WHEN IS A RECTOCELE SIGNIFICANT?
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Rectoceles are commonly investigated by barium proctography. This is a qualitative investigation and does not provide data on rectocele emptying. We have used a quantitative method [isotope defaecography (ID)] with the aim of differentiating between significant (SR) and non-significant rectoceles (NSR).

We studied 95 patients with a clinical diagnosis of rectocele. ID was performed using 100 MBq of 99mTc mixed with 100 ml of barium porridge. 71 of the 95 patients were found to have a rectocele. The percentage and rate of evacuation (%/sec) and also the percentage of isotope retained in the rectocele were calculated. Patients with 15% or more retention in the rectocele were defined as having a significant rectocele.

Results: 34 of 71 had a significant rectocele. The SR group had a significantly higher retention of the isotope than NSR (22.3 (1.4) vs 9.6 (0.4), p < 0.0005). Similarly the retention of the isotope as percentage of final rectal content was significantly higher in the SR than NSR group (52.6 (2.4) vs 33.1 (1.8), p < 0.0001). The rate of evacuation in the two groups was similar (0.97 (0.1) vs 1.3 (0.1), p > 0.05). There was no significant difference in the total percent evacuation between the no rectocele and NSR groups. There was a significant correlation between the presence of a significant rectocele and total percentage evacuation (r=0.61, p < 0.0001). There was no significant correlation between the presence of a SR or NSR and the rate of evacuation.

These data suggest that retention of 15% or more of the rectal contents in the rectocele influences the total percent evacuation resulting in impaired evacuation. This may be a useful way of differentiating between significant and non-significant rectoceles and selecting patients for surgical therapy.

DETECTION OF FAECAL INCO-TINENT EPISODES USING A NEW AMBULATORY WETNESS DETECTOR
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Internal anal sphincter amimalusatory assessment has suggested the anoctoreal pressure gradient may be reversed during faecal soiling. However patients are commonly unable to perceive these events. The aim of this study was to develop a wetness detector that would allow us to identify objectively episodes of faecal incontinence.

The wetness detector was constructed from a 5mm catheter with two copper electrodes set 3cm apart. A low voltage AC current was passed down the catheter and when the moisture levels increased, then electrical resistance between the two electrodes would reduce allowing an increase in conductivity indicating faecal incontinence. Simultaneous anoctoreal manometry was performed to correlate these events with changes in the anoctoreal pressure gradient.

10 patients (median age 58, range 44-76) with faecal incontinence were assessed for a median of 8 (4-18) hours. Episodes of faecal leakage were detected in all patients characterised by a rise in conductivity. A positive recto-anal pressure gradient was recorded for all of these events.

In conclusion, a sensor has been developed which can accurately and objectively detect episodes of faecal incontinence. The ability to detect occult episodes of faecal leakage has clear implications for the assessment of patients complaining of faecal incontinence.

EARLY INDOMETHACIN LESIONS IN RAT JEJUNUM: REDUCED VOCAL BLOOD FLOW AND SHORTENING OF VILLI PRECEDE ULCERATION

Background. Histologically, administration of indomethacin (indo) causes villus shortening, eosinophil infiltration and microvascular distortion, prior to ulceration. These changes may compromise blood flow and lead to mucosal necrosis.

Aim. This hypothesis was tested by correlating histological changes with changes in villus blood flow, measured in vivo using 125I-labelled red cells.

Methods. In two groups of rats (n=5 per group), oral indo (15mg/Kg) was given at 4 or 6 h preoperatively. Luminal and plasma levels were measured in order to determine the optimum dosing for subsequent experiments. After anaesthesia, exteriorised villi enclosed in a chamber were observed by fluorescent microscopy using iv FITC dextran and labelled red cells. Blood flow in surface arcade vessels was calculated from measurements of velocities and diameters (60-144 x 10^-6). In other groups indo was applied by simultaneous topical (100ug/ml) and iv administration (producing a peak plasma level of 100ug/ml) (n=5). Controls consisted of vehicle alone (n=5). Animals were sacrificed, perfusion fixed with 5% formal saline and processed for histology.

