W37

LACK OF EFFECT OF HIGH DOSE RANITIDINE ON THE POST-PRANDIAL PHARMACOKINETICS OF ALCOHOL

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Several studies have suggested that H_2-receptor antagonists may affect the rate or extent of absorption of alcohol. Various factors, such as time of day, gender, presence of food etc, may affect the absorption or metabolism of alcohol and hence may influence the results of interaction studies. The present double-blind two-way crossover study compared the effects of ranitidine 300mg qds and placebo on a single post-prandial dose of alcohol ($0.5g.kg^{-1}$) given at 3 different times of day to 18 normal caucasian male subjects (aged 25-45 years).

Medication started on day 1 and continued up to and including day 8. On day 4 a standard breakfast at 0745h preceded the 0800h dose of medication and the alcohol ($1.6mL.kg^{-1}$ vodka, 40%, made up to 200mL with orange juice) at 0830h. Eleven blood samples were taken at frequent intervals up to 1230h. These were rapidly frozen to await analysis by a fully validated GLC assay. Psychomotor tests, including digit symbol substitution and assessment of alertness using rating scales were carried out 10 min prior to alcohol and at 30, 60, 120 and 240 min after alcohol consumption. On day 6 a standard lunch was eaten at 1245h followed by the above procedures and similarly on day 8 after a standard dinner at 1745h.

There were no statistically significant differences between the effects of ranitidine and placebo on the psychomotor test results (MANOVA) or on alcohol C_{max}, AUC or t_{max} at breakfast, lunch or dinner time (ANOVA). Mean (±SD) results for C_{max} and AUC were:-

Parameter	Medication	Breakfast	Lunch	Dinner
AUC ($mg.h.L^{-1}$)	ranitidine	1123 (370)	1128 (380)	1007 (384)
	placebo	1115 (349)	1096 (458)	949 (384)
C_{max} ($mg.L^{-1}$)	ranitidine	464 (162)	487 (166)	438 (145)
	placebo	437 (102)	454 (164)	413 (151)

In conclusion, high dose ranitidine has no significant effect on blood alcohol concentrations or psychomotor function after a single dose of alcohol ($0.5g.kg^{-1}$) taken at breakfast, lunch or dinner time.

W39

QUANTIFICATION OF GASTROINTESTINAL BLOOD LOSS FOLLOWING THROMBOLYTIC THERAPY FOR ACUTE MYOCARDIAL INFARCTION

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Thrombolytic therapy has revolutionised the management of acute myocardial infarction, but is not free from adverse effects, the most common being bleeding. Gastro-intestinal blood loss is a well known complication, but usually recognised only when severe. Trace (subclinical) amounts of blood are lost from the gut in health. We wished to determine whether thrombolytic therapy with streptokinase or tissue plasminogen activator enhanced subclinical blood loss from the gut.

Serial daily stool samples were collected for up to 5 days from 57 patients admitted to the cardiac care unit with suspected myocardial infarction. Patients with a previously known gastrointestinal disorder likely to predispose to bleeding, as well as those with such bleeding at admission were excluded from the study. Stool haemoglobin concentrations were determined by measuring haeme derived porphyrins using fluorescence spectrometry. Each sample was measured three times and the mean calculated and expressed as mg of haemoglobin per gm of stool (mg/g).

A total of 88 stool samples were collected from 57 patients (42 male) aged between 34 and 85 years. Thirty eight patients received either streptokinase or tissue plasminogen activator, while 19 did not. However, some of the latter group did receive aspirin, warfarin or heparin. The faecal haemoglobin concentration in the group receiving thrombolytic therapy was 3.65 (2.2 - 5.1) mg/g (mean (95% confidence intervals)), while in the group not given thrombolytic therapy it was 1.45 (0.8 - 2.10). These differences were significant P=0.01 (Mann-Whitney U test).

These results suggest that thrombolytic therapy for acute myocardial infarction is associated with a significant increase in sub clinical blood loss from the gut.

Small bowel/nutrition W40–W51

W38

BONE MARROW TOXICITY FROM AZATHIOPRINE IN INFLAMMATORY BOWEL DISEASE: EXPERIENCE FROM 1663 PATIENT YEARS OF THERAPY.

