

## 1 Collagenous Colitis: Epidemiology, Associated Diseases, and Medical Therapy

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During the years 1992/1993, data on patients with collagenous colitis have been collected from most parts of Sweden. By the end of 1993, data on 113 patients were available. Epidemiological figures, associated diseases of inflammatory or autoimmune origin, and experience of medical treatment based on a retrospective analysis are presented.

**Results.** Distribution of patients: 96 women (85%), 17 men (15%). Mean age at diagnosis: 54 years (18–85 years). Prevalence in the Örebro area on Dec 31, 1993: 16.4/10<sup>5</sup> inhabitants (95% CI; 10.4–22.4/10<sup>5</sup>).

Associated diseases: Rheumatoid arthritis, 15 pat (13%); Thyroid disorders, 14 (12%); Celiac disease 6 (5%); among other diseases of inflammatory or autoimmune origin, diabetes mellitus, bronchial asthma, IBD, Sjögrens disease and psoriatic disease were represented.

**Treatment:** Out of 74 patients treated with sulphasalazine, 37 benefitted from this treatment, 9 had no effect, and 28 patients were intolerant. All 9 patients treated with some kind of penicillin responded. 18 of 28 patients treated with metronidazole, and 6 of 9 treated with erythromycine responded. Prednisolone had effect in 24 out of 27 patients.

**Conclusions.** Distribution of sex and age are in agreement with earlier reports. We estimate the prevalence to 16.4/10<sup>5</sup> inhabitants.

Our data confirm that collagenous colitis is associated with diseases of inflammatory or autoimmune origin.

Retrospective evaluation of different medical treatments, shows that treatment with sulphasalazine should have first priority, though a considerable number of patients are intolerant. Antibiotics often have beneficial but no sustained effect. Prednisolone is effective, and can be used for short term treatment.

## 2 Endoscopic Findings in Seropositive and Seronegative Asymptomatic Blood Donors According to Helicobacter Pylori (HP) Status

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We have reported an high frequency of peptic ulcer in 241 HP sero+ve asymptomatic donors. We now report the endoscopic findings of the total sero+ve population enrolled (n = 298) and those observed in 61 HP sero-ve asymptomatic donors who gave informed consent to endoscopy. Endoscopy was offered to 366 sero+ve and 111 sero-ve asymptomatic donors. After interviewing 298 HP +ve (81%) (M/F: 173/125; age range 18–65; mean 45 yrs) and 61 HP -ve (55%) (M/F 46/15; age range 18–65; mean 42 yrs) underwent endoscopy. Antral biopsies were taken for CP-TEST, culture and histology. IgG to HP were re-assessed.

**Results:** The endoscopic findings in the 298 sero+ve and 61 sero-ve donors were show in the table (N = endoscopically normal, AG/AE antral gastritis and/or erosion, ED = erosive duodenitis, U = ulcer, GC = gastric cancer)

	N	AG/AE	ED	U	GC
sero +ve	46	139	41	70	2
sero -ve	38	20	3	0	0

In 274 out of 298 (92%) sero+ve colonization was confirmed by Giemsa, CP-TEST and/or culture and high levels of IgG. In all of them active on chronic histological gastritis was found. Twentyfour subjects (8%) were not colonized by HP assessed by all the four methods. Two only out of 61 (3%) HP sero-ve were found to be colonized by HP assessed by Giemsa, CP-TEST and/or culture. In both of them active on chronic histological gastritis was found. Fifty-nine (97%) were not colonized by HP assessed by all the four methods, and no active on chronic gastritis was found. The sensitivity (SN) and the specificity (SP) of the tests are shown in the table (Giemsa = Gold Standard).

	Giemsa	CP-Test	Culture	IgG
SN (%)	100	98.6	82.8%	100
SP (%)	100	100	100%	92.8

**Conclusion:** We confirm in this larger population the high prevalence (24%) of peptic ulcers in sero+ve compared with none in sero-ve asymptomatic subjects. Our prospective data indicate the reliability of IgG for the diagnosis of HP infection.