Results. Oral indo resulted in peak luminal and plasma indo concentrations of 100mg/ml. In-vivo observation revealed groups of villi with vascular stasis. Histologically the villi were shortened, and had distorted epithelium and vessels. Combined topical and iv indo, given pre-operatively, induced immediate progressive slowing of blood flow in individual villi, and complete stasis within 15-45 mins in individual villi in all animals (Fig). Blood flow in adjacent villi was normal. At this time point, histology showed groups of shortened villi with distortion (but no loss) of surface epithelium overlying focci of vascular stasis, and normal surrounding villi. In both regimes lesions occurred only on the mesenteric border between vasa-recta. All control animals had normal blood flow (2.6 ± 0.1 nl/min) for 1.5hrs.

Conclusions. Oral dosing with indo, or combined topical and iv dosing at an ulcerogenic level, produces pre-ulcerative villus shortening, associated with severe focal interference of capillary blood flow. Thus focal ischaemic changes are likely to be involved in induction of lesions.

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SERUM SUCROSE: A NEW SCREENING TEST FOR COELIAC DISEASE
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An accurate non invasive test to screen for coeliac disease (CD) would be popular with patients and reduce the need for small bowel biopsy. Until recently such tests were inaccurate. IgA endomysial antibodies have been found to have a high sensitivity and specificity for CD. Small intestinal permeability tests involving urinary recovery of ingested markers are highly sensitive but not specific for CD. During the development of techniques to measure permeability in serum, an unidentfied peak was found in the serum from untreated CD patients but not in other sera. This peak was later found to be sucrose. The aims of this pilot study were to determine if serum sucrose is a marker for untreated CD and to compare the results with endomysial antibody titres. 20 consecutive newly diagnosed coeliacs, 15 controls on a strict gluten free diet for more than 12 months and 15 healthy normal controls were studied. All were given a drink containing approximately 8g of sucrose and had blood taken 30-45 minutes later: serum was deproteinised using the method of Somogyi and analysed using HPLC and pulsed amperometric detection for the presence or absence of sucrose. As Clin Biochem 1995 AR2:89-90). Sucrose was present in all 20 untreated coeliacs but in none of the treated coeliacs or normal controls. 17 untreated coeliacs were endomysial antibody positive; all the treated coeliacs and normal controls were negative. Serum sucrose separated untreated coeliacs from treated coeliacs and normal controls more accurately than endomysial antibodies. Serum sucrose shows promise as an indirect marker for villous atrophy and coeliac disease.
Microalbuminuria in Treated Adult Coeliac Disease.

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Background. We have observed that of 19 adults (13 males) with microalbuminuria (urine albumin excretion 20 to 200 µg/minute) associated with insulin-dependent diabetes mellitus (IDDM), 3 (16%) male patients had coeliac disease (2 newly diagnosed patients, each investigated because of unexplained anaemia, and 1 patient with coeliac disease diagnosed and treated with gluten free diet since age 5 years). We have therefore investigated the level of urinary albumin excretion in patients with treated coeliac disease compared with healthy adults.

Methods. 36 patients with treated coeliac disease (average age 48.3 years and average duration of gluten free diet (GFD) years) and 30 healthy volunteers (average age 40.2 years) were recruited. None of the patients or volunteers had diabetes mellitus. A 2 hour morning urine collection was obtained from patients and volunteers, and urine albumin (mg/g) and creatinine (mmol/l) concentrations measured using standard laboratory techniques. Results were expressed as albumin creatinine ratio (A/C ratio: mg/mmol).

Results. A/C ratio was significantly higher in patients than controls (0.99 ± 0.65 mg/mmol. p < 0.02, unpaired t test). There was no correlation between A/C ratio and duration of GFD (r=0.14, Spearman’s rank correlation). There was no difference in A/C ratio (0.89 ± 0.13 mg/mmol) in patients who had strict GFD (n=27) compared with those with occasional intake of gluten.

Conclusions. 1) Patients with treated coeliac disease have significantly increased urine albumin excretion. The clinical and prognostic significance of this remains to be determined. 2) The incidence of coeliac disease is known to be increased in IDDM, but perhaps those IDDM patients with microalbuminuria are particularly likely to have hitherto undiagnosed coeliac disease.


Introduction. To date most treatments for acute diarrhoea have been aimed at replacing fluid and electrolyte losses, slowing intestinal transit or treating the infection with antibiotics. In animal experiments 5-hydroxytryptamine (5-HT) has been implicated in cholera toxin (CT)-induced secretion and the 5-HT receptor antagonist, granisetron, has been shown to reverse 60-70% of intestinal secretion. If this finding were confirmed in humans then 5-HT, antagonists would emerge as a class of anti-secretory drugs, invaluable in mitigating the severity of diarrhoea.

