175 The Effect of Octreotide (OT) on Meal-Stimulated Gallbladder (GB) Emptying in Control Subjects and Acromegalic Patients

S.H. Hussain, S.P. Pereira, C. Kennedy 1, P. Jenkins 2, G.M. Murphy, J.A.H. Wass 2, R.H. Dowling. Gastroenterology Unit, Guys Hospital & Campus, UMDS, St Bartholomew’s Hospital, London, England; 1 Dept of Radiology, Guys Hospital & Campus, UMDS, St Bartholomew’s Hospital, London, England; 2 Dept of Endocrinology, St Bartholomew’s Hospital, London, England

Background: Up to 60% of acromegalic patients treated with octreotide develop GB stones – in part because of impaired GB emptying – but there is controversy about the influence of acromegaly itself on GB motor function, and whether the OT-induced dysmotility affects fasting (FV) or residual (RV) GB volume, the extent of GB emptying (ejection fraction or EF), and the delta volume or DV—that is, FV minus RV or the rate of GB emptying (RGE in ml/min).

Methods: To study this, we used a randomised, double-blind, placebo (saline)-controlled, cross-over design to examine the effects of a single dose (50 µg) of OT given sub-cut 30 min before a fat-rich liquid meal (“Ensures”), on all 5 parameters of GB emptying, assessed by ultrasound, in 6 non-acromegalic control subjects and 8 stone-free non-OT treated acromegalic patients. Results: Before OT, the fasting GB vol in the acromegalic patients (49.8 ± SEM 7.1 ml) was more than 3 times that in controls (15.8 ± 1.9; p < 0.005), but in response to the fatty meal, acromegalic GBs emptied faster (RGE 0.97 ± 0.19 vs 0.26 ± 0.04 ml/min; p < 0.005) and to a greater extent (DV 33.8 ± 6.5 vs 9.5 ± 1.2 ml; p < 0.005) than did those of the controls, and while the % GB emptying was also slightly greater (EF 74.3 ± 2.4 vs 66.3 ± 2.3%; p < 0.03), the RV in the acromegals (10.9 ± 1.2 ml) was still more than twice that in the controls (5.0 ± 1.0 ml; p < 0.02). OT markedly inhibited meal-stimulated GB emptying in the acromegicals with significant reductions in the DV (to 10.7 ml; p < 0.02), EF (to 23.1%; p < 0.002) and the RGE (to 0.44 ml/min; p < 0.02) and a significant increase in the RV (to 38.8 ml; p < 0.002), but OT’s effects were even more marked in the controls, where it completely abolished GB emptying. Summary/conclusions: These results confirm that acromegalic patients have cholcysto-megaly (larger GBs) than controls and show that in response to a meal, their GBs expel a greater than normal volume of bile (DV and EF) more rapidly than normal (RGBE) but despite this, are left with increased residual GB volumes. OT inhibits GB emptying more in controls than in acromegalic patients and since chronic OT treatment induces GBs, this suggests that the residual volume is more important than the speed of GB emptying, or the amount of bile expelled, in the pathogenesis of GBs.

176 Cholelithiasis in Diabetes Mellitus: Predisposing Factors

A. Golids, I. Sporea, C. Vernic, R. Strain. Gastroenterology Unit, University of Medicine Timisoara, Romania

The aim of our work was to study factors concerning the increased prevalence of cholelithiasis (CL) (gallstones or previous choledocholecystectomy) in adult subjects with diabetes mellitus (DM).

Materials and methods: 2000 DM patients: 1227(61.35%) females and 773(38.65%) males consecutively hospitalised in our Department with an average age of 58.34 ± 11.43 years were prospectively investigated.

Results: Among the 2000 DM patients, insulin-dependent DM (IDDM) was present in 353(17.65%) subjects and 49 (13.86%) of them presented CL, whereas among the 1647 (82.35%) non-insulin-dependent DM (NIDDM) patients, 401 (24.35%) presented CL, the difference between the 2 CL prevalences being statistically significant (p < 0.01). Overall 450(22.5%) of the DM patients had CL (154 gallstones and 296 previous cholecystectomies). After adjustment for age, body mass index and sex, using multiple logistic regression, the overall prevalence of CL in our DM patients was 22.1%.

