● CHARACTERIZATION OF MUCOSAL HLA-DR+ T CELLS IN ULCERATIVE COLITIS (UC) PATIENTS.

K.Kusugami, M.Shinoda, J.Haruta, M.Tanimoto, T.Ando, A.Kuroiwa, T.Matsuura, T.Yamaguchi, H.Yamamoto, T.Hosokawa, M.Ieda, H.Iokawa, and A.Ishihara. First Department of Internal Medicine, Nagoya University School of Medicine, and Daido Hospital, Nagoya, Japan.

Little information exists regarding the functional role of activated mucosal T cells in the pathogenesis of UC, although increased expression of HLA-DR has been demonstrated on the cell surface of intestinal T cells in the inflamed mucosa with UC. In the present study, we performed functional analysis of mucosal HLA-DR+ T cells using lamina propria mononuclear cells (LPMC) isolated from the UC-affected mucosa. We also made the follow-up study on their percentage among LPMC v.s. the clinical course of the patients, using endoscopic biopsies. [**Methods**] LPMC were isolated by enzymatic dispersion from colonoscopic or surgical specimens from actively inflamed mucosa with UC of chronic continuous type (CC-UC, n=17) or relapsing remitting type (RR-UC, n=20). Control LPMC were isolated from surgically excised normal mucosa with colon cancer (n=23). [**Results**] CC-UC LPMC had a higher proportion of HLA-DR+ T cells and secreted more sIL-2R than RR-UC LPMC. In the surgical UC specimens, mucosal HLA-DR+ T cells secreted significantly higher sIL-2R than HLA-DR- T cells. In RT-PCR analysis, the mRNA encoding TNF-α, IFN-γ and IL-2Rα was almost exclusively expressed in mucosal HLA-DR+ T cells but not in HLA-DR- T cells. Depletion experiments using LPMC expanded with rIL-2 demonstrated that CD4+, HLA-DR+ T cells and CD8+, HLA-DR+ T cells are mainly involved in TNF-α and IFN-γ secretion and cytotoxicity against colonic HT-29 cells, respectively. In the follow-up study, CC-UC LPMC continued (> 6 months) to have higher proportions of HLA-DR+ T cells whereas RR-UC LPMC exhibited decrease of their proportion during remission. [**Conclusion**] This study suggests that HLA-DR+ T cells are functionally activated cell populations and their enumeration using follow-up endoscopic biopsies may be useful for evaluation of the clinical course in UC.

ROLE OF INTESTINAL OBSTRUCTION IN BACTERIAL TRANSLOCATION DURING INTESTINAL SURGERY.

M.J. Laisné, F. Riché, P. Valleur, C. Briard, L. Raskine, P. Hautefeuille. Digestive surgery Department, Lariboisière Hospital, Paris, France.

Bacterial translocation (BT) is defined as the movement of viable enteric bacteria across the epithelial cell barrier to the mesenteric lymph nodes and other distant organ sites. BT during intestinal surgery has been described for inflammatory bowel disease, colon carcinoma and intestinal obstruction and may be responsible of post operative infections. The aims of the study were to evaluate: 1- the role of intestinal obstruction in BT, 2- the relation between the occurence of post operative septic shock (SS) and BT.

Patients and methods: 71 patients (pts) (mean age 51±21) were enrolled in a prospective study: Group 1 : 32 pts operated for an elective surgery: 17 colon carcinoma, 15 ulcerative colitis treated with corticosteroids , Group 2: 39 intestinal obstructions: 8 obstructive colon carcinoma, 17 small bowell obstruction, 7 radiation enteritis, 7 ileal Crohn's disease. A mesenteric lymph node was sampled immediately after laparotomy and sent for bacterial culture. All strains isolated were identified. The occurence of a post operative SS as defined by Bone was noted.

Results: Incidence of BT in non obstructive pts (Group 1) and in obstructive pts (Group 2) is shown in table:

	Group 1 n=32	Group 2 n=39
BT	2 (6%)	17 (43%)*
SS	1	2
BT+SS	0	2 (10%)

* p< 0.01

Bacteriological culture was polymicrobial in 8/16 cases (52%). E. Coli was the most commun isolate. SS associated with BT was rare (1/10 cases).

Conclusions: These results suggest that intestinal obsruction is a major risk factor for BT irrespective of etiology. This could be secondary to bacterial pullulation associated with intestinal obstruction. BT does not appears to be correlated with post operative SS.

● **SERUM LEVELS OF NITRIC OXIDE DURING PROGRESSION TO AIDS IN PATIENTS WITH HIV AND CHRONIC HCV LIVER DISEASE: POSSIBLE EXPLANATION FOR NORMAL HCV DISEASE SEVERITY IN HIV DISEASE.** G. Lake-Bakaar, D. Sorbi, and P. Abernathy. Dept. of Medicine, SUNY HSC Stony Brook and VAMC Northport, NY.