Aim. This is a placebo-controlled, cross-over study to investigate the effect of granisetron on CT-induced jejunal fluid and electrolyte transport in male subjects using an established model of human cholera.

Methods. Fasted subjects randomly received 3mg intravenous granisetron during one treatment period and placebo during a separate treatment period. Accurate placement of a triple-lumen perfusion tube in the proximal small intestine was confirmed by fluoroscopy. Two inflatable balloons on the perfusion tube isolated a 30cm closed segment of jejunum into which 20µg CT (Swiss Serum and Vaccine Institute, Berne) was introduced. After 3 hours incubation, perfusion with a plasma electrolyte solution (Na140, K4, CI104, HCO3, 40mmol/l) containing a non-absorbable marker, [14C]-PEG, was carried out to assess net water and electrolyte movement. 3x10min collections were taken.

Results. CT-induced secretion (median -6.19±6.1mllcm2/h [interquartile range -7.28 to -7.91]), n=6, was reversed to net absorption by 3mg granisetron (1.31 [2.97 to -1.21], n=8; p<0.013). Net chloride secretion (-905.4±428.2mllcm2/h [-818.1 to -987.1]) was reversed to absorption (13.6 [7.74 to -357.1]; p<0.005).

Conclusion. This study confirms our previous findings in rat small intestine that 5-HT, antagonism reverses CT-induced secretion and suggests that granisetron is an effective anti-secretory agent in humans.
**F246**

ENTEROCCOCCUS FAECIUM STRAIN PR88 - AN EFFECTIVE PROBIOTIC. Hunter J.Q., Lee A.J., King T.S., Barrat M.E.J., Lingood, M.A., Blades J.A. Department of Gastroenterology, Addenbrooke's Hospital, Cambridge and Unilever Research Laboratory, Sharnbrook, Beds.

The concept of administration of non-pathogenic bacteria (probiotics) to improve colonic fermentation has a long history but little scientific commentary. Enterococcus faecium may be a commensal in the healthy human gut and PR88 is a distinct strain which does not possess markers of pathogenicity including haemolysin, hyaluronidase or thermocleavage. Early weaning of piglets lead to transient partial villous atrophy, malabsorption and weight loss. Administering PR88 to piglets daily from 1 week of age had a dose-related effect in preventing these changes. As secretory diarrhoea is associated with increased cyclic AMP production, this was examined in K-1 cells from the Chinese hamster ovary. Pre-treatment with PR88 prevented elevation of cyclic AMP after administration of isoproterenol, forskolin and E coli heat labile enterotoxin. A feeding trial of 1011 organisms per day in rats revealed no harmful effects. To assess the viability of PR88 in the human gut 1010 organisms per day were administered for 12 weeks to 28 patients with high volume diarrhoea caused by food intolerances. PR88 was identified in the stools of all patients at counts of 1010 organisms per day. A culture of PR88 counts rose, there was a corresponding drop in Strep faecalis excretion which reversed when PR88 feeding stopped, PR88 being lost from the stools of virtually all subjects within 2 weeks. No effect on enterobacteria or total anaerobes were detected and haematological and biochemical screening remained normal. There was no serum antibody response to PR88. Symptoms improved in 19 subjects and faecal weights fell from 912 ± 67g to 610 ± 400g (p = 0.0005). Further clinical studies of PR88 are indicated.

**F247**

EFFECT OF SEX, ORGANISM, AND DURATION OF ILLNESS ON THE DEVELOPMENT OF POST DIARRHEAL IRITABLE BOWEL SYNDROME (IBS). J.M. Hebdon1, R.C. Spiller1, K.R. Neal2. 1Depts of Gastroenterology and Epidemiology, University of Nottingham Medical School, UK.

Although postdiarrheal irritable bowel syndrome (IBS) is well recognized the risk following bacterial gastroenteritis has not been quantified. The statutory notifications system was used to identify 665 people with gastroenteritis. A questionnaire covering medical history, the episode of gastroenteritis, bowel habit now and 12 months ago was mailed 6 months after the notification date. IBS was defined using the Rome criteria. Paired t-tests were used for analysis of symptoms before and after gastroenteritis and logistic regression to estimate relative risk (RR) and 95% confidence limits (CL). 436 questionnaires (66%) were returned.

