● LACK OF INDUCTION OF SUPPRESSOR T CELLS BY GUT EPITHELIAL CELLS FROM PATIENTS WITH INFLAMMATORY BOWEL DISEASE. THE PRIMARY DEFECT?? Lloyd Mayer and David Eisenhardt. Division of Clinical Immunology. Mount Sinai Medical Center New York, N.Y.

We have previously reported the selective induction of $T8^+$ antigen nonspecific suppressor T cells in antigen specific or allogeneic mixed lymphocyte cultures (MLR) containing normal Ia^+ gut epithelial cells as accessory or stimulator cells respectively. Since inflammatory bowel diseases(IBD), ulcerative colitis(UC) and Crohn's disease(CD) may reflect aberrancies in the handling of luminal antigen (i.e. processing and presentation), we sought to determine whether immune responses generated using IBD epithelial cells as accessory cells would be comparable to normal. Twelve patients with CD, 8 with UC, 5 with diverticulitis, 1 with ischemic colitis and 10 normals(cancer, volvulus, polyps) were studied. In contrast to normal epithelial cells, epithelial cells from all patients with CD(12/12) and 6/8 from patients with UC did not preferentially stimulate the $T8^+$ T cell population in MLR (T4/T8 ratios-normal range, 0.2-0.7; CD, 2.4-4.1; UC,1.8-2.8). This finding did not appear to relate to the presence of underlying inflammation in that epithelial cells from patients with diverticulitis and ischemic colitis were capable of selectively stimulating $T8^+$ cells(T4/T8 ratio range 0.3-0.7). Since cell staining may not be an accurate reflection of cell proliferation, T4 and $T8^+$ cells were isolated by panning after 48 hours of MLR cultures with either normal or CD epithelial cells and recultured alone for an additional 72 hours prior to pulsing with ^3H thymidine. There was significant proliferation of $T8^+$ cells in MLR cultures containing normal epithelial cells(stimulation index[S.I.]=33) whereas there was little stimulation of $T8^+$ cells in cultures containing CD epithelial cells(S.I.=3.1). In contrast, the $T4^+$ cells were significantly stimulated in these cultures(S.I.=24.5).

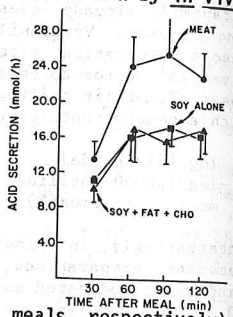
We next assessed the functional capacity of these stimulated cells. As we previously described, T cells stimulated in cultures containing normal epithelial cells significantly inhibited T cell proliferative responses to mitogen and antigen(range 25-90%) as well as B cell maturation. In contrast, T cells stimulated in cultures containing CD or UC epithelial cells significantly augmented T cell proliferative responses(range 20-52%) and enhanced Ig secretion from stimulated B cells. Taken together, these data suggest that there is a defect in the induction of suppressor T cells by epithelial cells from patients with IBD and that this defect may be primary, unrelated to inflammation. Such a defect may result in the unchecked and, in fact, augmented inflammatory response seen in these diseases.

● A VASOACTIVE INTESTINAL PEPTIDE (VIP) ANALOG DISTINGUISHES TWO SUBTYPES OF HIGH AFFINITY VIP RECEPTORS ON GUINEA PIG PANCREATIC ACINAR CELLS. K. McArthur, S. Pandol, J. Rivier. VAMC and UTHSCD, Dallas, TX, UCSD, San Diego, CA and Salk Institute, La Jolla, CA.

Previous studies indicate that guinea pig pancreatic acinar cells possess 2 types of VIP receptors that also interact with secretin. Both the high affinity, VIP-preferring receptor and the low affinity, secretin-preferring receptor are linked to cAMP generation, but only occupation of the VIP-preferring receptor causes amylase release. The VIP analog, $(4Cl\text{-}D\text{-}Phe^6, Leu^{17})VIP$ (PLV), inhibits VIP-stimulated amylase release but not secretin-stimulated cAMP generation from acinar cells. To determine the selectivity of PLV for the high and low affinity VIP receptors, we tested its ability to inhibit binding of ^{125}I-VIP or ^{125}I-secretin to guinea pig pancreatic acinar cells. PLV inhibited binding of ^{125}I-VIP over a wide range of concentrations: inhibition was detectable at 10 pM PLV, half-maximal at 1 uM PLV, and maximal at 30 uM PLV. However, although PLV also inhibited binding of ^{125}I-secretin, inhibition was not detectable until 10 uM PLV or half-maximal until 30 uM PLV. Thus, interaction of PLV with secretin receptors cannot explain the broad range of PLV concentrations required to inhibit binding of ^{125}I-VIP. A broad range of concentrations might be required because PLV occupation of the VIP receptor decreased receptor affinity (negative cooperativity). However, when ^{125}I-VIP bound to acinar cells was allowed to dissociate in the presence of no agents, 10 uM PLV or 1 uM VIP, the percentages of ^{125}I-VIP bound after 90 min were the same, 48 $\pm$ 8, 43 $\pm$ 9, and 41 $\pm$ 7 (mean $\pm$ SD), respectively; thus negative cooperativity was not present. Analysis of the abilities of PLV to inhibit binding of ^{125}I-VIP or ^{125}I-secretin to guinea pig pancreatic acinar cells indicates that there are 3 distinct VIP binding sites; two VIP receptor subtypes with the same high affinity (KD) for VIP but with different affinities for PLV (KD_{R1} = 30 nM PLV, KD_{R2} = 3 uM PLV), and a low affinity, secretin-preferring receptor (KD_{R3} = 30 uM PLV). Thus, $(4Cl\text{-}D\text{-}Phe^6, Leu^{17})VIP$ represents the first VIP-related peptide that distinguishes 2 high affinity VIP receptors in guinea pig pancreatic acinar cells.

