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CROHN'S DISEASE: A VASCULAR MODEL OF ANASTOMOTIC RECURRENCE

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It is not known why an intestinal anastomosis in Crohn's disease usually results in early localised recurrence. Microvascular injury and ischaemia may be important factors. This hypothesis was tested in a model of multifocal intestinal infarction in a series of 17 ferrets.

METHODS: At laparotomy isolated loops of small intestine were injected, via their feeding artery, with either styrene microspheres (20,000-30,000 microspheres/cm bowel - test loop), or saline (control loop). At 72 hours, following mucosal healing, a second laparotomy was performed. Test and control loops were divided and an end-to-end anastomosis was performed between either test loop and test loop (n=2), test loop and control loop (n=9), or control loop and control loop (n=2). In addition, two animals had an anastomosis alone without injection of microspheres, and two had microspheres alone, without anastomosis. Animals were sacrificed two weeks later and the intestine was examined microscopically and macroscopically. A total of 388 tissue blocks were examined with a minimum of 20 blocks/animal. Sections were reviewed in a blinded fashion. RESULTS: No abnormalities were seen in control loops and control anastomoses at two weeks. Macroscopic and microscopic abnormalities at 2 weeks were seen in 10 of the 11 test animals, were confined to the test loops, and were most prominent adjacent to the anastomosis. These changes included chronic, discontinuous and transmural inflammation (9/11), ulceration (6/11), and granuloma formation 4/11 cases. The changes became progressively milder further away from the anastomosis. CONCLUSIONS: These data confirm that the combination of two self-limiting ischaemic insults can produce a pattern of intestinal injury that is analogous to anastomotic recurrence of Crohn's disease. The study supports a role for ischaemia in the evolution of Crohn's disease.

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MEASURE OF THE QUALITY OF LIFE IN INFLAMMATORY BOWEL DISEASE (IBD).

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Indexes of IBD activity do not usually include a measure of the patients'subjective emotional and social problems which are important for a comprehensive assessment.

Aims of this study were to prepare and validate an instrument for assessing the quality of life (QL) specific for patients with Ulcerative Colitis (UC) and Crohn's Disease (CD). We prepared a 29-item questionnaire, which explored 4 aspects: intestinal and systemic symptoms, emotional and social functions. The instrument was tested for reproducibility and responsiveness in healthy subjects and patients. We then studied 72 controls and 90 patients with IBD (50 UC and 40 CD) of different disease activity.

Results: mean total score in controls was 6.0 ± 3.8 SD (maximum 87 points); in patients was:

	U C	C D
Remission	14.2 ± 3.8	14.8 ± 8.6
Mild activiy	21.4 ± 6.2*	28.8 ± 15.3*
Moderate activity	37.2 ± 11.1ç	47.0 ± 4.2ç

(* p<0.01, Student's unpaired t-test vs remission; ç p<0.005 vs mild activity). Not only patients with active disease but also those in remission had significantly higher scores for all functions, compaired to controls. Scores varied only 7% when stable patients were retested, while significantly fell in those who improved (from 37.6±9.2 to 23.6±6.3, p<0.005). The score modification, always agreed with the patients' and physician's overall opinion, while it was not always correlated to the biochemical tests'results

We conclude that: 1. the instrument developed is reliable and easy to use; 2. it allows a better definition of the patient's health status, identifying areas which may be overlooked but which may need intervention; 3. also patients in clinical remission have a significantly reduced QL; and 4. such instrument might be used in clinical trials in IBD, as a complement to the "biological activity" indexes.

F255

A FOLLOW-UP STUDY ON SELECTIVE AFFECTIVE BIASING IN IRRITABLE BOWEL SYNDROME (IBS).

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In a previous study of word recognition memory for emotionally loaded stimuli we found evidence of selective affective biasing in favour of negative material in both IBS and depressed patients. In addition the IBS group showed a unique receptiveness to emotionally negative material evidenced by a markedly elevated false-positive error rate for material of this kind. In depression such negative biases dissipate with clinical improvement. To investigate whether this would also occur in IBS, we repeated the word recognition memory task after an 8 month period (IBS n=23; depression n=20). The task involved memorizing a set of 24 emotionally loaded words (8 neutral, 8 positive, 8 negative) and then later picking the words out from a word list. Anxiety and depression were assessed by the Beck Depression Inventory (BDI) and the Hospital Anxiety and Depression Scale (HAD).

