CROHN'S DISEASE: A VASCULAR MODEL OF ANASTOMOTIC RECURRENT

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 with a different 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 anastomoses, and 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. Our 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.

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

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Indices 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 Crohn's and UC patients.

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

<table>
<thead>
<tr>
<th>Mode</th>
<th>UC</th>
<th>CD</th>
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<tr>
<td>UC</td>
<td>14.2 ± 3.8</td>
<td>14.8 ± 8.6</td>
</tr>
<tr>
<td>Mild activity</td>
<td>21.4 ± 6.2a</td>
<td>28.8 ± 15.2a</td>
</tr>
<tr>
<td>Moderate activity</td>
<td>37.2 ± 11.1c</td>
<td>47.0 ± 4.2c</td>
</tr>
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(1 p<0.01, Student's unpaired t-test vs remission; q p<0.005 vs mild activity). Not only patients with active disease but also those in remission had significantly higher scores for all functions, compared to controls. Scores varied only 7% when stable patients were restented, whereas significantly fell in those who improved (from 37.2 ± 11.1 to 23.0 ± 6.3, p<0.005). The score modification was 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 such instrument might be used in clinical trials in IBD, as a complement to the "biological activity" indexes.

Colorectal F255-F263

A FOLLOW-UP STUDY ON SELECTIVE AFFECTIVE BIASING IN IRRITABLE BOWEL SYNDROME (IBS) E. A. Sankey, A.A.M. Lewis, R.E. Pounder, A.J. Wakefield
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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=25; 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 rest, 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±10.9 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±2.6 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.

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 tract is suprasphincteric or extraspincteric. The other "deep-felt" fistula is one which occurs 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 treatment, but techniques employed preoperatively to date (filmtography and anal angioscopy) 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 fistula 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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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.

Methods: Small strips of muscle from both layers (n=30 strips from 5 abdomino-perineal resection specimens) were mounted for isometric recording in a modified organ bath at 37°C. Tone was initially established by loading the strips with the equivalent of a 1g weight. Subsequently, this spontaneously increased in IAS but decreased in CLC strips (187±4.9% of original tone vs. 21±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^-5 M). Hexamethonium (10^-6 M), a ganglionic blocking agent, had no effect on these responses but they were abolished by atropine (10^-4 M), a cholinergic (muscarinic) antagonist. Noradrenaline caused dose dependent contraction of both tissues (5x10^-6 - 10^-4 M), a response which was abolished by phentolamine (10^-5 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.

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


St Mark's and St Bartholomew's Hospitals, London, UK.

Dispute exists about the precise relationship between the different components of the striated muscle layer, 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 endosonography and to relate these images to dissection and histological findings.

Methods: Six anal sphincters removed whole at surgery and 5 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 endosonography and histology at serial levels. Finally, anal endosonography was performed in 60 multiparous women and 20 men. Healthy controls, assessing the distribution of the rectal and anal canal, determining 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 thickness of the 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 bone 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 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.

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 50, 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 endosonography.

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 these ending up C or D 2.66 ms, mean for final A or B 2.2, p<0.05). Resting and squeeze anal pressures pre-op did not predict outcome. Anal endosonography showed a defect in 19 patients: internal sphincter in 15, external in 2, and unknown, in 2. 10 patients have had 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.

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 multiparous, 36 nulliparous) had PNTML studies performed after 34 weeks gestation and 6-8 weeks after delivery. 14 were delivered by Caesarian section—7 electively 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, P<0.001). In the multiparous vaginal deliveries (n=30) the same pattern 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.
ANAL SPHINCTER DISRUPTION IN 32% OF VAGINAL DELIVERIES: PROSPECTIVE ULTRASOUND STUDY.
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St. Mark's and St Bartholomew's Hospitals, London, UK.

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 Caesarean section (C)) were studied in the last 6 weeks of pregnancy and again 6 weeks post delivery. Anal endosonography was performed using a Bruel & 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 sphincter (IAS) 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. Caesarean sections were mainly on primiparous women: there were no defects pre or post delivery.

Conclusions: New defects occurring 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.

EFFECT OF NICOTINE ON RECTAL MUCUS AND MUCOSAL ECOSYSTEMS.
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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 mucosal 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/kg/day respectively. After 14 days' treatment the rectum was removed and the visible adherent layer of mucosa was measured using phase contrast microscopy on thick sections. Rectal mucosal synthesis of mucus 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 [H]-glucosamine incorporation was unchanged. All prostaoylquin 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.

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, laxative use, pain, and well being. Proctography, pelvic floor relaxation (EMG and manometry) and transit time were measured pre treatment, and transit time reassessed post treatment. Biofeedback focused 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 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 benefited - 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 none with slow transit improve.

Helicobacter pylori

F264–F271

SEVERITY OF GASTRITIS AND VIRULENCE OF Helicobacter pylori

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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 gastritis, in acidic or motility, in dyspeptic patients. The aim of this study was to examine if there is 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 105 cells, all cells were stained with acridine orange. The severity of gastritis was assessed histologically according to the "syndrome system" for all 41 biopsy samples.

No association was found between severe gastritis (SG, found in 8 biopsies, 4 from the antrum) and levels of urease activity (urease activity up to 1/144 dilution of filtrates for nearly all strains), motility (26 strains were motile, 4 associated with SG), and strong degree of adhesion (EDA, i.e., EDA colonised with ≥50 organisms/cell); 30 strains showed EDA, 8 associated with SG). Similarly mild gastritis was not significantly associated with urease activity ≥1/64, and with mild or moderate degree of adhesion. Thus severity of gastritis is not associated with virulence characteristics of H. pylori.