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Although azathioprine has been shown to be helpful in the treatment of ulcerative colitis and Crohn's disease, bone marrow suppression may result in serious sequelae. We report here the experience of bone marrow toxicity in 739 patients treated at one hospital for inflammatory bowel disease with azathioprine over 27 years.

Methods: Between 1964 and 1991, 416 patients with Crohn's disease, 298 with ulcerative colitis and 34 with indeterminate colitis were treated with azathioprine (dose 2 mg/kg). Their case histories and corresponding blood counts which were performed regularly were reviewed.

Results: Leucopenia (WBC < 3.0) occurred in 28 patients (3.8%) necessitating azathioprine cessation or dose reduction. All 19 patients whose WBC remained above 2.0 were asymptomatic. Of the other 9 subjects (1.2%) in whom leucopenia was more severe (WBC < 2.0), 4 remained asymptomatic and 5 developed complications related to marrow aplasia (2 of these cases died). Severe leucopenia occurred at any time during azathioprine therapy (0.5-132 months after its introduction; mean=27.1 months), developing abruptly in 6 of the 9 cases and gradually in all other 3. Thrombocytopaenia (platelet count < 100,000) resulted in the withdrawal of azathioprine in 17 cases, 8 of whom had accompanying leucopenia. Only one individual developed symptoms related to thrombocytopaenia.

Conclusions & Recommendations: There is a definite but small risk of bone marrow complications with azathioprine for inflammatory bowel patients. Leucopenia is more common and significant than thrombocytopaenia. Bone marrow suppression may develop abruptly or gradually and can occur at any time during azathioprine treatment. Monitoring of the full blood count should be performed monthly throughout azathioprine therapy. In this way, asymptomatic patients with bone marrow suppression can be detected before serious complications develop. Dosage modifications are required when the WBC falls below 3.0 or platelet counts are less than 100,000.

W40

ANTIGLIADIN ANTIBODIES IN BLOOD DONORS IN NORTHERN IRELAND

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The prevalence of coeliac disease reported in the literature ranges from 1:300 to 1:2000 but these figures are based on detected symptomatic cases. Using an ELISA method for detection of antigliadin IgA, which has high sensitivity and specificity for coeliac disease (BMJ 1991; 303: 1163-5), we studied sera from 443 blood donors attending 11 centres in Northern Ireland. Patient ages ranged from 17 to 64 with a mean (SD) of 36 (11); 295 (67%) were male.

Five donors (1%) had positive values (≥ 100 ELISA units) ranging from 132 to 300. There appeared to be clustering of positive values among donors attending centres in the north-west (4 of 191 donors v. 1 of 252 elsewhere), although mean (SD) values were not significantly higher (27 (36) in the north-west v. 21 (25) elsewhere).

Thus, even amongst a blood donor population in Northern Ireland, from which anaemic patients are excluded, the prevalence of coeliac disease estimated from a highly sensitive and specific serum antigliadin IgA assay is 1:100 and may be higher in some areas. Testing patients with vague or atypical symptoms therefore seems worthwhile. However, the risks of long-term complications and the benefits of dietary gluten exclusion in asymptomatic patients are unknown and the need for serological screening, jejunal biopsy and treatment in this group is unclear.

W41

TRANSPLANTATION OF CULTURED SMALL BOWEL ENTEROCYTES.

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Autotransplantation of enterocytes from small bowel to colon, could increase absorptive mucosal surface area, without immunological sequelae. This study has evaluated isolation, primary culture and transplantation of small bowel enterocytes. Epithelial/mesenchymal cell clusters, containing pre crypt proliferative stem cells, were isolated from neonatal rat small intestine, by enzymatic digestion. Mesenchymal proliferation was inhibited by endogenous heparin and low concentrations of foetal calf serum. Enterocytes attached readily in culture, proliferated rapidly, increased in number and filled multi-wells within 10-14 days. Characterization studies showed that >90% cells in culture were epithelial, with expression of intestinal alkaline phosphatase and cytokeratins 8, 18 and 19. Electron microscopy confirmed surface microvilli, desmosomes and junctional complexes. After 72 hours in culture, enterocytes were combined with fetal mesenchyme and transplanted under the kidney capsule of adult AO inbred rats. Grafts retrieved at 14 days showed morphogenesis with villus formation and abundant goblet cells. This study has shown that small bowel enterocyte stem cells retain the capacity for pluripotent differentiation and morphogenesis, after culture and transplantation.

