studied. 11 subjects had no evidence of neuropsychiatric impairment, 37 had evidence of minimal HE and 34 had overt HE.

Methods: Unlocalised spectra were acquired from the entire head in 48 patients (TR 5s; 64 averages). Spectra from the basal ganglia (BG) were acquired in 34 patients, using a 3-D CSI technique (TR 5s; 2048 averages). pH_i values were calculated from the chemical shift difference between the inorganic phosphate (P_i) and phosphocreatine (PCr) resonances. The % P_i, PCr and βNTP signals relative to the total ³¹P signal and peak area ratios of P_i and PCr relative to βNTP were also measured.

Results: There were no pH_i differences between patients and volunteers in ³¹P MR spectra from the whole head or BG. There was no correlation between pH_i and the severity of HE or Child score. There was no change in spectra from the whole head, but in BG spectra, there was a significant increase in mean P_i/NTP (p=0.02) and PCr/NTP (p=0.009). The mean %P_i and %PCr were also increased (p=0.06; p=0.05). When the patients were classified according to the severity of HE, those with overt disease had a higher mean P_i/NTP and %P_i (p=0.03; p=0.01), compared to controls.

Conclusion: Our results suggest that there are detectable bioenergetic abnormalities in patients with minimal and overt HE and that any pH change, related to mitochondrial dysfunction, is probably a secondary, rather than a primary phenomenon.

081 HEMODYNAMIC CONSEQUENCES OF PRECONDITIONING IN LIVER ISCHAEMIA-REPERFUSION INJURY

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Background: Ischaemic preconditioning (IPC) may increase tolerance of the liver to ischaemic insults of surgery. IPC may be mediated via nitric oxide (NO). The hemodynamic changes of IPC have not been correlated to NO metabolism.

Material and Methods: Sprague Dawley rats were subjected to 45 mins lobar ischaemia followed by 2 hr reperfusion (IR). L-arginine or L-NAME were administered to stimulate or block NO synthesis. Study groups (n=6) had, (1) sham laparotomy, (2) IR, (3) IPC with 5 min ischaemia and 10 min reperfusion before IR, (4) L-arginine before IR, (5) L-NAME + IPC before IR. Hepatic tissue oxygenation was measured by near infrared spectroscopy (NIRS) and hepatic microcirculation (HM) by laser doppler flowmeter (LDF). Liver function tests and nitrates were analysed. Differences between groups and confidence intervals were established using analysis of variance (ANOVA) with Bonferroni test, and paired student's t test.

Results: IR injury produced significant reduction in HM (31.6% of preischaemic value, p=0.00 vs baseline). IPC improved the HM (49.5%, p<0.02 vs controls) upon reperfusion. IPC improved hepatic oxyhemoglobin and cytochrome oxidase (both p<0.05 vs controls). NO stimulation and blockade did not influence HM or hepatic tissue oxygenation. IPC as well as L-arginine treatment significantly increased nitrates and decreased liver enzymes. L-NAME administration with IPC prevented the rise in nitrates and decrease in liver enzymes.

Conclusion: IPC resulted in improvement of HM and hepatic tissue oxygenation following IR, but the effect may not be solely mediated by nitric oxide.

Oesophagus Posters: 082-111

082 REPEAT OESOPHAGEAL AMBULATORY pH MONITORING—IS IT WORTHWHILE? A RETROSPECTIVE ANALYSIS OF 6000 PATIENTS

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Introduction: Patients who have undergone oesophageal pH studies are re-referred for a variety of reasons, after varying time intervals. The aim was to determine if repeating the pH study was likely to alter the diagnosis.

Patients and methods: Data was reviewed from adult patients who were studied between January 1985 and June 2000. Over 6000 patients have had pH tests, of which there were 211 patients with two or more studies. As therapeutic interventions potentially alter the underlying pathology, only the 111 patients who had no therapy at any stage were included. Both initial and repeat referrals and subsequent diagnoses, were stratified and analysed. The total percentage of reflux (pH<4) time (TPR) and DeMeester score were examined. The initial TPR was also compared to the repeat studies.

Results: Patients diagnosed initially as normal (TPR<5.78 or DeMeester score<14.7) were unlikely (p<0.05) to have their diagnosis changed if their DeMeester score was less than 5.8 (average score 2.0 with SD 1.9). Non-intuitively, the TPR could not predict (p<0.05) whether an initial diagnosis of normal would change. In those initially diagnosed with gastro-oesophageal reflux disease (GORD), TPR and DeMeester score were not predictive (p<0.05). There was a poor correlation between the initial and repeat TPR, even in those whose initial diagnosis was confirmed by the second test (correlation coefficient R²=0.008). There was no consistency of TPR either, in specific groups where throughout the diagnosis was GORD (R²=0.016) or where throughout the diagnosis was normal (R²=0.025).

Conclusion: There is a high degree of intra-patient variation in TPR, in interval repeated studies. In those initially diagnosed as normal, surprisingly TPR is not predictive however a DeMeester score below 5.8 is a relative contra-indication to performing a repeat pH study.

083 THREE-HR POSTPRANDIAL pH MONITORING IS USEFUL IN EXCLUDING GASTRO-OESOPHAGEAL REFLUX DISEASE IN SYMPTOMATIC PATIENTS

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Introduction: Currently ambulatory 24hr oesophageal pH monitoring is the gold standard for the diagnosis of gastro-oesophageal reflux disease. This long period of oesophageal intubation is unpleasant. Thus the aim of this study was to determine if a 3hr postprandial study would be as sensitive as the 24hr study.

Patients and methods: Two hundred symptomatic patients (86 male, 114 female, average age 56yrs 3 months) were studied. A 3hr postprandial period was analysed and compared to a standard ambulatory 24hr oesophageal pH monitoring (Synectics Medical). A positive test was defined as >5.78% of the total period of pH<4. The De Meester score was also calculated from the 24hr study, with a score >14.72 regarded as positive.

Results: The 3hr post prandial oesophageal pH correlated well with the 24hr study (r=0.885, p<0.001), and the De Meester score (r=0.82, p<0.001). When only supine periods during the 3hr test was examined this again correlated well with the complete 24hr study (r=0.884, p<0.001), and the De Meester score (r=0.796, p<0.001). The negative predictive value of the 3hr study was 92% when compared with the 24hr test, and 88% when compared with the De Meester score.

Abstract 83, Table 1

	3hr pH vs 24hr pH	3hr pH vs De Meester score
Negative predictive value	92%	88%
Positive Predictive value	65%	80%
Sensitivity	88%	85%
Specificity	75%	82%

Conclusions: The 3hr post prandial study is a sensitive test for the detection of gastro-oesophageal reflux disease, and a negative 3hr test is useful in excluding disease in symptomatic patients.

084 CLINICAL ROLE OF OESOPHAGEAL MANOMETRY

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Background: Although several modalities are available to investigate oesophageal motility disorders, most gastroenterologists regard manometry as the gold standard. Manometry is increasingly available in district general hospitals but the clinical utility of the investigation in this setting remains unclear.

Aim: To evaluate the use and outcome of oesophageal manometry in a district general hospital setting.

Methods: Data on 100 consecutive oesophageal manometry procedures performed in Neath General Hospital between September 1998 and December 1999 (14 months) were analysed, taking into account the referral pattern, indications and results. Manometry was performed using the Synectics Polygraph with polygram software and Gaeltic triple solid-state transducer catheters.

Results: There were 46 male, 54 female patients, average age 52.8 years, range 15–81 years. Referrals were from six hospitals in south Wales and were from—surgeons (51 patients), physicians (47) and paediatricians (2). The indications for referral were gastro-oesophageal reflux (pre-operative assessment before fundoplication) (58), dysphagia (28), chest pain (12) and epigastric pain (2). Manometric diagnoses were made using standard pre-defined criteria and were as follows: normal (41), non-specific motility disorder (NSMD) (38), achalasia (15), diffuse oesophageal spasm (4) and scleroderma (2). Of the 58 patients who had undergone manometry as a pre-operative assessment of oesophageal motility before fundoplication, 27 (47%) were abnormal. Twenty-five (43%) had NSMD and 2 (3%) had achalasia. Forty-eight of these pre-operative cases were combined with 24 hour pH recording, which confirmed acid reflux in 35 (73%).