Further on we calculated OR = odds ratio (95% confidence interval) concerning the risk of appearance of CL for the following risk factors:

- DM: IDDM-OR = 0.50 (0.36 < OR < 0.70); NIDDM-OR = 2.00 (1.43 < OR < 2.78).
- Duration of DM: under 10 years-OR = 0.88 (0.70 < OR < 1.10) and over 10 years-OR = 1.14 (0.91 < OR < 1.43).
- Sex: females-OR = 3.05 (2.36 < OR < 3.95) and males-OR = 0.33 (0.25 < OR < 0.42).
- Obesity-OR = 1.91 (1.48 < OR < 2.46).
- Hyperlipoproteinemia (HLP)-OR = 1.16 (0.95 < OR < 1.35).
- Age: under 50 years-OR = 0.61 (0.48 < OR < 0.78) and over 50 years-OR = 1.64 (1.20 < OR < 2.16).

Conclusions: In our study, the factors which seem to determine the increased prevalence of CL in DM, are: NIDDM, female sex, obesity, age over 50 years, HLP, duration of DM over 10 years.

177 Colonoscopic Screening in First-Degree Relatives of Patients with Colorectal Cancer (CCR): A Prospective, Multicentre, Case-Control Study

E.A. Pariente, J. Lafon, C. Milan. Cooperative work of the Association des Gastroentérologues des Hôpitaux non universitaires and of the Registre Bourguignon des Canccrs Digestifs

First-degree relatives of patients with common CCR carry an increased risk of CCR. Feasibility and efficiency of colonscopy in this group are however not well defined.

The 488 first-degree relatives (R), aged from 40 to 75 years, of 196 patients with common colorectal cancer examined in 16 French general hospitals were invited to a colonoscopic screening. Each examined relative was matched by center with two controls (C) for sex, age and symptoms. Logistic regression taking into account of sex, age, center, and group (R or C) was used to determine the risk of colorectal tumor.

186 relatives (38% of total group), of mean age 54 years, were examined. Odds ratios (OR) for colorectal tumors observed in R vs C, adjusted for center, sex and age were as follows: adenomas OR = 1.5 (95% CI: 1.0-2.4); adenomas <1 cm OR = 1.2 (95% CI: 0.7-1.9); adenomas >1 cm OR = 2.5 (95% CI: 1.5-5.4); adenomas with villosus structures OR = 2.8 (95% CI: 1.0-7.9); adenomas with moderate to severe dysplasia OR = 3.1 (95% CI: 0.9-10.1); carcinoma OR = 7.2 (95% CI: 1.4-37.8).

Sex and age were preeminent risk factors for adenomas in R and C, but R seemed to be more prone to high risk adenomas (>1 cm, villosus structure, moderate to severe dysplasia) or cancer.

In conclusion, a history of CCR in a first-degree relative must be taken into account in CCR screening policy. Genetic predisposition to common CCR might concern adenomas growth.

178 Polypectomy of Adenomas in the Prevention of Clinical Colorectal Cancer. 10 Years Follow Up of a Prospective, Controlled Polyp Population Study in Telemark, Norway

G. Hoff, J. Saau, M.H. Vatn, S. Larsen, F. Langmark. Telemark Central Hospital, Skien; National Hospital of Norway, Oslo; Medstat Research, Lillestram; Norwegian Cancer Registry, Oslo

400 men and women aged 50-59 years (20 of each sex from each year of age) were randomly selected from the population registry of the municipalities of Porsgrunn and Skien in the county of Telemark, Norway, to be offered a screening examination of the rectum and sigmoid colon using a colonoscope. An equal control group was similarly drawn from the same registry. 324 individuals (81%) attended for the initial screening examination in 1983.

A finding of polyps qualified for full colonoscopy.

In the screening phase of the study neoplasms were found in 57 individuals, including one case of Dukes’ stage A carcinoma, two cases of intramucosal carcinoma and one individual with severe dysplasia in an adenoma. Controls were not at stage invited to have a screening examination.