At retest, anxiety and depression had decreased in depressed patients, BDI (15.7±6.5 vs 6.4±4.9; p<0.001) and HAD (27.4±5.7 vs 14.5±8.2; p<0.002) and IBS, BDI (9.0±3.8 vs 6.0±3.4; p<0.03) and HAD (17.1±8.2 vs 14.6±5.9, NS). On the word recognition memory task, the depressed group tended to show a reduction in their previous negative bias (84.0±0.9 vs 66±1.34; NS) which was not apparent in the IBS group (94±1.3 vs 91±0.9; NS) despite the fall in BDI score. Moreover, the significantly elevated false-positive error rate for negative material in the IBS group persisted (47±1.26 vs. 40±1.2) unlike the depressed patients in whom it decreased (21±1.0 vs 3±0.5; p<0.001).

Thus, the previously noted receptiveness to emotionally negative material in clinical IBS is persistent, which supports our previous contention that this may have a central role in the perpetuation of their somatic symptoms.

F256

IMAGING ANAL FISTULA WITH MRI

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The majority of anal fistulae are simple and relatively easy to treat. Fistulae are usually considered more difficult when the primary tract crosses the upper part of the external anal sphincter or when the track is suprasphincteric or extrasphincteric. The other "difficult" fistula is one which recurs despite skilled attention, in which additional internal openings or further secondary tracks may be responsible for the recurrences. Accurate delineation of total fistula anatomy, and especially in relation to the sphincter complex, is crucial to successful management, but techniques employed preoperatively to date (fistulography and anal endosonography) have been disappointing. Indeed, some consider the most accurate tool to be the experienced operator's digit.

MRI scanning demonstrates accurately the anatomy of the levator sling and sphincter complex, and the granulation tissue of fistulae tracks is revealed brightly on "STIR" sequences, requiring no contract enhancement.

Twelve patients with fistula-in-ano of varying complexity have been scanned with MRI, and the independent interpretation of the images has been identical in all cases to the findings at surgery (see figure).

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A COMPARISON OF THE PROPERTIES OF THE INTERNAL ANAL SPHINCTER AND THE CONJOINT LONGITUDINAL COAT OF THE ANAL CANAL.

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The internal anal sphincter (IAS) and the conjoint longitudinal coat (CLC) form two discrete layers of smooth muscle within the anal canal. The latter is the continuation of the longitudinal muscle of the rectum and has an unknown function. The purpose of this study was to compare the properties of the two muscle layers.

Small strips of muscle from both layers (n=30 strips from 5 abdomino-perineal resection specimens) were mounted for isometric tension recording in a perfused organ bath at 36 °C. Tone was initially established by loading the strips with the equivalent of a 1gm. weight. Subsequently, this spontaneously increased in IAS but decreased in CLC strips (187±4.3% of original tone vs. 21.7±7.1%, $p < 0.01$ unpaired t test). In this state, carbachol, a cholinergic agonist, caused dose dependent relaxation of IAS strips ($5x10^{-6}$ - 10^{-4} M) but contraction of CLC strips ($5x10^{-7}$ - 10^{-4} M). Hexamethonium (10^{-6} M), a ganglion blocking agent, had no effect on these responses but they were abolished by atropine (10^{-6} M), a cholinergic (muscarinic) receptor antagonist. Noradrenaline caused dose dependent contraction of both tissues ($5x10^{-6}$ - 10^{-4} M), a response which was abolished by phentolamine (10^{-6} M), an alpha-adrenergic receptor antagonist.

These results indicate that the behaviour of the two smooth muscle layers of the anal canal is different and suggests that defaecation may involve CLC contraction.

F258

REDEFINED ANAL SPHINCTER ANATOMY - ENDOSONOGRAPHIC, DISSECTION AND IN VITRO STUDIES.

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Dispute exists about the precise relationship between the different components of the striated sphincter muscle, the longitudinal muscle and circular smooth muscle of the internal anal sphincter (IAS).Previous anatomical details have been acquired mainly from post mortem dissection studies. This study aimed to precisely define sphincter anatomy in vitro using the newly developed technique of anal endosonography and to relate these images to dissection and histological findings.