Conclusion: Our experience reflects the published evidence that the use of manometry is changing. It is now more commonly used for assessment before anti-reflux surgery and for dysphagia, and the use in the assessment of chest pain is declining. Our findings confirm the importance of eliminating significant motility disorders (particularly achalasia) to avoid inappropriate anti-reflux surgery.

085 REFLUX SYMPTOM REPORTING AND ACID PERFUSION TESTING IN SCLERODERMA

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Gastroesophageal reflux disease causes significant morbidity in scleroderma (SSc) yet the reliability of reflux symptoms in the diagnosis is unclear. Acid perfusion testing (APT) has produced conflicting results regarding acid insensitivity in SSc patients. The aim of this study was to assess the value of reflux symptom reporting in predicting acid reflux in SSc and to assess the diagnostic value of acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system for each of heartburn and acid regurgitation with total minimum and maximum scores of 0 and 6 (0=<x1/month, 3=daily symptoms). APT was performed with normal saline infused at 8mls/minute for 5 minutes after which 0.1 N HCl was infused until either typical reflux symptoms occurred or 10 minutes had elapsed. The test was positive if typical symptoms were elicited by acid but not saline. Twenty-four hour ambulatory oesophageal pH monitoring then identified patients with normal (NEG) or abnormal (POS) pH profiles. The pH study was considered abnormal if any one of the total, erect or supine periods showed excess acid reflux. 22 patients were recruited. 21 had a positive acid perfusion test (96%) with a median time to onset of symptoms being 2 minutes (IQR 1–3). 14 (64%) had an abnormal pH profile. POS and NEG did not differ regarding symptom scores (POS v NEG, 4.1 v 3.6, $p=0.44$) or time to onset of typical symptoms (1.7 mins. v 3 mins., $p=0.12$). Only 64% of SSc patients with reflux symptoms have excessive oesophageal acid exposure yet 96% have a positive APT, the majority being positive in 2 minutes or less. This suggests that rather than acid insensitivity, SSc patients are very sensitive to acid exposure.

086 SWALLOWING CLINIC—A COMPLETE CARE PACKAGE

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In the East Yorkshire area, the Swallowing clinic is run as a Speciality referral clinic, with referrals from both General Practitioners and other nearby hospitals. We did an audit of the patients attending the clinic to assess the various disease patterns seen and the utility of the clinic over a two year period. The clinic provided single stop Consultation along with Upper GI Endoscopy followed by review and if need

be, fast track investigations. The clinic was run by a Consultant Gastroenterologist along with a Clinical Assistant, Specialist Registrar and a Nurse in the Endoscopy unit. The clinic attended to 197 pts. over a two year period. The mean age of the patients was 57.9 years. There were 109 females and 88 males seen. Eleven patients (5.6%) had Oesophageal cancer. Gastroesophageal reflux disease was seen in 116 pts. (58.9%), of which 36 pts. (18.3%) had oesophageal strictures which were dilated. Motility disorders were seen in 19 pts. (9.6%). Globus syndrome was seen in 19 pts. (9.6%). Two pts. had Achalasia (1%) and two pts. had Pharyngeal pouch (1%). Various other diagnoses were seen in 28 pts. (14.2%) including Gastric/Duodenal ulcer and Odynophagia. Thirty eight patients underwent Oesophageal dilatation. No pts. had any complications. Nineteen pts. underwent Oesophageal manometry/pH monitoring and 46 pts. had Radiological investigations. The mean waiting time for a clinic appointment was 2.76 weeks. Importantly, for pts. with cancer, this was only 1.75 weeks.

Conclusions: A speciality clinic provides patients with a single stop complete care package, which is fast, efficient and competent. The service is probably superior to a conventional open access endoscopy and to the new two week cancer waiting initiative by virtue of its complete care package.

087 DYSPHAGIA—WHICH TEST SHOULD BE FIRST

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Increasing demands to perform a definitive test for malignancy within 2 weeks has led to a reassessment of the order of investigations for dysphagic patients. Upper GI endoscopy is often the definitive test in detecting upper GI tumours but it has been widely accepted that barium swallow should precede this, due to the risks of endoscopy in high dysphagia. Carefully history taking in patients with dysphagia can lead to the diagnosis in over 80%, however localisation to the sternal notch has poor correlation with anatomical site. 100 cases of dysphagic patients were investigated prospectively, noting the final diagnosis, first test performed and the site of localisation, to ascertain whether endoscopy can safely be the first test. 6 patients were found to high causes of dysphagia (pouch, web, thyroid mass, cricopharyngeal spasm). All presented with high dysphagia and had a barium swallow as the first and diagnostic test. 53 had low causes of dysphagia, 51 described low symptoms and 48 had an endoscopy as the first test. 11 patients had gastro-oesophageal cancer, 10 described low dysphagia and an endoscopy was the first and diagnostic test (allowing biopsy). Of note most of these had progressive dysphagia to solids alone, for less than 3 months. Patients with peptic strictures (13) and oesophagitis (27) were 10 years younger, heartburn was commonest amongst the oesophagitis group and longer duration seen in the peptic stricture patients. 15 patients had dysmotility, dysphagia to solids and liquids was more common (33%). Upper GI endoscopy is a safe, definitive first test in patients with low dysphagia, allowing rapid diagnosis.

088 ACID EXPOSURE AT THE GASTRIC CARDIA: AN IMPORTANT DETERMINANT OF GASTRO-OESOPHAGEAL REFLUX

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Background: Episodes of gastro-oesophageal reflux are usually associated with low or absent gastro-oesophageal barrier pressures. However, on many occasions barrier pressure falls but acid reflux does not occur. We have therefore studied patterns of acid exposure at the gastric cardia and their relationship to episodes of reflux.

Methods: Ten asymptomatic volunteers and ten patients with gastro-oesophageal reflux were studied. A multi-lumen manometric assembly was used to monitor oesophageal body, lower oesophageal sphincter (LOS) and gastric pressures and a multi-channel pH electrode was used to measure pH, at 5cm above and at 2.5 and 10cm below the LOS for 30 min before and 2 hours after instillation of a test meal.

Results: 28 episodes of physiological and 182 episodes of pathological reflux were recorded. Most of the physiological episodes were associated with TLOS whereas most of the pathological episodes were associated with swallow-related relaxations. At 5 and 10 cm below the LOS, pH levels were largely below pH 4 whereas pH

was markedly variable 2 cm below the LOS (pH < 4 = 34.5 (2–100)% in the first post-prandial hour and 22 (2–100)% in the second post-prandial hour). TLOSR were twice as likely, and swallow-related relaxations were three times as likely to be associated with gastro-oesophageal reflux when pH at the cardia was less than 4 (p<0.05). Different patterns of acid exposure were seen at the cardia prior to episodes of gastro-oesophageal reflux suggesting different pathogenic mechanisms.

Conclusions: The gastric cardia is variably exposed to acid before and after a meal. The factors that determine this exposure are unknown but the presence of acid at the cardia increases the likelihood of both physiological and pathological reflux.

089 H. PYLORI (HP), INTRAGASTRIC (IG) PH AND OESOPHAGEAL ACID EXPOSURE (OAE)—THE GORD TRIANGLE

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Recent interest has focused on a possible preventive role of *Hp* in GORD. The inter-relation between *Hp*, IG pH and OAE is poorly understood.

Aim: To assess the role of *Hp* on IG pH, OAE and response to antisecretory therapy in patients with erosive oesophagitis (EO).

Abstract 89, Table 1

Baseline (Mean)	<i>Hp</i> + (n=10)	<i>Hp</i> - (n=31)	P
Age (y)	55.4	42.8	0.007
% time oesophageal pH < 4.0	17.5	11.6	0.12
# reflux episodes > 1min	215	190	0.6
# reflux episodes > 5 min	8.4	5.7	0.3
Mean IG pH	3.0	2.1	0.005
% time IG pH > 4.0	31.6	12.3	0.003

Methods: 41 EO patients (mean age = 46y; sd = 13; 54% men; 90% white) underwent dual probe pH testing. The distal probe was positioned in the gastric body / antrum; the proximal probe 5 cm above the OG junction. Patients underwent repeat pH testing at 1 (n=12) and 12 months (n=9) on therapy with lansoprazole 30mg once daily.