After 10 years, information invited to the Norwegian Cancer Registry has revealed presence of no new carcinomas in 324 attending for screening, one case in 76 not attending and 5 cases in the control group of 400 individuals. All cases of new carcinomas were diagnosed due to symptoms and not in the course of screening. 3 of the 6 cancer patients have died from their cancer. As far as we know, this is the first prospective, controlled study regarding the benefit of polypectomy in cancer prevention.

179 Diagnostic Value of Somatostatin Receptor Scintigraphy in Neuroendocrine Tumors

P. Tomassetti, B. Bellanova 1, N. Monetti 1, E. Del Vecchio, P. Faccoli, A. Pirazzoli, L. Guillo, L. Barbara. Institute of Medical Clinic, University of Bologna, Italy; 1 Gastroenterology and Nuclear Medicine Department, University of Bologna, Italy

Somatostatin receptor scintigraphy with 111 In-pentetetide, (Octreoscan 111), is a technique recently proposed for demonstrating the presence of receptor positive neuroendocrine tumors and their metastases. We performed this technique in 20 patients: 12 males and 8 females, ranging in age from 21 to 68 years; all patients had biochemical and/or histological diagnosis of neuroendocrine tumor (16 gastrinomas, 1 pancreatic somatostatinoma with hepatic metastases, 1 carcinoid with hepatic metastases, 1 medullary carcinoma of thyroid, and 1 nonfunctioning pancreatic islet cell tumor with hepatic metastases). Nine of the 16 patients with gastrinoma had familial multiple endocrine neoplasia type 1 (MEN I). One of these nine patients had a pancreatic gastrinoma with liver metastases and massive carcinoid proliferation of the gastric body. Each patient was studied at 4, 24 and 48 hours after injection of 180-220 MBq of Octreoscan 111 (Malinckrodt Diagnostica, Petten Holland). Total body planar imaging was performed using a Philips gamma camera (Gammadiagnost TOMO) equipped with a medium energy parallel
The Putative Mucosal Homing Receptor Integrin B7 is Upregulated in Human Intestinal Lamina Propria Compared with Peyer’s Patches and Appendix

I.N. Farstad, T.S. Halstensen, J. Norstein, P.J. Kihlshaw, P. Brandtzæg. Lab. of Immunohistochemistry and Immunopathology, The National Hospital, Oslo, Norway; Inst. of Pathology, The National Hospital, Oslo, Norway; Surgical Dep. B, The National Hospital, Oslo, Norway; AFRC Babraham Institute, Cambridge, CB2 4AT, England

Introduction. The integrin B7 may be coupled to a4 as the putative mucosal homing receptor a4B7, or to a2 as a2B7. a4B7 has been identified as a main Peyer’s patch homing receptor in mice partly because one of its ligands, MadCAM-1, is expressed by Peyer’s patch high endothelial venules. In this study we have compared the expression of integrin B7 in human small intestinal lamina propria with Peyer’s patches and appendix to evaluate its putative role in directing lymphocytes to these sites. Materials and methods. We have used a MoAb to mouse B7 that also recognizes human B7. Flow cytometry was performed on cells isolated from jejunal lamina propria (n = 7) and appendix (n = 5), including Raji cells as a positive control. Cytochemistry and immunostaining for normal jejunal (n = 2) and colicel (n = 2) mucosa, and from ileum containing Peyer’s patches (n = 2), were subjected to two- or three colour immunohistochemistry. Results. In flow cytometry, Raji cells as well as a fraction of lamina propria cells (median 37%, range 17–53%) expressed B7. In contrast, <5/10 appendix cells were B7+. Immunohistochemistry showed most intraepithelial (90%) and many lamina propria (40–50%) cells to be B7+; intra- and subepithelial cells showed highest staining. MoAb to B7 reacted mainly with T cells of memory phenotype. In Peyer’s patches scattered cells in the domes and interfollicular (T) cell zones were B7+

Conclusions. Integrin B7 is expressed primarily on T cells and much more frequently by lamina propria than by Peyer’s patch and appendix lymphocytes. This difference might be explained by the higher proportion of memory T cells in lamina propria. Integrin B7 could therefore be an important homing receptor for T cells primed in Peyer’s patches or the appendix and destined for distant lamina propria.