Methods: Six anal sphincters removed whole at surgery and 6 removed post mortem were studied ultrasonographically while dissected layer-by-layer in a water bath.Simultaneous endosonography was then performed in 10 patients during surgical dissection, to correlate the ultrasound images with true anatomy. Four specimens had a comparison of ultrasonography and histology at serial levels. Finally anal endosonography was performed in 60 nulliparous women and 20 men as healthy controls, taking note of the distribution and anatomical variation of the puborectalis, 3 components of the external anal sphincter (EAS),the IAS and longitudinal smooth muscle.

Results: The puborectalis, anal sub-epithelium, IAS, EAS and fatty layer were separately identifiable in all subjects. The longitudinal muscle layer varied in thickness and was more prominent in the male. The EAS could be divided into 3 components not by a demarcation line but by a change in its configuration. The ano-coccygeal ligament and the perineal body were seen more clearly in the men. The EAS in the female, unlike the male, was much shorter anteriorly than posteriorly. Normal variants of the EAS could be discernible by ultrasound.

Conclusions: Endosonographic images of the anorectal structures do correlate with dissection and histological findings and demonstrate accurate anatomical information. Anatomical differences can be demonstrated between the sexes. Recognition of normal sphincter layer variations should prevent the erroneous diagnosis of abnormalities.

F259

SIX YEAR FOLLOW-UP OF POSTANAL REPAIR FOR NEUROGENIC FAECAL INCONTINENCE: OUTCOME, PREDICTIVE FACTORS, AND ROLE OF OCCULT SPHINCTER DEFECTS DEMONSTRATED BY ULTRASONOGRAPHY.

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The long term results of postanal repair for neurogenic faecal incontinence are unknown, and the predictive value of preoperative tests remains controversial. The recent development of anal endosonography has highlighted that many patients with neuropathy and incontinence may have undetected sphincter defects, and this may account for some of the poor results of this operation.

Methods: 33 patients with neurogenic faecal incontinence, without a clinical sphincter defect, who underwent a post-anal repair between 1984 and 1986 (all female, mean age 59, range 30-76) were studied. Patients had pre-op physiology studies and post-op (1991) physiology studies, symptoms evaluation and anal endosonography after a mean follow-up of 6.3 years. Incontinence was scored as A-normal, B-incontinent to flatus, C-incontinent to liquid stool, D-incontinent to solid stool. Measurements included anal manometry pudendal nerve latency measurements, and endo-sonography.

Results: All patients were C or D pre-op; post-op 27% were A or B and 73% were C or D. Post-op 9 patients took constipating drugs, and 12 used laxatives for associated constipation (only 4 of whom had pre-op constipation). Of the pre-operative measurements, pudendal nerve latency prolongation predicted poor outcome (mean pre-op value for those ending up C or D 2.6 msec, mean for final A or B 2.2, $p < 0.03$). Resting and squeeze anal pressures pre-op did not predict outcome. Anal endosonography showed a defect in 19 patients: internal anal sphincter in 15, external in 13, both in 9.

Conclusions: Only a quarter of patients have a good long term result. More marked pudendal nerve damage predicts a worse outcome. Occult sphincter defects are common in patients with neurogenic incontinence, and contribute to many of the poor outcomes.

F260

PUDENDAL NERVE DAMAGE DURING CHILDBIRTH: PROSPECTIVE STUDY PRE AND POST DELIVERY.

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Vaginal deliveries are thought to cause pudendal nerve damage but previous studies have not included pre-delivery nerve latency measurements. We have prospectively assessed pudendal nerve terminal motor latency (PNTML) pre and post delivery, including changes occurring separately on each side.

Methods: 100 pregnant women (64 nulliparous, 36 mutli-parous) had PNTML studies performed after 34 weeks gestatation and 6-8 weeks after delivery. 14 were delivered by Caesarian section - 7 elective and 7 in labour. PNTML was measured on each side using a finger mounted electrode, with a stimulus of up to 50V, 0.1 ms, 1Hz.