● SOY VERSUS MEAT MEALS: LESS GASTRIC ACID SECRETION AND GASTRIN RELEASE WITH EQUIVALENT NUTRITION. K.E. McArthur, C.T. Richardson. VAMC and UTHSC, Dallas, Tx.

Soy protein is a low cost, widely used, nutritious substitute for meat protein. The effect of soy protein on gastric acid secretion is not known. We compared the effects of soy and meat protein on acid secretion and serum gastrin concentrations in 10 normal subjects (6 male, 4 female; ages 22-51 yr). Basal and pentagastrin-stimulated (6 ug/kg) acid outputs were 4.0$\pm$1.0 and 36.2$\pm$2.8 mmol/h, respectively (mean $\pm$ SE). After a 10 h fast, one of the test meals, in random order, was infused into the stomach through a nasogastric tube. The meat meal contained steak, bread and butter [26 g protein, 9 g carbohydrate (CHO) and 19 g fat]. The soy meal contained 26 g soy protein with quantities of bread and butter added to mimic the CHO and fat content of the meat meal. We also studied the effects of 26 g soy protein alone. Acid secretion was measured for 2 h by in vivo intragastric titration to pH 5.0. Serum gastrin concentrations, (Courtesy, Dr.JH Walsh), were determined at -5,0,15,30,60,90 and 120 min in relation to each meal. As shown in the Figure, mean ($\pm$ SE) postprandial acid secretion was significantly lower ($P<0.05$) following the soy meal than the meat meal (30.4$\pm$4.7 and 43.2$\pm$5.6 mmol/2 h for the soy and meat meals, respectively). Average serum gastrin rises were also significantly lower ($P<0.05$) after the soy meal (45.0$\pm$8.3 and 61.7$\pm$13.3 pg/ml for the soy and meat meals, respectively). Soy protein given alone stimulated the same amount of acid secretion (30.7$\pm$4.4 mmol/2 h) but a markedly and significantly lower ($P<0.05$) average serum gastrin rise (15.0$\pm$8 pg/ml) than the complete soy meal. We conclude: Soy stimulates less acid secretion and gastrin release than meat whether given as part of a complete meal or alone. The effects of chronic ingestion of soy protein, as occurs in many parts of the world, on acid secretion and gastrin release remains to be determined.



PREVALENCE OF CAMPYLOBACTER-LIKE ORGANISMS IN PATIENTS WITH GASTRO-ESOPHAGEAL REFLUX DISEASE VERSUS NORMALS. R.W. McCallum, V. DeLuca, B.J. Marshall, C. Prakash., Depts. of Medicine, University of Virginia, Charlottesville, Va., and Griffin Hospital, Derby, CT.

Campylobacter-like organisms [CLO] are associated with peptic ulcer and gastritis, but there is little information on their prevalence in patients with gastro-esophageal reflux disease [GERD], or in normals. To address this issue, we retrospectively examined antral and esophageal mucosa from 21 consecutive GERD patients (20 males, 1 female, mean age 53, range 28-68 yrs), and 20 endoscopically normal, healthy volunteers (13m, 7f, mn. 30, rg. 19-46 yrs). Patients were studied only if they had symptoms and endoscopic findings of esophagitis, abnormal esophageal histology, a positive Bernstein test, and a normal stomach and duodenum. Biopsy specimens were stained with H&E to assess for gastritis, and a with Giemsa stain to demonstrate bacteria.

We found that 75% of GERD patients had histological evidence of gastritis using Whitehead's criteria, compared to 10% of the normals ($p<0.005$). 60% of the GERD patients had CLO identified, compared with 5% of the normals ($p<0.002$). In both groups, gastritis was more common when CLO were detected ($p<0.001$). CLO were not seen in any of the esophageal biopsy specimens. In the GERD group, stimulated acid secretion tended to be higher when CLO were present, (31 versus 16 meq/hr. $p=0.07$).

We conclude that both CLO and histological gastritis are more often present in GERD patients than in normals. We hypothesize that GERD patients may be at higher risk for infection with CLO because of chronic antacid consumption. Alternatively, CLO may be invoked in the pathophysiology of GERD.