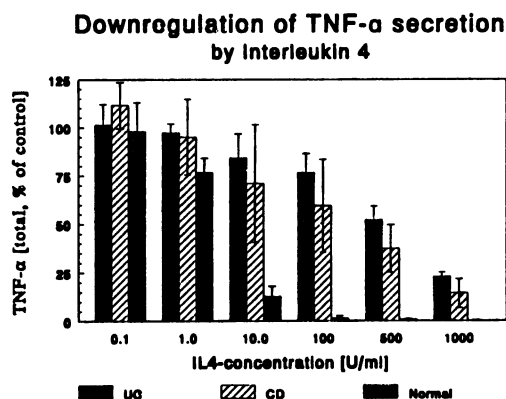
## 3 Impaired Deactivation of Intestinal Lamina Propria Macrophages by IL-4 in Inflammatory Bowel Disease

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**Introduction:** Active inflammatory bowel disease (IBD) has been shown to be associated with increased priming and activation of peripheral as well as intestinal monocytes/macrophages.

**Methods:** Lamina propria mononuclear cells were isolated from colonic biopsies by collagenase digestion. The state of activity was determined by the capacity to secrete proinflammatory cytokines (TNF- $\alpha$ , IL-1 $\beta$ ), the IL-1-receptor antagonist (IL-1ra) or superoxide anions after stimulation with FMLP. TNF- $\alpha$  and IL-1- $\beta$  gene transcription was studied by semiquantitative polymerase chain reaction. The presence of IL-4 receptors (IL-4-R) was assessed by ligand binding studies with <sup>125</sup>I-rIL4.

**Results:** The secretion of TNF- $\alpha$ , IL-1 $\beta$  and superoxide anions is increased in IBD intestinal macrophages in comparison with normal controls. IL-4 deactivates both IBD and normal intestinal macrophages in a dose dependent manner and specifically inhibits IL-1 $\beta$ , TNF- $\alpha$  and superoxide anion generation. In addition, secretion of IL-1-ra is induced by IL-4. However, IBD macrophages require 50–100 fold greater amounts of IL-4 in comparison with normal controls to induce similar levels of inhibition. We addressed the mechanism of this defect by determining TNF- $\alpha$  and IL-1- $\beta$  mRNA levels. IL-4 induced downregulation of pro-inflammatory cytokine secretion in IBD macrophages is defective at the transcriptional level. In addition, IBD monocytes express less IL-4-R on their surface than normal monocytes. As an additional control we employed IL-10 and found no defects in dose dependent downregulation of IBD intestinal macrophages.



**Discussion:** IBD intestinal macrophages are in an enhanced state of activation in comparison with normal cells. The increased levels of pro-inflammatory cytokine secretion (TNF- $\alpha$ , IL-1 $\beta$ ) and superoxide release can be downregulated by IL-4. However, in comparison with normal cells IBD intestinal macrophages need 50–100 fold greater amounts of IL-4 for level of downregulation similar to normal cells. A diminished number of IL-4-receptors may contribute to this defect in IL-4 induced deactivation of IBD macrophages which may be caused by a decreased downregulation of TNF- $\alpha$  and IL-1- $\beta$  gene transcription. The defect is specific to IL-4 as IL-10 deactivates IBD and normal monocytes/macrophages with similar dose response characteristics.

## 4 Laparoscopic Nissen Fundoplication; Clinical and Radiological Evaluation

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Between January 1991 and July 1993, 357 patients underwent laparoscopic anti reflux surgery for gastroesophageal reflux disease. Conversion to conventional laparotomy was required in 5 patients. 2 patients with severe persistent dysphagia were reoperated 6 months after the initial procedure. At the time of study (March 93); 111 patients presented with a minimum follow-up period of 12 months. (median 16.2 months, range 12 to 26 months). 63 patients volunteered for clinical evaluation and radiological study. 3 patients were previously submitted to endoscopic dilation for persistent dysphagia and presented without symptoms. 3 patients (4%) had occasional dysphagia when swallowing some types of food. 9 patients (14%) noticed a modification of their swallowing habits. Upper gastro-intestinal barium studies were normal in all patients. There were 3 symptomatic recurrences of gastroesophageal reflux (4.8%); the upper GI series were abnormal (1 slipped Nissen, 1 too large (?) valve, 1 disrupted valve). 8 patients complained of gaz bloat syndrome,