Results: Primiparous vaginal deliveries (n=56) resulted in prolonged PNTML bilaterally, but significantly (P=0.02) more so on the left (1.96 v 2.05 ms, pre v post. $P < 0.0001$). In the multiparous vaginal deliveries (n=30) the same phenomena occurred. In the elective Caesarian section group the PNTML did not change. In the Caesarian section during labour group (n=7) the PNTML became prolonged, to a greater extent on the left side (1.95 v 2.13, $P < 0.05$).

Conclusions: Vaginal delivery affects pudendal nerve function. In contrast to other studies this prospective study shows that pudendal nerve damage persists at 2 months after delivery. Secondly, women who have had a C/S during labour may also suffer the consequences of a pudendal neuropathy. Thirdly, the pudendal nerve damage may be asymmetrical in its extent.

F261

ANAL SPHINCTER DISRUPTION IN 32% OF VAGINAL DELIVERIES: PROSPECTIVE ULTRASOUND STUDY.

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The development of faecal incontinence in middle age has been previously attributed primarily to pelvic nerve damage during childbirth with subsequent progressive pelvic floor denervation. However, occult anatomical lesions may occur during childbirth. We have prospectively studied the incidence of damage to the anal sphincters during childbirth, using anal endosonography.

Methods: 134 women (113 vaginal delivery: 72 primiparous (A); 41 multiparous (B); 21 Caesarian section (C) were studied in the last 6 weeks of pregnancy and again 6 weeks post delivery. Anal endosonography was performed using a Bruel and Kjaer rotating 7 MHz probe, withdrawn down the anal canal at 1cm intervals to image the whole length of the sphincter. Anal manometry was performed using a 1cm stationary pull-through technique with an air-filled microballoon catheter.

Results: (A) All primiparous vaginal delivery patients had a normal sphincter pre delivery; post delivery 32% had an internal anal (IAS), 12.5% had an external anal sphincter (EAS) defect; a total of 32% developed a defect. Only three of these patients developed flatus incontinence. (B) 49% of multiparous patients had a preexisting lesion: IAS 46% and EAS 20%. IAS lesions worsened post delivery in 26% and 5% developed a new EAS lesion. 50% of patients with IAS defects had low resting pressures and 49% of EAS defects had low voluntary squeeze pressures. Caesarian sections were mainly on primiparous women: there were no defects pre or post delivery.

Conclusions: New defects occuring in both parts of the sphincter are common after vaginal delivery.Most are asymptomatic. The later development of incontinence is therefore likely to be due to the combination of occult defects with the progression of neuropathy.

F263

SYMPTOMATIC AND OBJECTIVE BENEFITS WITH BIOFEEDBACK FOR INTRACTABLE CONSTIPATION.

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There are few objective assessments of the benefit of biofeedback for intractable constipation. It is also not clear which type of patient benefits, and which symptoms improve. We have prospectively evaluated the success of treatment in patients with pelvic floor inco-ordination and slow colonic transit.

Methods: 30 consecutive patients with reduced bowel frequency or excessive need to strain or both, who had not responded to fibre or laxatives, entered the study. Week-long diaries were recorded pre- and 6 weeks post treatment to record bowel frequency, straining digitation, laxative use, pain, and well being. Proctography, pelvic floor relaxation (EMG and manometry) and transit time were measured pre treatment, and transit time remeasured post treatment. Biofeedback focussed on relaxing the pelvic floor, using visual EMG, and transmitting expulsive force to an intrarectal balloon. Patients had 2-6 45 minute sessions.

Results: 10 patients did not complete treatment. Of the remaining 20 patients: (i) 2 with slow transit only did not benefit. (ii) All 8 with pelvic inco-ordination only decreased time spent straining. (iii) Of 10 patients with pelvic inco-ordination and slow transit, 8 benefitted - 9 decreased straining (mean 30 v 8 mins, pre v post, $p<0.05$), 3 reduced or stopped digitation. Mean proportion of retained markers significantly decreased (66% v 23%, $p<0.02$). For all 18 with pelvic inco-ordination (i & ii) the bowel frequency increased (mean 4 v 6/week, pre v post, $p<0.05$), straining time decreased (mean 29 v 11 min, $p<0.01$) and straining episodes decreased (mean 5 v 2/week, $p<0.01$). Pain was not improved in all groups.