Results: Although, IG acid suppression with lansoprazole in *Hp*+ subjects was significantly better (p<0.001), OAE or change in OAE was not different between the two groups at either 1 or 12 months post-therapy (P > 0.05).

Conclusions: Although *Hp*+ GORD patients are significantly older and have higher IG pH than those who are *Hp*-, they have numerically more OAE. This may be due to effects of age, *Hp* infection, or both on the lower oesophageal sphincter.

090 RABEPRAZOLE 20 MG IN FUTURE OF ACID SUPPRESSION THERAPY (F.A.S.T.) TRIAL: ACUTE HEARTBURN RELIEF IN PATIENTS REFRACTORY TO OMEPRAZOLE AND LANSOPRAZOLE

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Background: Clinical effectiveness of rabeprazole 20 mg once daily in symptoms associated with endoscopically confirmed erosive esophagitis was studied in the F.A.S.T. Trial, including patients who had reported ineffective relief with prior proton pump inhibitor (PPI) therapy.

Methods: An open-label, multicenter, clinical trial of 2449 efficacy evaluable patients diagnosed with erosive GERD was conducted. Within this group, 290 omeprazole recipients and 212 lansoprazole recipients reported prior ineffective relief in the 3 months prior to study entry. After recording baseline daytime and nighttime heartburn at enrollment, patients used an interactive telephone response system within 36 hours to report symptoms for the first 7 days of therapy and at week 4. 4-point Likert scale responses were recorded (0=no symptoms; 3=severe symptoms). Complete relief was computed daily as the percentage of baseline symptomatic patients with a score of 0 divided by all reporting patients who had been symptomatic at baseline.

Results: For heartburn relief in all patients, rabeprazole 20 mg once daily effectively relieved both daytime and nighttime symptoms on Day 1 and throughout the first week, with this treatment effect maintained at week 4. Similar findings were noted in those patients reporting prior ineffective relief with either omeprazole or lansoprazole, with their symptomatic response equaling the all-patient population at week 4.

Abstract 90, Table 1

Percent of patients with Complete Relief	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Wk. 4
Daytime Heartburn								
All patients	64.0	70.8	75.3	76.7	78.2	80.0	81.1	81.1
Prior Omepr ineff relief	51.4	59.6	64.6	67.1	66.5	66.7	65.6	82.2
Prior Lanso ineff relief	54.1	66.9	70.0	73.5	72.0	74.1	75.5	81.0
Nighttime Heartburn								
All patients	69.2	78.1	80.9	82.3	83.8	85.8	85.7	85.7
Prior Omepr ineff relief	57.4	62.7	72.7	72.5	74.2	75.0	77.3	82.3
Prior Lanso ineff relief	62.0	78.1	71.9	74.3	72.8	82.9	76.8	84.4

Summary: Rabeprazole 20 mg demonstrated symptom relief on Day 1 of therapy, even in patients reporting prior ineffectiveness with other PPI's.

091 HELICOBACTER PYLORI INFECTION AND THE MANAGEMENT OF GASTRO-OESOPHAGEAL REFLUX DISEASE. A SYSTEMATIC REVIEW OF THE LITERATURE

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Background: Despite research on the potential link between *H pylori* infection and gastro-oesophageal reflux disease, there is to date no formal systematic review evaluating the overall picture.

Objectives: To evaluate the role of *H pylori* in reflux disease through a systematic review of the literature.

Search strategy: We searched the Cochrane Upper Gastro-intestinal and Pancreatic Disorders group specialised register (August 2000), the Cochrane Controlled Trials Register, CRD Database of Abstracts of Reviews of Effectiveness, Cochrane Database of Systematic Reviews, Medline, Embase and reference list of articles (Jan 1996 to Aug 2000). We obtained recent literature by hand searching recent issues of key journals and contacted manufacturers and researchers in this field.

Selection criteria: Cohort and case-control studies comparing prevalence of *H pylori* in reflux disease with controls. Randomised, quasi-randomised and cohort studies comparing the effect of *H pylori* (presence or absence) on oesophagitis and/or reflux symptoms.

Data collection and analysis: Two reviewers independently assessed trial quality. Data was extracted from eligible trials on a standardised form by a single investigator that was checked by a second investigator.

Preliminary results: Twenty three studies were included in the systematic review, which evaluated 2665 patients and 1730 controls. *H pylori* prevalence was 37% in reflux and 46% in controls. Following successful *H pylori* eradication in 531 patients with duodenal ulcer, heartburn symptom had decreased from 162 patients at baseline to 132 patients at a mean follow-up period of 18 months. In 257 patients with reflux oesophagitis evaluated at 3–57 months, no significant difference in terms of amount of proton pump inhibitors required to maintain remission, dyspepsia scores, and mean reflux values was found between *H pylori* positive and *H pylori* negative patients.

Conclusions: Preliminary results, subject to further statistical refinement, do not suggest a protective role for *H pylori* in reflux disease. The value of eradication in patients with gastro-oesophageal reflux remains open.

092 A BENEFICIAL EFFECT OF H PYLORI ERADICATION IN REFLUX PATIENTS IN THE COMMUNITY

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Theoretical concerns have been raised about *H pylori* eradication in patients with reflux disease. The effect of *H pylori* eradication in patients in general practice with reflux is not known. These patients

tend to present with heartburn as their main symptom or with oesophagitis diagnosed on endoscopy.

Aim: To assess a *H pylori* test and treat strategy in patients on maintenance therapy with either uninvestigated heartburn or endoscopy positive oesophagitis. This was undertaken within the context of a community nurse led clinic during the ACID1 study.

Methods: Two patient groups were studied: 1) Heartburn with no previous GI investigation (n=204); & 2) Endoscopic oesophagitis (n=267). We defined maintenance therapy as ≥ 3 prescriptions / year for PPI and/or H₂RA therapy and the patients in group 1 all reported heartburn as their predominant presenting symptom. *H pylori* status was determined using ¹³C urea breath testing. Symptoms were assessed before and 6 months after treatment, using the Glasgow Dyspepsia Severity Score (GDSS). A significant change in the GDSS was defined as a change of ≥ 3 points.

Abstract 92, Table 1

Change in GDSS	Heartburn		Oesophagitis	
	<i>H pylori</i> eradicated	<i>H pylori</i> negative	<i>H pylori</i> eradicated	<i>H pylori</i> negative
Improved ≥ 3	32.7%	21.7%	28.8%	31.1%
Deteriorated ≥ 3	7.9%	3.6%	4.5%	3.9%
Unchanged	59.4%	74.7%	66.7%	65%
Drug therapy 1 year post Rx				
% off therapy	35.6%	15.7%	27.3%	16.1%
% change to PPI	2.7%	4.2%	4.1%	4.0%

Conclusion: *H pylori* eradication in the community is of benefit in patients on therapy with uninvestigated heartburn. *H pylori* eradication does not adversely affect patients with endoscopic oesophagitis on maintenance therapy and may be beneficial in reducing prescribing costs.

093 A POTENTIAL NEW INDICATION FOR PROTON PUMP INHIBITORS: CHRONIC COUGH ASSOCIATED WITH OESOPHAGEAL DYSMOTILITY

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It has been reported that the chronic cough of patients with proven gastrooesophageal reflux (GOR) may respond to proton pump inhibitors (PPI), but less is known about those cough patients who have oesophageal dysmotility.

Methods: Over an 18-month period, 40 patients (21 female) with chronic cough mean age 57.5 years (range 37 to 76), mean cough duration of 9.3 (0.16 to 50) years underwent oesophageal manometry and 24-hour pH monitoring. 31 patients had reflux symptoms while 9 did not. Patients with abnormal results received standard doses of PPI. GOR was diagnosed if pH below 4.0 was recorded in 3.5% or more of total time. Dysmotility was diagnosed when more than 30% of non-transmitted oesophageal peristaltic waves were recorded during 10 wet swallows.

