The advantages of the en face technique over routine histopathologic sectioning include: 1) A perspective on mucosal topography corresponding to gross examination of the mucosal surface is provided;

2) Large surface areas of mucosa can be examined easily; 3) Fewer paraffin blocks are required, thus reducing cost; 4) Sampling is more adequate; and 5) Quantitative studies and mapping of lesions are feasible. In our studies using the en face technique, approximately 60 to 70 percent of the submitted mucosa appears in the histologic sections. The technique does have disadvantages: 1) The orientation of the tissue and sections is unusual and requires a period of adjustment both by the histotechnologist and pathologist to gain familiarity; 2) Only the mucosa is adequately demonstrated; 3) The levels of the epithelium visualized within the crypts vary because of unavoidable undulation in the tissue; 4) Mucosa which is thin or has prominent semilunar folds is difficult to process satisfactorily; 5) Practical applicability in surgical pathology is not established, but at present the technique remains a research tool.

References

1. Hamilton SR, Bussey HJR, Morson BC: En face histopathologic technic for examining colonic mucosa of resection specimens. Am J Clin Pathol 78:514-517, 1982.

2. Hamilton SR, Bussey HJR, Morson BC: En face histologic technic to demonstrate mucosal inflammatory lesions in macroscopically uninvolved colon of Crohn's disease resection specimens. Lab Invest 42:121, 1980.

3. Hamilton SR, Bussey HJR, Boitnott JK, Morson BC: Active inflammation and granulomas in grossly uninvolved colonic mucosa of Crohn's disease resection specimens studies with en face histologic technic. Gastroenterology 80:1167, 1981.

4. Hamilton SR, Stephens RB, Natuzzi E, et al: Morphologic analogy of intestinal tract carcinogenesis in adenomatous polyposis and the azoxymethane-treated rat model. Lab Invest 46:33A, 1982.

11-7-83

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REVIEW OF THE RECENT LITERATURE

Thompson JJ, Zinsser KR, Enterline HT: Barrett's metaplasia and adenocarcinoma of the esophagus and gastroesophageal junction. Human Pathol 1983; 14:42-61.

SUMMARY

Based largely on the biopsy study of Paull and colleagues (NEJM 1976; 295:476-480), Barrett's epithelium has been classified into three morphologic subtypes: specialized columnar, junctional and fundic. These three subtypes have been assumed to occupy distinct zones in the esophagus with specialized columnar being the most proximal and fundic the most distal. Controversy has existed concerning the different cell types present in each type of epithelium. Thompson and co-workers have comprehensively evaulated the columnar epithelium in resected specimens from eight patients with Barrett's esophagus and adenocarcinoma or dysplasia; some of the data are contrasted with findings from nine cases of adenocarcinoma at the gastroesophageal junction area that were not associated with Barrett's esophagus. The techniques employed included dissecting microscopy, specimen radiography, scanning electron microscopy and mapping of the specimens with complete histologic evaluation of the entire mucosal surface.

In contrast to the concepts mentioned above, Thompson and colleagues found that Barrett's epithelium is a mosaic of cellular, glandular and architectural types. With the possible exception of gastric fundic epithelium, there was no evidence of zonation. Surface mucous, goblet, absorptive, mucous neck, mucous gland and neuroendocrine cells were not only found in all cases but were randomly distributed. Paneth, parietal

and chief cells were seen in approximately half of the cases. Chief and parietal cells were found at all levels from the lower esophageal sphincter, but had a slight tendency for distal distribution. The authors claim that mucosa with a villar architecture lined by goblet and absorptive cells is unique and therefore diagnostic of Barrett's esophagus on biopsy. Multifocal dysplasia and carcinoma in situ were found in all but one case. Two cases had adenomas, one of which resembled a villous adenoma of the colon. The mean age, age range, sex ratio and symptom complex for the patients with adenocarcinoma of the gastroesophageal junction area not associated with Barrett's esophagus were the same as for the patients with Barrett's epithelium. Because of this observation, the authors postulate that adenocarcinomas of the gastroesophageal junction region also arise from Barrett's epithelium, but that the tumor overgrows it so that it can no longer be recognized.

COMMENT

This detailed study makes important observations about the morphologic spectrum of Barrett's esophagus. The dissecting microscopic photographs demonstrate five different patterns of surface architecture, and the meticulous mapping and complete sectioning document that these various patterns are distributed at random with respect to distance from the lower esophageal sphincter. The mapping technique also demonstrates that the various cell types in Barrett's epithelium are randomly distributed, with the exception that parietal and chief cells tend to be concentrated distally. These findings should help resolve the controversy surrounding the distribution of cell types in Barrett's epithelium. The expected strong association between dysplasia, carcinoma in situ and adenocarcinoma in Barrett's epithelium has been confirmed.