Nitric oxide (NO) is a free radical gaseous molecule which mediates several vital physiological functions. It is increasingly recognized as an important component of non-specific immune response to infection. Transcriptionally induced isoforms of NO synthase, iNOS, have been described in hepatocytes and macrophages and may contribute to enhanced cytoxicity against tumor cells and microbial pathogens. NO inhibition of HSV 1 and ectromelia virus replication have been well described. HIV disease is characterized by progressive immune paresis. However, chronic RES activation is also a feature, which could generate increased NO production.

Since HCV is considered to be cytopathic, increased liver disease severity would be expected in patients with simultaneous HIV/HCV infection. However, this is not a recognized feature in clinical practise. We hypothesized that increased NO production generated by chronic RES activatiion in HIV disease, may in part account for this lack of increased cytopathicity. Therefore, we compared serum NO levels in HIV infected patients with chronic HCV liver disease, during progression to AIDS. **METHODS**:

Serum metabolites of nitric oxide, NO_2 /NO_3 were measured in three groups of patients chronically infected with HCV: non-HIV infected; HIV infected; and patients with AIDS. Stored sera were deproteinized with 35% sulfosalicylic acid before analysis. NO_2 was determined with the Griess reaction; NO_3 was measured after oxidation of nitrites to nitrates with potassium permanganate and reaction with Brucine. **RESULTS**: Analysis of variance revealed no significant within group variability in age, sex, bilirubin, AP or total serum protein. NO metabolites were present largely as NO_3 in serum.

	HIV neg (n=7)	HIV pos (n=8)	AIDS (n=6)
AST iu/l (m±sd)	43.6±12.8	39.4±10.8	46.2±47.8 ns
ALT iu/l	43.6±22.4	52.1±29.6	36.5±22.4 ns
NO_2/NO_3 uM	52.9±14.1	61.8±19.6	172.2±48.2p<.0001
WBC	9.01±3.9	5.4±1.9	4.5±0.9 p<0.01
Age yrs	35±6.9	37.3±7.2	36.5±3.7 ns

SUMMARY: a. Mean ALT and AST were similar at all stages of HIV infection. b. Total WBC was lower in AIDS reflecting the immune paresis c. Serum NO_2/NO_3 was significantly increased in patients with chronic HCV and AIDS.

CONCLUSION: NO production increases significantly with HIV disease progression in patients with chronic HCV liver disease. This could, in part account for the lack of increased HCV cytopathicity in AIDS.

LOCALIZATION OF EPIDERMAL GROWTH FACTOR (EGF) PROHORMONE IN FECES ADHERING TO THE SITE OF INFLAMMATION IN AN EXPERIMENTAL MODEL OF RAT COLITIS.

J. Lakshmanan, P. Hoffmann, F. Procaccino, J. Zeeh, A.R. Patel, P. Ngo and V. E. Eysselein, Division of Gastroenterology, Harbor-UCLA Medical Center, Torrance, CA.

Background: We recently reported that exogenous EGF administration in rats one hour prior to induction of colitis by 2, 4, 6 trinitrobenzene sulfonic acid/ethanol reduced the severity of inflammation by 50-75% as assessed by changes in microscopic ulceration and myeloperoxidase activity. In an attempt to understand the role of endogenous EGF which is predominantly produced by salivary glands and the pancreas, we examined the inflamed colon for EGF after the induction of colitis. Our initial immunohistochemical study revealed presence of EGF immunostaining in feces adhering to the site of inflammation. This prompted us to examine its molecular nature. Methods: Adult male Sprague Dawley rats weighing 250-300 gm after an overnight fast were induced colitis via the infusion of 2, 4, 6 -trinitrobenzene sulfonic acid through a soft pediatric catheter introduced 10 cm from the anus. Animals were sacrificed 8 hr after the induction of colitis. Feces adhering to the mucous at the site of inflammation was carefully removed, homogenized in phosphate buffered saline and the extracts were centrifuged. The supernatants were mixed equal volumes of 2x Laemmili's electrophoretic sample buffer, heated in a boiling water bath for 8 min, cooled and centrifuged. The samples were subjected to immunoblotting analysis with an antiserum raised against EGF isolated from rat submaxillary gland. The radioactive bands were identified after incubation with ^{125}I-goat anti-rabbit IgG. Results: Feces of normal rat contained predominantly 200 kDa and 52 kDa EGF proteins which were barely detectable on the autoradiogram. In animals with colitis, the radioactive intensity of both proteins was 2-10 fold greater in the feces collected from the site of inflammation. Conclusion: The increased levels of EGF prohormone and its principle 52 kDa metabolite in feces adhering to the site of inflammation suggest that these molecules may have anti-inflammatory functions. We speculate that the salivary glands and the pancreas, the organs that express high levels of EGF prohormone mRNA, are the most likely sources for luminal EGF prohormone.