W42

THE RELATIONSHIP OF CELL VOLUME TO CELL HEIGHT AND WIDTH: A COMPARATIVE STUDY BY COMPUTERIZED IMAGE-ANALYSIS.

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In various malabsorption syndromes in which mucosal flattening occurs, the surface enterocytes are reduced in height (height profile). However, because of altered epithelial cell proliferation-dynamics, in which cell losses from the flattened surface may exceed production, the apparent reduction in cell height may merely reflect increased coverage of basement membrane, resulting in a more squamous-type cell, but without necessarily altering its volume. These possibilities have been explored with the use of computerized image-analysis of appropriate small intestinal biopsy specimens. **Methods**: 1μ toluidine-blue-stained epon sections of upper jejunal mucosa from 21 disease-controls (Group 1) and 20 untreated coeliac patients (Group 2) were analysed in terms of enterocyte height; width; area and volume. For the latter, cells were either assumed to be cylinders (I), or inverted truncated conoids (II). Similar dimensions for enterocyte nuclei were calculated based on an assumed shape of prolate spheroids. **Results**: There were significant differences in cell height [37 vs 33μm: $p<0.001$], cell width [5.1 vs 4.7μm: $p<0.01$], cell area [184 vs 152μm^2: $p<0.0001$] and cell volume I [790 vs 604μm^3: $p<0.001$] or cell volume II [822 vs 621μm^3: $p<0.0001$] but not between group 1 and 2 mucosae in respect of nuclear dimensions. In assessing the relationship between volume and linear measurements, good correlations were found between cell volume (method I or II) and cell width [$r=0.901$: $p<0.0001$] but not cell height [$r=0.457$]. Random measurements of the width of epithelium (brush border to basement membrane, i.e. "barrier thickness") did not differ significantly from mean measurements of height of individual enterocytes (Group 1 mucosae, 39.8$\pm$3.0μm vs 36.9$\pm$3.2μm and Group 2 mucosae, 32.6$\pm$3.1μm vs 33.3$\pm$3.2μm, respectively). Height/width ratios did not differ between group I (7.3$\pm$1.0μm) and group II (7.2$\pm$1.1μm) mucosae, suggesting that flattening of cells involves parallel alterations in height as well as width. **Conclusions**: 1. The volume of enterocytes in untreated coeliac mucosae is reduced in comparison with normal mucosae. 2. Average cell width correlates best with cell volume, rather than height. 3. Random measurement of epithelial "barrier" width is equally effective as the measurement of the mean heights of individual cells.

W43

EFFECT OF GRADED ORAL GLUTEN CHALLENGES ON MUCOSAL MORPHOLOGY AND DYNAMICS, AND EPITHELIAL LYMPHOCYTES

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The assumption that in coeliac disease, gluten is directly damaging to jejunal enterocytes, and that an increased loss of surface enterocytes is followed by compensatory crypt hypertrophy ("mucosal haemolysis theory") may not be correct. The present study addresses this problem in a systematic evaluation of time/dose responses of treated coeliac mucosae to gluten challenge with one of a series of graded doses of gliadin digest. **Methods**: 26 known coeliacs, with good mucosal responses were recruited. As previous studies showed that disease-control subjects show no response to gluten challenge these were not studied any further. Each challenge comprised one oral dose of a peptic-tryptic digest of gliadin (PTD) (0.1; 0.5; 1.0; 1.5; 3; 6 and 12g): some coeliacs were challenged with varying doses at different times. After a control mucosal specimen was obtained by Crosby capsule, the selected challenge was taken, and further biopsies obtained (12, 36, 60 and 84h). After processing and staining with toluidine blue, sections were subjected to computerised-image-analysis in respect of volume of surface (V_{SE}), crypt (V_{CR}) and lamina propria (V_{LP}): surface (sIEL) and crypt (cIEL) lymphocyte responses: mean IEL diameter, and mitotic index; and crypt cell mitotic activity. **Results**: Doses of PTD from 0.1-1.5g evoked dose-related elevations of sIEL without architectural change: cIEL started to rise with 1.5g PTD and remains elevated throughout challenges with 3, 6, 12g PTD: maximal rise (cIEL) exceeded that of sIEL at all dose levels. The first mucosal change was crypt hypertrophy with 3g PTD, occurring before significant villous flattening occurred (late with 6g (60-84hr), early with 12g (12-60hr) PTD). Changes in V_{LP}, mean IEL diameter and mitotic activity were only seen in late challenges with 6 and 12g, in which significant villous flattening occurred, which were also associated with demonstrable increases in crypt cell mitotic activity. **Conclusions**: 1. In becoming flat, the mucosa is first infiltrated by IEL: the second phase involves continuing lymphoid infiltration together with crypt hypertrophy; thirdly, villous flattening is the last event to be seen. 2. 'Haemolysis' is not the mechanism of villous flattening: rather, the process of flattening occurs through a series of events analogous to cell-mediated immunity in graft-versus-host mucosal lesions. 3. Enterocyte damage only appears late, and is clearly not a prime mover in this evolving sequence.