4 reported frequent hiccup. 51 patients maintained the ability to belch. Excellent or good results (Visick grade 1 and 2) were obtained in 55 patients (88.7%). The main reason for unsatisfaction was abdominal meteorism. Radiological evaluation demonstrated normal continent valve, without stenosis in 50 patients (80%). 6 patients had an intrathoracic wrap without symptoms. 6 patients had a partially or completely disrupted valve. 1 patient had a slipped Nissen. The radiological findings corresponded to the described symptoms in 60 patients (95%). Twenty four hours pH monitoring is the more sensitive and sensible to detect gastroesophageal reflux.

However, upper GI barium series is certainly more easily accepted by the patients and may help in selecting the patients who will need further evaluation.

These results of the early experience with laparoscopic antireflux surgery are encouraging.

## 5 Combined Liver/Small Intestinal Transplantation in Children

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A small group of patients with intestinal failure will develop total parenteral nutrition (TPN) induced liver failure. The only therapeutic option that offers the potential for long term survival is combined liver/small intestinal transplantation (L/ITX). Over the past 4 years, we have performed 5 L/ITX in 5 children. During this same time period, 6 other patients with TPN induced liver failure died awaiting transplantation (average 106 days; range 20-261). Donors were pretreated with antilymphocyte therapy & bowel prep (mechanical and antibiotics). The average cold ischemia time was 8 hours. All patients received a composite graft of liver and small intestine only; arterialization of the graft was provided through an aortic conduit. The recipient portal vein was anastomosed end-to-side to the donor portal vein. Donor and recipient intestine were anastomosed proximally with the distal end of the donor bowel brought out as a terminal ileostomy. Immunosuppression consisted of induction therapy with OKT3 combined with cyclosporine and prednisone ( $n = 3$ ) and FK506 ( $n = 1$ ). One patient was converted to FK506. Infection prophylaxis consisted of acyclovir, immunoglobulin, and intravenous Amphotericin B. Three patients were able to discontinue TPN; 4, 5, and 15 weeks postoperatively. Histologic evidence of rejection was present in 3 patients precipitating the removal of the intestinal allograft in 1 patient and conversion to FK506 in another. In another patient necrotizing arteritis precipitated the removal of the small bowel allograft. There was no clinical evidence of graft vs. host disease in any of the patients nor has any patient developed a post transplant lymphoproliferative disorder. Motility studies were performed in 1 patient demonstrating normal migratory motor complexes. Survival of the 5 patients was 811, 390, 368, 80 and 7 days; 2 of the patients have died. *Conclusion:* Our experience with L/ITX demonstrates the relative safety and effectiveness of this procedure. The major obstacle to its application is a lack of suitable donors.

## 6 Intraoperative Peroral and Transpapillary Cholangioscopy

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1090 Intraoperative cholangioscopies and 14 transpapillary cholangioscopies were performed between 1975–1993. Most frequently (820 patients) cholangioscopy was performed for choledocholithiasis and for (708 patients) cholangitis. In the remaining patients we diagnosed: duct neoplasms, non-neoplastic obstructions, iatrogenic damages or bile ducts cysts. The results of intraoperative cholangioscopy were compared to those of intraoperative cholangiography and ERCP. We observed that the effectiveness and sensitivity of cholangioscopy was higher as compared to radiological findings. Youden index for the bile ducts diseases in case of cholangioscopy ranged from 0.96 to 1.0, while in case of cholangiography or ERCP from 0.01 to 0.69. Peroral transpapillary cholangioscopy was performed after endoscopic papillotomy. The indication for the examination was suspected bile ducts neoplasm and extrahepatic ducts obstruction. Obtained results recommend cholangioscopy as the most effective method in diagnosing bile ducts diseases.