Gut-Specific, HLA-DQ-Restricted Small Intestinal T Cells Secrete Cytokines That May Explain Several Features of the Coeliac Lesion

E.M. Nilsen, K.E.A. Lundin, P. Krajci, H. Scott, L.M. Solliød, P. Brandtzæg. 1) Laboratory for Immunohistochemistry and Immunopathology (LIPIAT), Institute of Pathology, Oslo, Norway; 2) Institute of Transplantation Immunology (ITI), University of Oslo, The National Hospital, Rikshospitalet, N-0027 Oslo, Norway

Coeliac disease (CD) is precipitated in susceptible individuals by ingestion of wheat gliadin or other gluten-related prolamins from various cereals. The disease is strongly associated with certain HLA-DQ heterodimers, DQ2 (DQα1*0501, DQβ1*0201) in most patients and apparently DQ8 (DQα1*0301, DQβ1*0302) in a small subset. T-cell recognition of gluten peptides presented by such class II molecules may be immunopathogenically important. We recently established HLA-DQ-restricted, gluten-specific T cell clones (TCC) from the small intestinal mucosa of CD patients, and have now examined their antigen-induced secretion of cytokines. Altogether fourteen TCC (DQ2- or DQ8-restricted) from three patients were investigated. Cell culture supernatants were prepared by stimulation with gluten peptides in the presence of DQ2α or DQ8α EBV-transformed B cells as antigen-presenting cells. Supernatants were analyzed for cytokines by bioassays, ELISA, and CELISA. Cellular cytokine mRNA was analyzed semiquantitatively by Northern blotting and PCR. All TCC were found to secrete large amounts of IFN-γ. The DQ2-restricted TCC produced small amounts of IL-4 but no IL-5 or IL-6, and some of them produced in addition TNF-α; this profile is typical of Th1-like cells. Conversely, the DQ8-restricted TCC secreted in addition to IFN-γ substantial amounts of IL-4, IL-5, IL-6, and TNF-α, a pattern more compatible with Th2-like cells. Very little IL-2 was found in the supernatants from all the TCC but could be readily detected by mRNA analysis. The cell supernatants from both varieties of gluten-stimulated TCC induced upregulation of HLA-DR and secretory component (SC or poly-Ig receptor) in the colonic adenocarcinoma cell line HT-29. The characterized cytokine profiles thus substantiated the possibility that mucosal T cells activated in situ by gluten in a DQ-restricted fashion play a central role in the pathogenesis of CD.

Advantages and Drawbacks of Adding Flexible 60 cm Sigmoidoscopy to Hemocult-II in Screening for Colorectal Neoplasia

O. Kronborg, O.D. Joergensen, C. Fenger. Department of Surgery and Pathology, Odense University Hospital, Odense, Denmark

The aim is to assess benefit and costs of adding flexible sigmoidoscopy (S) to Hemocult-II (H) in asymptomatic persons between 50 and 74 years of age. At random, 3000 persons are invited to H+S and other 3000 to H alone at Funen in Denmark. Other centres within EU are extending these figures, and the final number of 40,000 persons is approached to evaluate the feasibility of screening with H+S. So far, 929 persons have had H+S and H was positive in 25. Colosonoscopy was done in 157, because of positive H (25) or because of polyps found during S. Cancer was found in 4 and adenomas in 91 (91/25=3.7). To detect the H alone, in 1222 persons, resulted in 23 with positive test; until now 20 have had colomocscopy, cancer being detected in 2 and adenomas in 7 (5±1 cm).

In conclusion, no more than 41% accepted H+S, whereas 54% accepted H alone. However, the first strategy resulted in detection of a number of cancers, which may be higher than that for H alone, and the number of large adenomas was significantly higher than that found by H alone. A higher acceptability would be wanted and resources for extended colonscosopy service are needed before embarking upon a mortality study.

3rd UEGW Oslo 1994