W44

TERMINAL ILEAL DYSFUNCTION IN CYSTIC FIBROSIS.

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Excessive faecal bile acid (FBA) losses have been demonstrated in the majority of patients with cystic fibrosis (CF) although FBA excretion is significantly less in patients with liver disease (LD). Previous in vitro studies suggest that a defect in the terminal ileal bile acid active transport mechinism may be responsible for the excessive FBA losses observed in CF. The aim of the present study was to assess in vivo intestinal bile acid absorbtion in CF patients using the 7 day retention of orally administered selenium labelled homotaurocholic acid (SeHCAT), a bile acid absorbed via an ileal active transport mechanism. the study population included 24 patients(15 male;median age22yrs) with CF, with(N=6) and without(N=18) LD and 8 control subjects(CS)

One microcurie (37kBq) SeHCAT at a specific activity of 68.5mCi/mmol was administered orally in caspule form to each subject. Whole body retention (% of administered dose) of selenium radioactivity was measured on two occasions using a shallow shield whole body counter (Camberra Accuscan) 2 hours and 7 days after ingestion.

Eight (33%) of CF patients had 7 day SeHCAT retention <10% (normal retention>20%). SeHCAT retention in CF patients with LD was comparable to CS (30.0+/-SEM8.3%v36.8+/-5.9%;P=NS) while SeHCAT retention in CF patients without LD was significantly reduced (19.9+/-3.8;p<0.05).

The results indicate that terminal ileal function is abnormal in patients with CF without LD and that a defect in the ileal absorbtion bile acids is a contributary factor to excessive FBA in these patients.

W45

RELATIONSHIP OF IMMUNOPATHOLOGY OF HIV POSITIVE DUODENAL BIOPSIES TO ADVANCING HIV DISEASE AND OPPORTUNIST INFECTION.

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The relationship between immunopathology of the gastrointestinal tract, advancing HIV disease and the development of gastrointestinal opportunist infections (GIOI) was investigated. Methods: 15 HIV-positive patients (6 CDC II and 3 CDC IV on no therapy, 6 with GIOI) and 8 controls with non-ulcer dyspepsia had duodenal biopsies from the third part of the duodenum at upper GI endoscopy. Biopsies were snap frozen , and cut in 6μ sections. Monoclonal antibodies RFD1 (interdigitating/antigen presenting cells), RFD7 (mature phagocytic macrophages), RFT4 (T helper lymphocyte subset), RFT8 (T suppressor/cytotoxic lymphocyte subset) and EBM11 (CD68, all macrophages) were used. An indirect immunoperoxidase and a double immunofluorescent method was used. Results: there was a depletion of RFT4 cells in the lamina propria (LP) of all HIV-positive patients (Wilcoxon Rank Sum, $p<0.05$), but no difference in RFT8 LP cells nor in RFT8+ intraepithelial lymphocytes. EBM11 (all macrophages) was similar in all HIV-positive groups, but there was a decrease in RFD1+ macrophages in those with CDC IV disease compared to CDC II ($p<0.05$). RFD7+ macrophages were increased in all HIV groups compared to controls ($p<0.05$). RFD1/RFD7 doubly-positive macrophages were decreased in those with CDC IV disease compared to CDC II and controls ($p<0.05$). Conclusions: RFT4 lymphocyte depletion is seen early in HIV and the development of GIOI cannot be due to the loss of these cells in the duodenal LP alone. While there was no loss of macrophages with advancing HIV disease, there were alterations in the expression of macrophage markers with HIV disease that may reflect functional changes.