Conclusions: Biofeedback improves bowel frequency and symptoms of straining, digitation and well being. It significantly reduces transit time when prolonged. Pain is not relieved. Patients with pelvic inco-ordination are most likely to benefit, although some with slow transit improve.

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EFFECT OF NICOTINE ON RECTAL MUCUS AND MUCOSAL EICOSANOIDS

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Anglo-Dutch Nicotine Intestinal Study Group

Colitis is largely a disease of non-smokers and nicotine may have a beneficial effect on the disease. To examine the effect of nicotine on rectal mucosa 32 rabbits were allocated into 4 groups, controls and 3 treatment groups. Nicotine tartrate at low, medium and high doses was administered subcutaneously via an Alzet osmotic mini-pump in doses of 0.5, 1.2 and 2 mg/K/day respectively. After 14 days' treatment the rectum was removed and the visible adherent layer of mucus was measured using phase contrast microscopy on thick sections. Rectal mucosal synthesis of mucin and mucosal eicosanoids were also measured.

Serum nicotine concentrations (ng/ml) were 0.4±0.1, 3.5±0.4, 8.8±0.8, and 16.2±1.8 in control and treated groups respectively. Thickness of adherent mucus was reduced with low dose and increased with high dose nicotine (p 0.026 and 0.0001 respectively). Correlation coefficient for serum nicotine concentration and mucus thickness = 0.446, $p<0.05$. Rectal mucin synthesis measured by ^{3}H-glucosamine incorporation was unchanged. All prostaglandin levels were significantly reduced by nicotine with inverse dose dependence - greatest inhibition with lowest dose.

Nicotine and possibly smoking may affect colitis by an action on mucosal eicosanoids and surface mucus thickness in the rectum and large bowel.

	Control	Low dose	Medium dose	High dose
Mucus thickness μ	36.0±2.0	*22.2±1.3	29.4±3.0	*44.7±2.8
Rectal mucin synthesis (dpm/g wet wt)	106,985	103,304	100,669	92,480
$F_2\alpha$	73.7	9.5*	23.6*	41.8*
PF $F_2\alpha$	13.6	2.7*	4.8*	7.1*
HHT (dpm/mg wet wt)	22.8	8.4*	14.8*	17.2*

* significant difference from control.

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SEVERITY OF GASTRITIS AND VIRULENCE OF *HELICOBACTER PYLORI*

N Figura, L Di Gregorio *, M Bugnoli **, D. Armellini **, E Esposito *, L Abate *, P E Bayeli * (introduced by J E Crabtree)
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An association has been recently observed between the mucosal recognition of a 120 kDa protein of Helicobacter pylori (HP) and the severity of antral gastritis in dyspeptic patients. The aim of this study was to examine if an association exists between severe gastritis and putative virulence factors of HP: motility, urease activity and adhesion.

41 HP strains were tested in all: 13 strains were isolated from the antrum, 14 from the body, and 14 from the fundus of the stomach of 14 dyspeptic patients. Motility was tested in semi-solid brucella broth with 10% fetal calf serum (FCS). Strains were grown in brucella broth with 5% FCS at 150 oscillations per min for 72 hours. After centrifugation and filtration (0.22 μm) dilutions of broth culture were assayed for urease activity using a "urease test broth"; samples were read after incubation at 37°C for 60 min. The degree of adhesion of strains was assayed with Int 407 cells; after 3 hours incubation with 1.5 X 10^7 organisms/ml, cells were stained with acridine orange. The severity of gastritis was assessed histologically according to the "Sydney System" for all 41 biopsies.

No association was found between severe gastritis (SG, found in 8 biopsies, 4 from the antrum) and levels of urease (urease activity was detectable up to 1:64 dilution of filtrates for nearly all strains), motility (26 strains were motile, 4 associated with SG), and strong degree of adhesion (SDA, i.e. 100% of cells colonized with ≥ 50 organisms/cell; 30 strains showed SDA, 8 associated with SG). Similarly mild gastritis was not significantly associated with absence of motility, urease activity ≤ 1:64, and with mild or moderate degrees of adhesion. Thus severity of gastritis is not associated with virulence characteristics of H. pylori.