## 7 Clinical Results of the Rectoscopic Surgery

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Surgical intervention in the middle or upper region of the rectum is technically difficult because of the anatomical inaccessibility of the site. We have developed a practical rectoscopic technique using a Buess' transanal endoscopic microsurgery system, and applied this for 30 patients with 15 creeping

adenomas, 14 rectal carcinomas and a rectal carcinoid. Performing such rectoscopic surgery is less aggressive than other procedures. In all cases, the postoperative course was uneventful, with no complication and the patient was discharged at the latest on the eighth day after the operation.

This technique for rectoscopic surgery involves minimal intervention and short hospitalization.

## 8 Biliary Stones Lithotripsy. Comparison of Different Methods

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"Difficult" bile duct stones are defined those whose conventional endoscopic treatment is unable to clear them from the common bile duct. We have compared our experience on Electrohydraulic lithotripsy (EHL), External shock wave lithotripsy (ESWL), Alexandrite laser lithotripsy (ALL), Mechanical lithotripsy (ML) and solvent dissolution with MTBE.

42 patients with "difficult" bile stones were treated with these methods singly or in combination, eventually with a percutaneous endoscopic approach and according to the availability of the methods. When all the methods failed to clear the stones from the bile ducts, a biliary endoprosthesis was inserted.

*Results* The first treatment for all the patients was as follows, after diagnostic ERC, ES and nasobiliary drainage:

MTBE	5	failure 3
ML	16	failure 8
EHL	9 (5 PTC)	failure 2
ALL	5	failure 4
ESWL	7	failure 3

Stones' clearance was achieved in 38 pts. 4 pts had biliary endoprosthesis. No deaths were seen. Related complications were 1 after MTBE and 1 after ML. The patients with endoprosthesis are well after 2 years of follow-up.

*Conclusions* The results of the different methods depend on stones' composition. EHL is the method with the significantly better results while ML results depend on technical problems.

## 9 Submucosal Fibrin Adhesion – Early Elective Endoscopic Therapy for Treatment of Ulcer Bleeding

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Submucosal Fibrin Adhesion (SFA) has proved an effective therapy for ulcer hemorrhage. Together with the concept of early elective endoscopy (that means close endoscopic follow-up and postadhesions until the stigmata have disappeared and the ulcerground is clean) it is more effective than thermal and sclerosing techniques. The aim at the initial bleeding is (1) the hemostasis, (2) additionally, a clear endoscopic improvement must be seen that means: the visible vessel thin, submucous clots around, ulcerground swollen. SFA does not induce tissue destruction, as histological examination shows. That's why the new concept of early elective endoscopic therapy by postadhesions could be developed. Early elective endoscopy means: (1) close endoscopic follow-up and (2) postadhesions until the ulcer ground is clean. Our results in more than one thousand bleeding patients from 1987 to 1993 show low rates of relapse bleedings (<1%), of urgent surgery (<1%), or mortality related to the bleeding (<1%). About 40% of the patients treated so far needed repeated application of fibrin glue, because of persisting stigmata, thus clearly indicating the high risk that a rebleeding occurs during the period of three days that follow a bleed. The frequency of postadhesions cannot be predicted. This way, a new concept of early elective endoscopy with prophylactic treatment of bleeding stigmata (esp. the visible vessel) has been established and has to be compared with the concept of early elective surgery.

*Conclusion:* SFA offers an effective, nonoperative treatment for ulcer hemorrhage, even for patients at high risk (high age, severe underlying diseases). Special care should be given to the purely technical details of handling the DUO-probe and the adhesive. Precondition, furthermore, is the strict maintenance of close endoscopic follow-up (daily!) and postadhesions.

The VIDEO shows the technique, handling of probe and material, special examples of treatments, difficulties and pitfalls of the method, our results as a summary.

## 10 Endoscopic Diagnosis of Colon Hamartoma in an 8-Month-Old Infant

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Colon hamartoma is a very rare tumor which is revealed with age. We ob-