W46

GROWTH IN CROHNS' DISEASE (CD) IS ASSOCIATED WITH HIGHER ENERGY REQUIREMENTS.

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Growth failure occurs in up to 30% of adolescents with CD. Deficiency of dietary energy substrates appears to be a major contributor, but the energy requirements of these patients is unclear. Six adolescents with inactive CD, assessed to be growing during the previous 12 months (group A, mean age 17.3 yrs), five who had ceased growing (group B, mean age 19.6) and 6 growing healthy controls (age and sex matched with group A) were studied. In each subject nutritional status was assessed by anthropometric measurements from which body mass index (BMI), arm muscle circumference (AMC), fat percentage and fat free mass (FFM) were calculated. Resting energy expenditure (REE) was measured with subjects fasted using a Deltatrac indirect calorimeter.

Weight, BMI and fat percentage were significantly reduced in patients of both group A (mean 51.5 SEM±4.8 kg, 19.3±1 kg/m², 13.6±2.8%, $p<0.05$) and group B (56.4±2.5 kg, 20.1±1 kg/m², 15.3±2.8%, $p<0.05$) compared with controls (63.4±3.4 kg, 23.5±0.5 kg/m², 22.5±2.3%). FFM and AMC were not different between groups. REE/kg of body weight was significantly higher in group A (31.7±2.3 kcal/kg/24h, $p<0.001$) but not group B (26.7±1.4) compared with controls (23.9±1.3). No difference was found between the two groups of patients. However, REE/kg FFM was significantly higher in patients in group A (36.3±2.1 kcal/kg/24h, $p<0.05$) compared with patients in group B (31.5±0.7) and controls (31.0±1).

These results suggest that (i) lower body weights in adolescents with inactive CD is due to a reduction of fat mass and (ii) such subjects who are growing have significantly higher energy expenditure. Thus, although food intake may appear adequate, it is appropriate to consider nutritional supplementation in adolescents with CD.

W47

A PREMEAL OF L-PHENYLALANINE RELEASES CHOLECYSTOKININ AND REDUCES SUBSEQUENT FOOD INTAKE IN HUMANS.

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Exogenous administration of cholecystokinin (CCK) reduces food intake in humans. Oral administration of L-phenylalanine increases endogenous secretion of CCK from the duodenum. The aim of this study was to investigate the effect of oral L-phenylalanine on food intake in humans. **Methods:** On separate occasions 6 non-obese fasted subjects were given a pre-load of 10g L-phenylalanine or placebo 20 min before being presented with a standard test meal of known calorie content. The amount of food offered was far in excess of the amount subjects were likely to eat. Preliminary experiments had shown that peak plasma concentrations of CCK were obtained 20 min after giving L-phenylalanine. The test meal was given to coincide with this peak. Visual analogue scales to assess hunger, fullness and desire to eat were completed pre-meal, post-meal and at hourly intervals thereafter for 5h. Blood was taken before giving phenylalanine/placebo, immediately pre- and post-meal and stored for measurement of CCK by bioassay. The total number of calories consumed was determined. **Results:** Total calorie intake (mean ± SEM) after placebo was 1587 ± 174kcal compared to 1089 ± 122 kcal after a phenylalanine pre-load ($p<0.03$). Visual analogue scales to assess hunger and desire to eat did not predict subsequent food intake. Basal levels of CCK were 1.10 ± 0.12pmol/l; 20 min after the phenylalanine pre-load CCK levels increased to 5.49 ± 0.83pmol/l. There was no increase in CCK following placebo (0.99 ± 0.06pmol/l; $p<0.04$). **Conclusions:** Pre-prandial administration of L-phenylalanine resulted in a rise in plasma concentration of CCK and this was associated with a significant reduction in food intake. These results suggest that the effect was due to the early rise of CCK induced by phenylalanine and that endogenous CCK is a major regulator of food intake in humans.