The authors state that a mucosal biopsy with villiform surface architecture lined by goblet and "absorptive" cells is, for practical purposes, diagnostic of Barrett's "metaplasia". They comment that these changes are seen in atrophic gastritis, but only rarely. Before accepting this concept, I would like to see a more detailed study of the mucin histochemistry and electron microscopy of Barrett's epithelium compared with intestinal metaplasia in gastric mucosa. The authors do not make it clear if the cells they call "absorptive" are like those found in the normal small intestine or whether they are the "intermediate" cells described in metaplastic epithelium by others (J Clin Pathol 1981;34:866-870). Until a blinded study documents specific consistent differences between Barrett's epithelium and intestinal metaplasia in gastric mucosa, I would require knowledge of the site of origin of the biopsy before making the diagnosis of Barrett's esophagus.

Recent studies on intestinal metaplasia in both the esophagus and stomach (J Clin Pathol 1981;4:866-870); Gastroenterology 1981;80:1282; J Clin Pathol 1980;33:801-810) suggest that this can be separated into three or more subgroups by mucin histochemistry, and that metaplastic epithelium containing sulfated mucosubstances is more likely to be associated with an adenocarcinoma.

Thompson and co-workers found that adenocarcinoma arising at the gastroesophageal junction area but not associated with Barrett's esophagus has epidemiologic features in common with adenocarcinoma in Barrett's esophagus. This interesting observation has been the subject of two recent abstracts (Lab Invest 1982;46:44A; Gastroenterology 1981;80:1264) and confirms observations made over ten years ago by MacDonald (Cancer

1972;29:724-732). The lower 1-2 cm of the esophagus is normally lined by columnar epithelium (Thorax 1961;16:36-41), but in individuals with Barrett's esophagus, this lining extends proximally above the usual position of the squamocolumnar junction and becomes recognizable by endoscopy as a columnar epithelial lined esophagus. One could speculate that adenocarcinomas of the gastroesophageal junction area that are not associated with a Barrett's esophagus arise through a process of intestinal metaplasia and dysplasia in the normal esophageal columnar epithelium, just as they apparently do in Barrett's epithelium and in the stomach.

The authors make interesting speculations about the pathogenesis of Barrett's esophagus, and about why surgical therapy fails to cause its regression. I urge you to read this important contribution to the literature on Barrett's esophagus.

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Pathologist-in-Charge of
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Baptist Memorial Hospital
Clinical Associate Professor
of Pathology
University of Tennessee Center
for the Health Sciences
Memphis, Tennessee

Whipple's Disease: Scourge of the Western World

David F. Keren, M.D.

Significant advances in Whipple's disease have been relatively slow in their appearance. Since its original description in 1907 by George Hoyt Whipple, there have really been only a handful of major useful discoveries about this fascinating disease. It was clear from Whipple's original description that this was a systemic disease and was probably related to a rod-shaped microorganism. The discovery that the foamy macrophages stained with PAS provided a useful histologic marker for tissues involved with Whipple's disease.

The most significant finding was that antibiotic therapy could cure Whipple's disease, but that it had to be used for long periods of time. The next most significant finding was the description in the same year by Yardley and Hendrix (1) and Chears and Ashworth (2) of encapsuled bacilliform bodies in the involved tissues of Whipple's disease patients.

There has been considerable difficulty in culturing a single agent from patients with Whipple's disease. Further, there have been no reproducible animal models of the disease. Consequently, there was controversy as to whether Whipple's disease was due to an immune defect allowing infection by a wide variety of bacteria or whether Whipple's disease was due to a single bacteria perhaps with a subtle defect in the immune system. This question was largely answered by the finding that the foamy macrophages in patients with Whipple's disease react with a constant staining pattern (Table 1) when stained with a variety of bacterial grouping sera (3). Immunoelectron microscopic studies have demonstrated that these antisera are staining the actual microorganisms themselves within the foamy macrophages (4). This staining pattern has been confirmed by several other reports (5-7).

Most recently, Du Boulay (8) using a sensitive immunoperoxidase technique has demonstrated that if one dilutes the bacterial grouping serum sufficiently, only the group B streptococcal antisera cross react with the foamy macrophages of Whipple's disease. However, she was not able to absorb out the staining activity with the Group B streptococcus itself. This raises questions regarding the specificity of the reactivities. However, it is clear that the immunofluorescent pattern is of great importance in confirming foamy macrophages as being due to Whipple's disease versus, for instance Mycobacterium avium as has been recently reported in cases of AIDS syndrome (9).