Results: 10 patients had normal results, interestingly 9 of those had reflux symptoms. 22 patients had positive 24-hour pH monitoring and 19 patients had an abnormal motility profile (11 patients overlapped, 4 of this overlap group had no reflux symptoms). Cough responded well to PPI therapy in 19 patients (86.4%) with positive pH recording and 14 patients (73.7%) with abnormal motility profile.

Conclusions: The absence of reflux symptoms does not exclude abnormal oesophageal motility or abnormal 24-hour pH recording. Oesophageal manometry has identified a subgroup of chronic cough patients with manometric abnormalities who respond to PPI therapy. A randomised trial is needed to verify these pilot results.

094 IN VITRO REFLUX RESISTANCE IN ALGINATE RAFTS

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Introduction: The anti-reflux products Liquid Gaviscon (LG) and Gaviscon Advance (GA) form strong, buoyant alginate rafts on contact with gastric acid, providing a barrier to acid reflux into the oesophagus. The objective of this study was to compare the *in vitro*

performance of LG and GA in tests designed to be representative of the forces involved in reflux into the oesophagus. Rafts were forced to extrude or rupture through an orifice similar in cross sectional area to the relaxed lower oesophageal sphincter and resistance to reflux was measured with a Texture Analyser.

Methods: Rafts were formed by adding a maximum dose of product (20ml of LG or 10ml of GA) to 150ml of 0.1M HCl at 37°C, inside a cylindrical forward extrusion cell fitted with a base disc giving an extrusion orifice of either 10, 15 or 20mm diameter, in a beaker. After stabilisation for 30 minutes, resistance to reflux by extrusion was tested by a plunger fitted to the Texture analyser. Resistance to reflux by rupture was tested by a 9mm diameter cylindrical rod fitted to the Texture analyser. Typical weights and volumes of rafts were also measured.

Results: The force required to extrude GA through a 10mm orifice (3.0Kg) was significantly greater than that required for LG (2.3Kg). The force required to extrude both products decreased with increased orifice size, but at the largest orifice size (20mm) there was no significant difference. The force required to rupture GA rafts (47.4g) was significantly greater than that required for LG rafts (25.2g). GA rafts typically had weights of 20–25g and volumes of 30–42ml. LG rafts typically had weights of 30–35g and volumes of 90–100ml.

Discussion: Rafts of GA are more resistant to simulated reflux than those of LG, either by an extrusion or a rupture mechanism. GA produces a more dense gel, and also the LG raft contains much more CO₂. The same alginate dose (1g) thus creates a buoyant but weaker raft in LG, which may be less likely to suppress reflux than the stronger GA raft.

Conclusion: Gaviscon Advance performs better than Liquid Gaviscon in *in vitro* tests designed to assess the ability of alginate products to resist reflux.

095 TREATMENT OF UNEXPLAINED CHEST PAIN: A DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF AMITRIPTYLINE

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Background: 10–20% of patients undergoing coronary angiography for investigation of chest pain have no significant coronary artery stenoses. Visceral hypersensitivity plays an important role in the pathogenesis of unexplained chest pain (UCP). Tricyclic antidepressants have visceral analgesic effects and may be useful in the treatment of UCP.

Aim: To determine the effects of low dose Amitriptyline on the frequency of chest pain, oesophageal sensitivity and quality of life of patients with UCP.

Methods: Thirty-nine patients with UCP were entered into the study following baseline assessment of psychosocial profile, quality of life, oesophageal manometry, oesophageal sensitivity and 24-hour ambulatory oesophageal pH monitoring. Patients were randomised in a double-blind fashion to Amitriptyline 25 mg nocte (21 patients), or placebo (18 patients) for 4 weeks. Daily records of chest pain frequency and severity were maintained for 2 weeks prior to entry and for the duration of the trial. Intra-oesophageal balloon distension was performed at the end of the treatment period to reassess oesophageal sensitivity. The Short Form-36 (SF-36) quality of life questionnaire was completed at the end of the treatment period.

Results: Sixteen patients in each of the 2 treatment groups completed the study. There was no difference in mean age, gender, baseline psychosocial profile, quality of life scores, oesophageal manometry, oesophageal sensitivity and pH monitoring between the 2 groups ($p > 0.05$). Patients on Amitriptyline showed no significant improvement in chest pain frequency ($p = 0.66$) or severity ($p = 0.71$) when compared with patients on placebo. Oesophageal sensory and pain thresholds of patients on Amitriptyline were not significantly altered ($p = 0.98$ and $p = 0.54$) when compared with patients on placebo. Patients on Amitriptyline had no improvement in their SF-36 scores ($p > 0.05$) when compared with placebo patients.

Conclusions: Low dose Amitriptyline does not improve the symptom of chest pain or quality of life of patients with UCP. Visceral sensitivity in these patients is not altered by low dose amitriptyline.

096 PSYCHOSOCIAL PROFILE, OESOPHAGEAL FUNCTION AND QUALITY OF LIFE OF PATIENTS WITH UNEXPLAINED CHEST PAIN

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Background: 10%-20% of patients undergoing coronary angiography for investigation of chest pain have normal coronary arteries. Oesophageal dysfunction, psychiatric abnormalities and visceral hypersensitivity are possible aetiological factors. Despite a good prognosis, most patients continue to experience chest pain with impairment of functional status and quality of life.

Aims: To compare the psychosocial profile, oesophageal manometry, oesophageal sensitivity and quality of life of patients with unexplained chest pain (UCP) with those of healthy age and sex-matched controls (HC). To determine the incidence of gastro-oesophageal reflux disease in UCP patients.

Methods: Sixty-one patients with UCP and 19 HC were recruited. All subjects completed the Hospital Anxiety and Depression (HAD) Scale, Interview Schedule for Social Interaction (ISSI) and Short Form-36 (SF-36) quality of life questionnaires. Subjects then underwent oesophageal manometry and intra-oesophageal balloon distension. 24-hour ambulatory oesophageal pH monitoring was performed on UCP patients.

Results: UCP had higher mean anxiety (8.7 vs 4.7, $p<0.001$) and depression (4.7 vs 1.5, $p<0.001$) scores. 21/59 (36%) of UCP and 0/19 (0%) of HC had abnormal HAD scores ($p<0.001$). Their mean ISSI ADAT score was higher (8.2 vs 6.6, $p=0.02$) but mean AVAT, AVSI and ADSI scores were not significantly different from those of HC. All the SF-36 scores were lower in UCP ($p<0.001$). 11/48 (23%) of UCP and 2/17 (12%) of HC had abnormal oesophageal manometry ($p>0.05$). UCP had lower sensory (11.2 ml vs 17.9 ml, $p<0.001$) and pain thresholds (15.3 ml vs 20.5 ml, $p=0.002$) on intra-oesophageal balloon distension. 26/48 (54.2%) of UCP had positive pH studies.

Conclusions: UCP patients have a higher tendency to anxiety and depressive disorders but have good social support. Their quality of life is impaired due to continuing chest pain. The incidence of oesophageal dysmotility is not significantly different from that of healthy controls. However, UCP patients show evidence of visceral hypersensitivity and have a high incidence of gastro-oesophageal reflux disease.

097 DOES PNEUMATIC DILATATION AFFECT THE OUTCOME OF LAPAROSCOPIC CARDIOMYOTOMY?

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Background: Controversy surrounds the use of laparoscopic cardiomyotomy as the primary treatment of achalasia or as a second-line treatment following the failure of non-surgical treatment. Laparoscopic cardiomyotomy may be technically more difficult following pneumatic dilatations and the aim of this study was to compare the outcome of primary laparoscopic cardiomyotomy to that performed following failed pneumatic dilatation.

Methods: Laparoscopic cardiomyotomy was performed in 7 patients following a median of 4 pneumatic dilatations (group A) and in 5 patients as their primary treatment (group B). Outcome was measured using manometry, modified DeMeester symptom scoring system and a quality of life questionnaire.