W48

INSULIN IMPROVES NITROGEN BALANCE OVER AND ABOVE OPTIMAL PARENTERAL NUTRITION

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Nutrition must be given parenterally in conditions associated with obstruction or malabsorption in the gut. Despite the provision of adequate calories and nitrogen negative nitrogen balance will persist if there is supervening infection or cancer. Insulin has been shown to be anabolic in animals in vivo and in humans in vitro. We wish to observe any additional effect of insulin on nitrogen balance in the parenterally fed state. 5 healthy male volunteers were fed parenterally for about 20 hours with a balanced feed providing approximately 1.3 times Resting Energy Expenditure and 12.4 grams nitrogen per 24 hours. After a mean run in period of 11 (6-15) hours whole body protein turnover was measured over 2 periods of 2 hours using constant 13C-leucine infusion technique. In random order turnover was measured on and off a euglycaemic hyperinsulinaemic clamp employing an infusion of 40mu/m2 body surface area/min actrapid insulin and a variable intravenous infusion of potato starch glucose to establish hyperinsulinaemia with stable blood glucose. The mean and standard error of mean of the rates of leucine flux calculated from plasma 13C-ketoisocaproate (QKIC), oxidation of leucine (Oxid), synthesis of leucine into protein (S) and leucine appearance (B) are expressed as umol/kg/hr.

	plasma insulin	QKIC	Oxid*	S	B	S-B*
clamp (m)	84	141	22	119	112	7
(sem)	12	9	2	8	8	2
no clamp (m)	18	151	26	125	122	3
(sem)	8	7	2	7	6	2

*p<0.05

Infusion of supraphysiological doses of insulin results in decreased oxidation of leucine and increased net nitrogen retention over and above that achieved by parenteral feeding and may thus prove to be a useful adjunct in catabolic states.

W49

PARA-AMINOBENZOIC ACID (PABA) AS A MARKER FOR 24 HOUR URINARY UREA EXCRETION IN PARENTERALLY FED PATIENTS.

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Provision of adequate nitrogen in parenteral feeds depends upon measurement of 24 hour urinary urea (N) excretion. Accurate urine collection is difficult clinically. PABA is quantitatively excreted in urine and given orally is advocated for checking the completeness of urine collections. We examined the feasibility of adding a known amount of PABA to parenteral feeds and using the ratios of urine concentrations of urea to PABA in spot samples to estimate 24 hour urinary urea excretion. 6 patients (4 males) were studied. 200mg PABA were added to their routine "3 in 1" complete parenteral feeds. Spot urine samples were collected into bottles containing boric acid at 4,8 and 24 hours after starting the feed. An accurate 24 hour urine collection coincided with the constant infusion of the feed by pump. After storage at 4 deg C aliquots were analysed for urea concentration (urease) and for PABA metabolites (colorimetric assay). Measured 24 hour urinary urea excretion was compared with the excretion calculated from the ratio of urea to PABA concentrations in spot samples multiplied by (a) the known input of PABA, and (b) the measured 24 hour excretion of PABA. The 24 hour excretion of PABA metabolites (47.7 ± 15.4 sd) was less than the expected 100% of the administered dose. The ratio of urea to PABA concentration in urine in the spot samples at the three time points was not constant so a mean of the three ratios in each patient was employed.

	24hr urea(measured) (u)	24hr urea(calculated) (a)	(b)
MEAN	428	1020	419
SD	156	667	164
R (calc/measured)		0.94	0.98

Our data show that PABA is not quantitatively excreted given in this way. It may be bound to the feed container and giving set in which case our approach could be used if the concentration of the PABA in the feed entering the patient could be measured; but with current techniques the feed interferes with such an assay. If this problem were solved PABA could prove useful but at present it cannot be recommended.

W50

TOTAL URINARY NITROGEN MEASUREMENT BY NEAR INFRARED REFLESSOMETRY. COMPARISON WITH CHEMICAL METHODS.