Using the strict Rome criteria 28 people (7%) had developed IBS for which the risk factors were female sex RR= 2.9 (95% CL – 1.2-6.9) and duration of gastroenteritis RR= 2.1 (95% CL – 1.3-3.4) for each week of symptoms. The number of cases of new IBS by infecting organism were campylobacter 17,228, salmonella 3,104, shigella 3,159, giardia 1,109 and cryptosporidium 3,109, 0.05% varicella. Lesser changes in bowel habit were surprisingly common being reported in 107 patients. The mean±SEM of the number of days per week on which symptoms were experienced are shown below. Table.

<table>
<thead>
<tr>
<th>symptom</th>
<th>loose stools</th>
<th>bloating</th>
<th>slience</th>
<th>hard stools</th>
<th>urgency</th>
</tr>
</thead>
<tbody>
<tr>
<td>before</td>
<td>2.4±0.9</td>
<td>1.3±0.9</td>
<td>0.5±0.1</td>
<td>1.4±0.9</td>
<td>0.7±0.9</td>
</tr>
<tr>
<td>after</td>
<td>2.5±0.9</td>
<td>1.2±0.9</td>
<td>0.4±0.1</td>
<td>1.3±0.9</td>
<td>0.6±0.9</td>
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<tr>
<td>p value</td>
<td>&lt;0.001</td>
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</table>

In conclusion, 25% reported altered bowel habit largely characterized by increased frequency of loose stools. IBS developed in 7% of patients. Infection with shigella and cryptosporidium were more likely to result in IBS than salmonella. Female sex and increasing duration of illness significantly increased the risk of developing IBS.

**Pharmacology F248–F253**

INHIBITION OF ACID SECRETION BY INTERLEUKIN-1β AND TUMOR NECROSIS FACTOR-α IN CULTURED RABBIT PARIETAL CELLS INVOLVES MULTIPLE PATHWAYS. Ian L., P. Brelas and John Calam. Gastroenterology Unit, Royal Postgraduate Medical School. London, UK.

The pro-inflammatory cytokines interleukin-1β (IL-1β) and tumor necrosis factor α (TNF-α) are potent inhibitors of gastric acid secretion when administered in vivo. The site and mechanism of action is not yet understood. Therefore we have studied the effect of these cytokines on the acid secretion capacity of parietal cells. Methods: Rabbit parietal cells were isolated by collagenase-EDTA digestion, enriched by centrifugal elutriation and cultured for 40 hours. Intracellular accumulation of 31C-aminopinic acid (AP) over 30 mins was used to assess acid secretion in response to receptor dependent or independent stimuli. Results: Both IL-1β and TNF-α (0.1-100ng/ml) dose dependently inhibited AP uptake stimulated by 0.1mM histamine (maximal inhibition II. β 25±5.5%, p<0.01, TNF-α 21±5.6%, p<0.05), 0.1 mM carbachol (II. β 47±4.5%, TNF-α 57±9.2%, both p<0.001) and 0.1 μM gastrin (II. β 66±14%, TNF-α 57±8%, both p<0.01). Near maximal inhibition occurred with 10 μM of cytokine. Inhibition was maximal with 15 mins preincubation but was seen at all time points up to 18 hours. There was no alteration in binding of 125I-gastrin or 3H-histamine. Both cytokines at 10 ng/ml also inhibited AP uptake stimulated by 10μM forskolin (II. β 15±5%, TNF-α 16±4%, both p<0.05) and the calcium ionophore A23187 (1μM) (II. β 55±15%, TNF-α 65±16 % p<0.001), but had no effect on stimulation by dibutyryl-cAMP. The inhibition of histamine and forskolin action by both cytokines was completely blocked by pretreatment with pertussis toxin (200mg/ml) but this had no effect on inhibition of carbachol or A23187 stimulation. Pretreatment with the tyrosine kinase inhibitor herbimycin A (1μM) also abolished the inhibition of histamine and forskolin stimulation and significantly reduced the inhibition due to TNF-α with carbachol and A23187 but had no effect on IL-1β inhibition of these stimuli.

Conclusions: IL-1β and TNF-α directly inhibit parietal cell function by multiple pathways, including inhibition of adenylate cyclase and also further steps downstream of the Ca2+ signalling pathway. Inhibition involves tyrosine kinase dependent and independent pathways.