Results: There were no significant differences between groups A and B in sex, age, preoperative modified DeMeester score or mean barrier pressure. Six of 7 group A patients had evidence of peri-oesophageal and submucosal fibrosis at surgery, but this was not detected in group B patients. Operative time was slightly longer in group A patients. There was no difference in complication rates (a primary haemorrhage in group A and an oesophageal perforation in group B) and both groups had a significantly improved modified DeMeester score at 6 weeks and at long-term follow up (median 26 months). Eleven of 12 patients would choose laparoscopic cardiomyotomy as their primary treatment if newly diagnosed with achalasia.

Conclusions: Laparoscopic cardiomyotomy is safe and effective as a primary or second-line treatment following previous pneumatic dilatations in patients with achalasia.

098 LAPAROSCOPIC CARDIOMYOTOMY FOR ACHALASIA

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Introduction: Laparoscopic cardiomyotomy is an accepted treatment for achalasia. It has advantages over the standard surgical approaches of thoracotomy and laparotomy. This series compares patients treated with laparoscopic cardiomyotomy *de-novo* with those who had undergone previous failed balloon dilatation.

Methods: Twenty-two patients underwent a single anterior cardiomyotomy for achalasia. Twelve had previously undergone minimum of 2 (range 2-7) balloon dilatations. Ten patients had no previous treatment.

Results: Mucosal tears were seen in 4 patients in the previously dilated group, there were none in the *de-novo* group. In those patients with no previous treatment there was no requirement for post-operative dilatation. In the previously dilated group, 2 patients required further dilatation. Operative time was significantly longer (median 150 mins vs 120 mins, $p<0.05$ Mann-Whitney) in the previously dilated group, despite the fact that this group had fewer simultaneous anti-reflux procedures. Post-operative stay was significantly reduced in the non-dilated group (median 2 vs 4 days, $p<0.05$ Mann-Whitney).

Conclusion: Laparoscopic cardiomyotomy provides relief from the symptoms of achalasia even in patients who have undergone previous balloon dilatations. However, there is a significant increase in complications, operative time and post-operative stay in those patients who have undergone previous balloon dilatation. This series supports the concept that the best first line treatment for achalasia is laparoscopic cardiomyotomy.

099 QUALITY OF LIFE AFTER LAPAROSCOPIC ANTI-REFLUX SURGERY

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Laparoscopic treatment of gastro-oesophageal reflux disease (GORD) has largely replaced open surgery. This study compared the impact of laparoscopic anti-reflux surgery on quality of life (QL) compared to chronic proton pump inhibitor therapy. Prospective clinical data of 53 consecutive patients (33 men, mean age 48) undergoing laparoscopic anti-reflux surgery and 25 patients (18 men, mean age 49) on proton pump inhibitors for more than 12 months awaiting surgery were compared along with questionnaires validated for use in patients with GORD. Three patients required revisional surgery (2 for recurrent reflux). 41 patients, (77% response rate) who had undergone fundoplication and 20 (80% response) patients on medical therapy returned questionnaires. After fundoplication, patients reported significantly fewer digestive problems interfering with daily activities, sleep and eating ($p<0.001$) than patients receiving proton pump inhibitors. Fewer problems with worry and anxiety ($p<0.001$) were also reported. Overall QL scores from patients who had undergone fundoplication were significantly better ($p<0.0001$) than scores from patients awaiting surgery. These data show that laparoscopic fundoplication is an effective procedure that controls reflux and produces a good QL. Quality of life data contribute to informed decision making for patients with GORD.

100 DEOXYCHOLIC ACID AND APOPTOSIS IN OESOPHAGEAL CARCINOMA CELL LINES

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Background: Previous studies have demonstrated that bile acids can damage oesophageal mucosa. However the concentrations of bile acids that were used, are not normally seen in the oesophagus in gastro-oesophageal reflux disease. The aim of this study was to assess if physiological concentrations of bile acids can damage oesophageal cells.

Method: OE21 (oesophageal squamous carcinoma) and OE33 (oesophageal adenocarcinoma) cell lines were used. Cells were grown to 50% confluence using serum supplemented RPMI 1640 medium.

They were exposed to 0, 5, 10 and 100 micromoles/l of deoxycholic acid (DCA) for 24 hours at pH7.4. The ability to cause cellular damage was assessed by the induction of apoptosis. The induction of early apoptosis was detected by FACS scanning using Annexin V FITC and Propidium Iodide.

Results: There was a significant effect on early apoptosis seen in OE21 cells ($p=0.030$, Friedman's test). The most marked effect was seen at 5 micromoles/l of DCA, the median percentage of cells in early apoptosis increasing from 1.65 at 0 micromoles/l to 2.60% at 5 micromoles/l of DCA. There was also a significant effect of DCA seen on early apoptosis in OE33 cells ($p=0.041$, Friedman's test). The most marked effect was seen at 100 micromoles/l of DCA. The median percentage of cells in early apoptosis increased from 1.90% at 0 micromoles/l to 3.10% at 100 micromoles/l of DCA.

Conclusions: Physiological concentrations of deoxycholic acid can damage oesophageal cells at pH7.4. Bile acid induced damage may have an important role in the complications of gastroesophageal reflux disease, especially when oesophageal pH is greater than 4.

101 THE ROLE OF ANTRODUODENAL DYSMOTILITY IN GASTRO OESOPHAGEAL REFLUX DISEASE AND BARRETT'S COLUMNAR LINED OESOPHAGUS

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Aims: Antroduodenal dysmotility has been implicated in the pathogenesis of duodeno gastro oesophageal reflux (DGOR), which in turn is thought to be particularly pertinent in the delivery of bile to the distal oesophagus. The role of alkaline reflux and its implication in GOR and its sequelae is well recognised. Non invasive assessment of antroduodenal motility, utilising electrogastrography (EGG) and antral ultrasound (AS), in GORD is well documented, there are however no previous comparative studies with Barrett's CLO.

Methods: A prospective study group of 7 asymptomatic control patients, 15 patients with Barrett's CLO (mean age 60, no evidence of high grade dysplastic changes, 4 patients with short segment Barrett's CLO) and 30 patients with varying grades of endoscopic oesophagitis (mean age 52, 5 patients with grade IV Savary Millar changes, the remainder had grade I - 11 changes) was undertaken. Each patient underwent initial preprandial EGG and AS analysis, followed by a standardised test meal (500 Kcal) and subsequent post prandial EGG and AS analysis for an identical time period.

Results: Our results reveal that the mean pre and post prandial frequencies for all patient groups fall within normal limits ie slow wave activity is greater than 70 % in all patient groups. However, the degree of antroduodenal dysmotility (both pre and post prandial values) was more marked in the Barrett's CLO and GORD groups respectively in comparison to the control group ($p = 0.001$). In addition, postprandial frequencies were delayed in the Barrett's CLO group in comparison to the GORD group ($p = 0.08$). Increased antral diameters were identified in the post prandial phase in the Barrett's CLO group in comparison to GORD patients and asymptomatic controls.

Conclusion: This study suggests that antroduodenal dysmotility is more marked in a Barrett's CLO patient group in comparison to a GORD and an asymptomatic control group. This may partly explain the increased presence of bile in the oesophageal refluxate in Barrett's CLO patients and be associated with their recognised increased morbidity.

102 IS MUCOSAL SENSITIVITY A RELIABLE PREDICTOR OF DISEASE SEVERITY IN BARRETT'S COLUMNAR LINED OESOPHAGUS?

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Aims: The metaplastic epithelium in Barrett's columnar lined oesophagus (CLO) has both premalignant potential and reduced sensitivity to long standing acid reflux. The role of alkaline reflux and its particular implication in Barrett's CLO and its sequelae, oesophageal adenocarcinoma is well recognised, however, there are no studies acknowledging the sensitivity of the metaplastic epithelium to alkaline reflux.