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Chemical methods for the measurement of total nitrogen in urine are complex and therefore rarely used; urea nitrogen is the most used alternative, but it often underestimates urinary losses. Aim of this study was to assess the analytical efficacy of near infrared reflectance (NIRA) in the measurement of total urinary nitrogen. This method provides the results in about one minute, simply injecting the sample in a termostated cell of the equipment. The comparison was performed both on fresh urines (40 samples: 28 from GI patients, 8 of whom on enteral and 5 on total parenteral nutrition; 4 operated, 4 nephrotic and 4 burned patients) and on thawn urines (70 samples from GI patients, 20 of whom in enteral, 8 in total parenteral nutrition). These had to be acidified and warmed to obtain a clear solution. Two different calibration curves had to be obtained for fresh and thawn urines. This was done by a multiparametric regression, comparing the results of the Kjeldahl method with the reflectance values at 19 different wavelenghts. Results: we found a range of NIRA nitrogen concentration of 0.35-2.04% in fresh, of 0.1-1.7% in thawn urines. A coefficient of correlation of 0.97 and of 0.93 was obtained between the mineralometric and the NIRA nitrogen concentration in fresh and thawn urines respectively. An intraassay coefficient of variation of 6.6 and of 9.6% was found for fresh and thawn urines respectively (3 samples measured 20 times). In fresh urines, a correlation coefficient of 0.95 was found between the NIRA total nitrogen and the urea nitrogen.

In conclusion, the near infrared reflectance analysis represents a quick and reliable alternative to the complex chemical methods for the day-by-day study of the nitrogen balance.

W51

ETHANOL FLUSH FOR THE PREVENTION OF CATHETER OCCLUSION

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Catheter occlusion by lipid material has been associated with the use of compounded nutrient solution containing lipid. We have studied 51 patients in whom either a saline or ethanol flush has been used prior to a heparin lock in patients receiving parenteral nutrition with such solutions in order to determine whether improved catheter survival and a lower incidence of catheter occlusion could be achieved.

METHOD

Following overnight infusion of parenteral nutrition the giving set was disconnected from the extension set and either 20 ml of isotonic saline solution (n=23) or 10 ml aqueous solution of 20% ethanol (n=28) was flushed through the catheter. A spigot was then placed on the extension set and a heparin lock of 5,000 units heparin was injected through the spigot. Catheter occlusion was recognised by increasing resistance during the flush or by activation of the occlusion alarm of the infusion pump. Catheters were removed if they were occluded, or if there was no further need for parenteral nutrition.

RESULTS

The incidence of catheter occlusion was significantly ($p<0.001$, χ^2 test) lower in patients who received the ethanol flush (2/28) when compared with patients who received the saline flush (13/23). In addition catheter survival was significantly ($p<0.01$, logrank test) longer in patients who received the ethanol flush. No complications of the flush were observed in either group.

CONCLUSION

Ethanol flush is a simple, safe and effective method of reducing the incidence of catheter occlusion with compounded solutions.

Liver W52–W59

W52

FIBRINOLYTIC ACTIVITY IN CIRRHOSIS

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Although there is in vitro evidence for increased fibrinolytic activity in cirrhosis, in vivo evidence of fibrinolysis is indirect and controversial, because both pro and antifibrinolytic components need to be measured simultaneously, together with an index of thrombus degradation to distinguish primary from secondary fibrinolysis. We evaluated 51 cirrhotics (26 alcoholic, 13 PBC, 12 non-alcoholic non-biliary) measuring fibrinogen, activators of fibrinolysis(tissue plasminogen activator-TPa ,which is solely endothelial derived, inhibitors of fibrinolysis (plasminogen activator inhibitor-PAI-1, also solely endothelial derived; antithrombin III-ATP III; antiplasmin,ATP) as well as x-linked fibrin degradation products (XDP) -only present if thrombus degradation occurs- and whole blood fibrinolysis (clot lysis index) by thromboelastography which has been used clinically as an index of fibrinolysis. TPa was elevated in 77% of alcoholics, 31% of PBC and 75% of the remainder , as was the PAI-1 in 58% alcoholics, 62% PBC, and 58% of the others , with an expected correlation ($p<0.02$). However the hepatic derived inhibitors, AT III and ATP were low in 90% and 88% of the total group but fibrinogen levels were low in only 25%. Clot lysis index was only abnormal in 8(16%), and it correlated with fibrinogen ($p<0.02$) and ATP ($p<0.025$), but not with TPa, PAI-1,or their ratio. In 4 of these XDP were not elevated suggesting primary fibrinolysis. XDP were raised in 18(53%) of the total, 13 of whom had raised TPa levels suggesting that these 13 had a degree of secondary fibrinolysis. This study shows that both primary and secondary fibrinolysis exist. Further investigation will clarify which tests are the most useful in a clinical setting such as bleeding, sepsis, ascitic recirculation or surgery.