Lastly, there has been evidence suggesting an immune deficit in patients with Whipple's disease. Reports have variously described almost total energy in this population (10,11) to other reports where the cell-mediated immune function even in active Whipple's disease was relatively normal (12). Further, it is also clear that at least some patients with

TABLE 1

INTENSITY OF MACROPHAGE FLUORESCENCE WITH ANTIBACTERIAL SERA

	Whipple Cases				Normals	
Antisera to	Keren 1 2 3	Kirkpatrick 4	Kujada 5	Bhavgavan	1 2 3	Celiac-like
Salmonella polyvalent	0 0 0	-	0	0	0 0 0	0
Shigella A	0 0 0	-	0	0	0 0 0	0
Shigella B	3 3 4	3	-	3	0 0 0	0
Streptococcus group A	3 3 3	2	4	3	0 0 0	0
Streptococcus group B	3 3 3	4	2	3	0 0 0	0
Streptococcus group C	1 3 2	2	3	0	0 0 0	1
Streptococcus group D	1 2 1	-	2	0	0 0 0	0
Streptococcus group F	0 1 1	-	3	0	0 0 0	0
Streptococcus group G	4 4 4	4	4	4	0 0 0	0

Whipple's disease have normal cytotoxic functions of their mononuclear cells (10). It is most likely that patients with Whipple's disease do suffer from a subtle defect in their cell-mediated immune response to a particular microorganism (or family of microorganisms) which prevent adequate activation of macrophages for intracellular killing.

In summary, progress in Whipple's disease has been slow but is being made. The advent of immunohistochemical staining for bacterial antigens is highly useful to the diagnostic pathologist. It can be performed even on formalin-fixed, paraffin-embedded tissues (4,7). Future research efforts in Whipple's disease will likely be helped by the recent availability of monoclonal antibody technology and fluorescent activated cell sorters. These tools will help direct studies to the subtle immune response defect likely responsible for the overwhelming infectious disease seen in these patients.

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Editor's Comment:

The readers undoubtedly will have noted that there are 33 separate authors listed in Dr. Keren's bibliography, and several authors appear multiple times. This prompted a quick review of the English-language literature on Whipple's disease to determine the case/author indices. There were 32 separate reports covering 113 total cases, probably many of which were reported multiple times. These 32 reports were written by 115 authors, again several of whom were repeaters or chronic offenders, depending upon your orientation. In fact, three of the Club members have accounted for at least 10 of these authors, a remarkable feat of literary manipulation. Needless to say, these data may be evaluated in a number of ways. For instance, there is a 1:1 case:author ratio based upon 113 cases and 115 authors. However, there is also a 2:3 case:author ratio (0.67) if the median members of authors and cases are used for all the reports, clear evidence of what we had expected all along, namely that no single author, in general, is ever allowed to have his own private case of Whipple's disease. Then, there is a more personalized version of the indices. Dr. Yardley has been involved in the reporting of 8 cases by 13 authors, an index value of 0.62, almost identical to that from the literature at large. Dr. Keren, however, in an effort to "one-up" his mentor, contributed to the reporting of 10 cases by 19 authors, an index of 0.53, a figure well on the way to the desired level of ½ case of

Whipple's disease per author. Finally, Dr. Dobbins, in an attempt to reverse the 1 case, 1 author ratio has assisted in the reporting of 41 cases by only 10 authors, a dismal index of 4:1, a number for which he should be ashamed. Imagine, his attempting to establish a trend of fewer than 1 author per case of Whipple's disease. We are recommending that he be tarred and feathered and ridden out of the Club on a rail.

The Club Marches On

(Reflections of an almost ex-past-president)

Harvey Goldman

Do you remember the small seminar room at the 1979 IAP meeting in San Francisco, being exhorted by Henry (did he ever sit down?) to share our polyps and mucin stains or, at least, our dues? After a few hundred votes and applying our names to all those yellow pages called committees, we were committed (?differentiated?) and on our way. By 1982, the IAP hierarchy realized, because they couldn't get in, that GI was for real and needed the biggest room.

By 1984, as further evidence that Orwell was off the mark, the GPC will extend its educational activities to the clinical GI meeting and to the IAP congress, the programs of which are listed in this newsletter. After seemingly endless, but actually routine, negotiations with the clinical groups, we are now part of the Digestive Disease Week and hopefully this will be an annual event. It will afford us the opportunity to develop alternative scientific sessions and to work more closely with the clinician-morphologists who have been so supportive of our club.

In creating a symposium for the IAP Congress, we managed to parlay our effort and joined forces with our sibling groups in Britain and France. Take a look at the Congress menu--only our symposium is genuinely international. But, we wish to add a further step at the meeting by offering a reception for all groups and persons interested in GI pathology. At the time, we can explore the potential for future, collaborative efforts by the various societies. The reception is tentatively scheduled for Wednesday, September 5 at 6:00 p.m. (or 1800, if you prefer); final plans will be provided at our March meeting. For all Club members who will be attending the Congress, and for all who will be passing by to and from the Epcot Center, please come and help to host the reception, and maybe, start another five-year plan. Henry, bring the yellow sheets.