Methods: A prospective study group of 8 asymptomatic control patients, 22 patients with Barrett's CLO (mean age 64, no evidence of high grade dysplastic changes, 5 patients with short segment Barrett's

CLO) and 40 patients with varying grades of endoscopic oesophagitis (GORD) (mean age 51, 9 patients with grade IV Savary Millar changes, the remainder had grade I - 11 changes) was undertaken. Perfusion of the recognised endoscopic abnormality, following the placement of a fine bore nasogastric tube with 3 different solutions of 30 ml 0.1M hydrochloric acid, 30 ml 0.1 M sodium bicarbonate and 30 ml normal saline was undertaken. The patients were unaware of the composition of the solutions and were asked if the infusion of the above solutions induced heartburn and if so, to grade it on a scale of 0 (asymptomatic) - 3 (severe symptoms). Symptom onset, was also noted and calculated with a score of 1 for immediate heartburn, 2 for intermediate and 3 for late onset symptoms.

Results: Using the independent t test, mucosal sensitivity in the Barrett's CLO group was reduced to both acid and alkaline infusion in comparison to asymptomatic controls ($p < 0.001$) and reduced to acid infusion alone in comparison to the GORD patient group ($P < 0.001$). Symptom onset was delayed in the Barrett's group in comparison to the GORD and asymptomatic groups respectively.

Conclusion: The reduction in mucosal sensitivity in Barrett's CLO to both acid and alkaline perfusion, may explain why a significant number of patients with this condition present de novo with severe disease or an occult malignancy.

103 ACID SUPPRESSION IN BARRETT'S OESOPHAGUS: DEMOGRAPHIC AND CLINICAL FEATURES AS PREDICTORS OF ADEQUACY

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Barrett's oesophagus (BO) is a premalignant condition. Recent evidence suggests that a reduction in oesophageal acid exposure promotes differentiation and limits proliferation in Barrett's mucosa. The aim of this study was to determine the value of demographic and clinical features in the identification of those patients with BO demonstrating an inadequate response to acid suppression. Patients with BO were recruited from routine endoscopy lists and outpatient clinics. Inclusion criteria included a Barrett's segment of at least 3cm with specialised intestinal metaplasia on biopsy. Demographic and clinical features were recorded including time interval from diagnosis, smoking and alcohol history, length of Barrett's segment, presence of dysplasia or neoplasia and presence of mucosal inflammation on biopsy. Twenty-four hour oesophageal pH monitoring was performed on maintenance acid suppression therapy when rendered asymptomatic (reflux ≤ 1 /month) to determine the adequacy of treatment. Thirty-three subjects were recruited. Seventeen (51%) had abnormal acid exposure despite acid suppression therapy.

Abstract 103, Table 1

	Normal pH n=16	Abnormal pH n=17	p value
Gender (M:F)	9:7	12:5	0.49
Mean age	56.4	56	0.74
Smoking history (%)	7 (44%)	9 (53%)	0.15
Alcohol history (%)	11 (69%)	14 (82%)	0.28
Median duration (IQR)	3 (1-3)	3 (1.75-8.25)	0.21
Median length (cm) (IQR)	6(4.75-9.25)	6 (5-8.5)	0.83
Low grade dysplasia (%)	3 (19)	1 (6)	0.53
Mucosal inflammation (%)	14 (88)	12 (71)	0.42

A significant number of Barrett's patients are undertreated yet no single demographic or clinical feature predicts inadequate therapy. The use of pH monitoring would ensure adequate acid suppression is achieved.

104 SYMPTOM REPORTING AND THERAPEUTIC REQUIREMENTS IN BARRETT'S OESOPHAGUS

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Patients with Barrett's oesophagus (BO) are relatively insensitive to oesophageal acid exposure. Consequently they may be undertreated with the risk of ongoing oesophagitis, stricture formation and possibly malignant transformation. The aim of this study was to assess the reliability of reflux symptom reporting as a guide to the adequacy of acid

suppression therapy in BO and to determine therapeutic requirements in refractory cases. Patients with BO of 3cm or greater in length and specialised intestinal metaplasia on biopsy were recruited from endoscopy and outpatient lists. Maintenance acid suppression was noted with current reflux symptom status using a scoring system for heartburn and acid regurgitation with total minimum and maximum scores of 0 and 6 ($0 \leq x \leq 1$ /month, 3=daily symptoms). Twenty-four hour ambulatory oesophageal pH monitoring was then performed on treatment. In those subjects with abnormal pH profiles acid suppression was increased by double dose increments with repeat pH monitoring at each increment until oesophageal acid exposure was normalised or a maximal dose allowed was reached. Thirty-three patients were recruited. Twenty-three (70%) were maintained on standard once daily maintenance doses of acid suppression with the remainder on varying larger doses. Seventeen (51%) had an abnormal pH profile despite acid suppression therapy. Acid suppression doses were not significantly different between the groups. However, frequency of therapy differed significantly with twice daily dosing more common in the normal group ($p=0.01$). Median reflux symptom scores did not differ between normal and abnormal (1 vs 0 , $p=0.42$). Of the 17 abnormal cases 13 were subsequently normalised, 10 (77%) requiring 1 dose increment and 3 needing 2 increments. Three withdrew before normalisation and 1 had refractory reflux at maximal dosing. Symptom reporting is minimal in BO and does not reflect treatment success. Twice daily dosing is more effective than once daily and in the majority of resistant cases only modest dose increments are required.

105 HUMAN AND MURINE DATA SUGGEST CRITICAL ROLE FOR TGF- β IN THE AETIOPATHOGENESIS OF BARRETT'S OESOPHAGUS

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Transforming growth factor- β (TGF- β) is important for oesophageal embryological development and cell differentiation. Dysregulation of TGF- β 2 receptor (T β R-2) expression is implicated in oesophageal carcinogenesis. Mice null for TGF- β or Thrombospondin-1 (TSP-1, a TGF- β activator) may have altered cell differentiation in the distal oesophagus (J Lawler, Cell 93, 1998). TGF- β null mice also have elevated levels of Th-2 cytokines and we have shown a Th-2 phenotype in BE patients.

Methods: The gut was harvested from TSP-1 null ($n=6$) and control mice ($n=4$) and examined histopathologically. Alcian blue and PAS stains for mucins, and immunohistochemistry for cytokeratin 8/18, were performed. Total TGF- β was examined by RT-PCR and active TGF- β immunohistochemically. Endoscopic biopsies from patients with normal oesophagus, oesophagitis and BE were analysed for TGF- β mRNA levels by competitive RT-PCR. Protein levels of TSP-1 and TGF- β were analysed (Western blotting and ELISA) and tissue localisation of TGF- β isoforms and receptors were examined (immunohistochemistry).

Results: Genotyping of tail-DNA confirmed mice identities. Total oesophageal TGF- β levels were unchanged but active TGF- β levels were reduced in the TSP-1 null mice. There was no macroscopic BE. However, there were focal distal histopathological appearances of a PAS-positive, mucin-secreting columnar-epithelium with minimal inflammation in 5/6 TSP-1 null mice. The metaplasia was less marked post-weaning (32 weeks compared with 3 day old mice). Human studies revealed a reduction in TGF- β mRNA levels in BE compared with uninfamed or inflamed squamous oesophagus (4.0×10^6 , 10.2×10^6 8.9×10^6 molecules/ μ g RNA respectively, $p<0.05$). TSP-1 protein levels were similar for all tissues. Surface epithelium showed a progressive reduction in TGF- β 1 staining in squamous oesophagus, oesophagitis and BE, ($p<0.05$). T β R-1 and T β R-2 staining was also reduced in BE ($p<0.001$).

Conclusions: The role of oesophageal levels of TGF- β in the aetiopathogenesis of BE merit further investigation.

106 ALTERATION OF PHASE II DRUG DETOXIFYING ENZYME LEVELS IN BARRETT'S METAPLASIA COMPARED TO NORMAL OESOPHAGEAL EPITHELIUM

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Background: The pathogenesis of Barrett's oesophagus and the subsequent development of oesophageal adenocarcinoma are topical due to the marked increase in cases of oesophageal cancer. Phase II detoxifying enzymes, including GSTs (Glutathione S-transferases), AFAR (Aflatoxin B1 Aldehyde Reductase) and AKR (Aldoketoreductase) protect the mucosa from carcinogens which can cause oxidative damage to cells. Therefore a reduction in these anti-oxidant enzymes can increase the risk of carcinogenesis.

Aims: To discover whether the levels of GST, AFAR and AKR alter due to metaplasia in oesophageal tissue as compared to normal tissue. GST alpha, mu, pi and microsomal GST were studied, along with AFAR and AKR.

Method: Paraffin-embedded sections were analyzed immunohistochemically for expression of different phase II enzymes, using specific polyclonal antibodies. Biopsy specimens from 12 patients with the diagnosis of Barrett's Metaplasia were compared with an equal number of specimens from normal oesophageal and gastric mucosa. The slides were examined microscopically and allocated a visual score representing the density of staining.

Results: Expression of the GST enzymes was generally lower in Barrett's tissue compared to normal oesophageal tissue. Conversely, AFAR and AKR appeared to be expressed to a greater extent in Barrett's tissue. Nuclear staining was also witnessed in certain sections, though with no definite pattern.

Conclusion: Barrett's Metaplasia involves the reduction of certain GST enzymes. This alteration is critical as it would render the Barrett's tissue more prone to neoplastic transformation, due to reduced protection against carcinogens. The nuclear staining also suggests GSTs may act as transcription factors, recruited at times of stress to enhance the resistance of cells against damage.

107 ALTERED EXPRESSION OF ANTI-APOPTOTIC STRESS PROTEINS IN BARRETT'S METAPLASIA

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The human oesophageal epithelium is under unique environmental pressures, being exposed to thermal stress, unmetabolized chemicals and refluxed acid or bile, that may play a role in the development of ulceration and neoplasia. An *ex-vivo* organ culture system has been used to identify the major stress protein, named SEP70, that is induced by thermal injury in human oesophageal epithelium. A micro-purification scheme was developed to isolate SEP70 protein by radiolabeling the polypeptide in organ culture after heat shock to facilitate its detection throughout chromatography. Monoclonal antibodies were developed to SEP70 protein and used to show that it localizes predominantly to suprabasal cells of the squamous epithelium. The SEP70 protein is induced by exposure of cultured cells to low pH or glucose starvation, indicating that it is a functional GRP homologue. Proteomic analysis was further used to produce a molecular protein fingerprint of stress protein expression in normal squamous epithelium and Barrett's metaplastic cells. These studies demonstrated that SEP 70 is the major stress response protein in squamous oesophageal mucosa with down regulation of the more ubiquitous HSP70. In Barrett's SEP 70 expression is lost. This suggests that SEP 70 is the major molecular chaperone expressed in the oesophagus, loss of its acid related protective effect may be involved in gastric metaplasia of the oesophagus

108 EXPRESSION OF COX-2 LINKS BARRETT'S METAPLASIA, DYSPLASIA AND ADENOCARCINOMA IN THE OESOPHAGUS

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Background: Barrett's oesophagus is a pre-malignant condition and progresses in a step-wise fashion to adenocarcinoma. The factors leading to this progression are far from clear. Increased cox-2 expression has been shown to be tumorigenic in in-vitro studies. Furthermore, epidemiologic studies have shown an inverse association between aspirin consumption and the risk of oesophageal cancer.

Aim: To investigate the expression of cox isoforms in Barrett's metaplasia, dysplasia and adenocarcinoma.

Method: Oesophageal biopsies from a retrospective sample of patients with Barrett's oesophagus were obtained. Paraffin embedded sections were stained with monoclonal antibodies for cox-1 and cox-2. A semiquantitative assessment was made.

Results: Constitutive expression of cox-1 was seen but no significant difference in the pattern of expression was observed within the subgroups. There was a clear progressive increase in cox-2 expression at the deep glandular level from normal to Barrett's ($p=0.006$) to dysplasia ($p=0.03$) to adenocarcinoma ($p=0.03$). The table shows the mean (SE) cox-2 expression at the surface (s) and deep glandular (d) level:

Abstract 108, Table 1

Pathology	Cox-2 (s)	Cox-2 (d)	p value
Normal	0.20 (0.20)	0.00 (0.0)	ns
Barrett's	0.17 (0.17)	1.00 (0.0)	0.04
Dysplasia	0.80 (0.37)	1.80 (0.2)	0.11
Adenocarcinoma	1.44 (0.29)	2.11 (0.42)	0.03

Conclusion: The progressive increase in cox-2 expression particularly at the deep glandular level may play an important role in the metaplasia to carcinoma sequence in Barrett's oesophagus.

109 PALLIATION OF OESOPHAGEAL CARCINOMA: A 10-YEAR AUDIT OF CLINICAL PRACTICE

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Background: The majority of patients with oesophageal carcinoma are not suitable for surgical resection and instead require palliative treatment. The aim of this study was to evaluate the indications for non-operative management and the outcome following palliation in a specialist unit.

Methods: 657 patients with oesophageal carcinoma have undergone surgical evaluation in this unit from 1/6/90 to 1/6/00. Staging investigations included thoraco-abdominal CT, endosonography from 1997 and a detailed fitness evaluation. 278 patients underwent subtotal oesophagectomy with curative intent with the remaining 379 patients (58%) requiring palliative treatment modalities.

Results: The median age of palliative patients was 73 years (range 27-97) with a male to female ratio of 1.6:1 and a predominance of adenocarcinoma ($n=201$) versus squamous cell carcinoma ($n=178$). Reasons for declining surgery were distant metastases ($n=83$), unresectable loco-regional disease ($n=167$) and poor fitness ($n=129$). 78% (65/83) of patients with distant metastases had adenocarcinoma whereas 60% (100/167) of patients with unresectable loco-regional disease had squamous cell carcinoma; $\chi^2=32.5$; 2df, $p<0.001$. 13% had no active treatment whilst the initial treatment was an endoprosthesis in 25%, external beam radiotherapy, brachytherapy or chemotherapy in 60% and argon beam in 2%. These were evenly distributed amongst the three patient subgroups although many patients ultimately had multiple treatments. The median survival for all patients from the time of diagnosis was 196 days (range 1-2394 days). Patients with distant metastatic disease had a significantly worse survival (median 168 days) compared to those with unresectable loco-regional disease (median 186 days) and those considered unfit (median 249 days), log rank=16.73; 2df, $p=0.0002$.

Conclusions: Patterns of dissemination and inoperability vary according to histological subtype. Patients selected for palliation are heterogeneous with different survival characteristics and this must be recognised in trials of palliative therapy.

110 CONTINUING RISE IN INCIDENCE OF OESOPHAGEAL ADENOCARCINOMA IN ENGLAND AND WALES

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Background: In the US and several other western countries the incidence of oesophageal adenocarcinoma (AC) has been rising rapidly. No recent data has been reported from England and Wales. The

present study is based on the data from the whole population of England and Wales between 1971-1993 released by Office of National Statistics.

Methods: 99280 cases of oesophageal cancer registered by regional cancer registries were analysed. Age-adjusted incidence rates of AC (ICD-O codes 8140-8380) and squamous cell carcinoma (SCC) (ICD-O codes 8050-8080) were calculated using European Standard Population. Rates were corrected for the proportion of cases with no histology in the early 1970s and no sub-site specification throughout the study period.

Results: Age adjusted incidence rates per 10^5 of AC increased from 1.49 and 0.42 in 1971 to 5.24 and 1.12 in 1993 in men and women respectively. The rate of increase was greater in older age-groups. The increase was seen in all sub-sites of the oesophagus. The same figures for SCC were 2.64, 2.08, 2.74 and 2.42. Gastric cardia AC also increased from 2.42 to 5.98 in men and 0.65 to 1.63 in women during the same time period.

Age adjusted incidence rates in England and Wales

Conclusion: AC incidence is increasing rapidly in both sexes (almost tripled during 22 years). In men rates are already higher than in the US and other European countries. SCC has remained unchanged in men while increasing in women possibly due to increases in cigarette smoking in women.

111 PATHOLOGY OF EARLY ADENOCARCINOMA OF THE OESOPHAGO-GASTRIC JUNCTION: THERAPEUTIC IMPLICATIONS

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Background: Endoscopic treatment modalities are increasingly being utilised for early oesophago-gastric tumours as an alternative to surgery. The aim of this study was to evaluate local growth patterns and regional dissemination of early adenocarcinoma (ACA) of the oesophago-gastric junction (OGJ) in surgically resected specimens in order to clarify the optimal therapeutic strategy to manage such tumours.

Methods: The clinico-pathological data of 64 consecutive patients with ACA of the OGJ confined to the mucosa or submucosa who underwent surgery from 1/4/90 to 1/10/00 were studied. Patients with lower oesophageal ACA ($n=49$) underwent radical transthoracic subtotal oesophagectomy whereas a transhiatal radical total gastro-oesophagectomy was employed for tumours of the cardia ($n=15$).

Results: The median age was 66 (31-79) with a male to female ratio of 4:1. The incidence of adjacent intestinal metaplasia for oesophageal tumours was 96% (47/49) compared to only 47% (7/15)

for cardia tumours ($p < 0.001$). Of the 22 patients with a preoperative endoscopic diagnosis of high-grade dysplasia (HGD) invasive ACA was found in the resected specimen in 59% (13/22). Pathological depth of tumour invasion was in-situ in 9 (14%) mucosal in 19 (30%) and submucosal in 36 (56%). 51% (28/55) of patients with mucosal and submucosal ACA had evidence of adjacent multi-focal HGD. Nodal metastases were found in 13% (8/64) all of whom had submucosal disease. Nodal disease occurred in 50% (6/12) of submucosal cardia tumours compared to only 8% (2/24) of submucosal oesophageal tumours ($p < 0.01$). Overall 30-day mortality was 6% with three and five year survival rates of 87% and 77% respectively. There was no significant difference in survival rates between in-situ, mucosal and submucosal lesions ($p = 0.65$) nor between node positive and node negative tumours ($p = 0.45$).

Conclusions: Endoscopic treatment modalities should be applied with caution given the multifocal distribution of dysplasia and its association with underlying invasive ACA. The incidence of nodal disease from submucosal ACA indicates that surgery should remain the mainstay of treatment. Irrespective of depth of invasion, surgery provides excellent long-term survival.

Stomach/Duodenum Posters: 112-142

112 EFFECT OF *HELICOBACTER* GASTRITIS ON GASTRIC ANTIBIOTIC SECRETION IN MAN

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Introduction: Subgroup analysis of *Helicobacter* eradication trials suggests that patients with more severe gastritis have a higher rate of treatment success.

Aim: To test the hypothesis that *H. pylori* gastritis increases gastric secretion rates of metronidazole, amoxicillin and clarithromycin by studying patients before and after treatment.

Methods: 22 patients and 9 healthy volunteers underwent gastroscopy to diagnose gastritis and *H. pylori* status. Subjects received a intra-gastric phenol red infusion and an intravenous antibiotic infusion, after a five day pretreatment with omeprazole and an overnight fast. Samples of plasma and gastric juice were obtained for 4 hours and later analysed by HPLC. Pyloric losses were corrected for by phenol red recovery. 9 patients returned at least 6 months later for a gastroscopy to confirm resolution of their gastritis, followed by a further naso-gastric sampling session.

Results: Gastric clearance of antibiotics (ml/min) (table 1).

Abstract 112, Table 1

Antibiotic	Amoxicillin	Clarithromycin	Metronidazole
<i>H. pylori</i> -ve volunteers	0.270 ± 0.205	6.61 ± 2.82	1.85 ± 1.03
<i>H. pylori</i> +ve patients	0.434 ± 0.418	5.66 ± 6.14	1.76 ± 0.76
<i>H. pylori</i> -ve patients post-treatment	0.362 ± 0.361	10.18 ± 7.70	-

Conclusions: Contrary to expectations, *Helicobacter* gastritis did not significantly increase gastric antibiotic transfer. This may be due to the large inter-subject variability in gastric antibiotic secretion rates, which limits the usefulness of human experiments for examining gastric antibiotic secretion mechanisms. PV Sherwood was supported by an Astra Research Fellowship.

113 EFFECTS OF GENOTYPICALLY DIFFERENT STRAINS OF *HELICOBACTER PYLORI* ON HUMAN MICROVASCULAR ENDOTHELIAL CELL PROLIFERATION IN VITRO

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Background/Aims: *H. pylori* infection is associated with delayed healing of peptic ulcers. Ulcer healing is dependent upon angiogenesis or new blood vessel formation. Proliferation of endothelial cells (ECs) is a crucial process in angiogenesis. This study aimed to determine whether genotypically different strains of *H. pylori* inhibited the proliferation of ECs *in vitro*.

Methods: Three *H. pylori* strains were tested on human dermal microvascular ECs (HuDMECs): a *cagA+* *vacA* s1/m1 (toxigenic) strain, its *VacA-* (non-toxigenic) isogenic mutant and a *cagA-* *vacA* s2/m2 (non-toxigenic) strain. *Campylobacter jejuni* and *Escherichia coli* were also tested. An MTT assay quantified overall HuDMEC viability. Dual staining using Hoescht and Propidium Iodide distinguished between apoptosis/necrosis and allowed total viable cell counts to be determined. HuDMECs were seeded into 96 well plates and exposed to 50µl aqueous extracts of bacteria or PBS. The two assays were performed after 24, 48, 72 and 96 hours.

Results: Cell viability and total cell number increased significantly ($p < 0.01$) at all time points upto 96 hrs in both PBS and *E. coli* treated cells. However, no increases in viability or total cell number were observed at any time point with *H. pylori* or *C. jejuni* treated cells. This anti-proliferative effect observed with *H. pylori* and *C. jejuni* was not accompanied by apoptosis or necrosis.

Conclusion: All *H. pylori* strains decreased the proliferation of HuDMECs due to a cytostatic but not cytotoxic effect. This effect also appears to be associated with the *Campylobacter* family. Inhibiting the proliferation of ECs would prevent angiogenesis at the ulcer site. This may explain the delay in ulcer healing associated with *H. pylori* infection.

114 ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF *HELICOBACTER PYLORI* ISOLATED IN SCOTLAND

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Helicobacter pylori is the principal cause of chronic active gastritis and peptic ulcer disease. Multi-drug antimicrobial therapies include combinations of proton pump inhibitors and one or several antimicrobial agents. Resistance of *H. pylori* to antimicrobial agents has been associated with treatment failure. Between December 1999 and August 2000, we obtained 243 antral biopsies from patients undergoing endoscopy in Edinburgh. A total of 67 *H. pylori* strains were isolated (27.6%). Antimicrobial susceptibility patterns of amoxycillin (AMX), ciprofloxacin (CIP), clarithromycin (CLA), erythromycin (ERY), tetracycline (TET) and metronidazole (MTZ) were determined by E test. Mutations in the 23S rRNA conferring macrolide resistance were investigated by PCR and DNA sequencing. MIC₅₀ and MIC₉₀ values are shown below. Resistance to clarithromycin and erythromycin was found in 12% (8/67) and 13% (9/67) of the *H. pylori* strains, respectively. All clarithromycin-resistant isolates had erythromycin MIC of >256 mg/L. Metronidazole resistance was demonstrated in 6 isolates (9%). Two of them had clarithromycin and erythromycin resistance. Tetracycline resistance (intermediate) was found in one of the 67 isolates (1.5%). Resistance to amoxycillin and ciprofloxacin was not detected.

Abstract 114, Table 1

	AMX	CIP	CLA	ERY	TET	MTZ
MIC ₅₀ (mg/L)	<0.016	0.032	<0.016	0.023	0.023	<0.016
MIC ₉₀ (mg/L)	0.02	0.06	3	>256	0.064	0.75

Mutations in the 23S rRNA gene were examined in the nine macrolide-resistant *H. pylori* strains. Seven of the nine isolates had mutation at position 2143 (A to G). Two of the seven isolates had an additional T to C mutation at either position 2182 or 1934. Mutation at position 2182 (T to C) has previously been found not to be associated with macrolide resistance. However, the mutation at position 1934 has not previously been reported. Of the nine isolates, one carried only a T to C mutation at position 2182 and one had no mutation in the 23S rRNA, implying that other mechanisms are responsible for the resistance in these strains. The results show that macrolide resistance, occurring by different mechanisms, is currently found in 13% of our *H. pylori* isolates.