(PCS & MCS). Measurements were taken at baseline 1 (B1), two weeks later at baseline 2 (B2), approximately 8 weeks later at end of treatment (P), and a further 10 months later at followup (F).

Results: There were no differences between the groups in terms of sex ratio, age, duration of IBS, and B1 outcomes measures. A repeated measures MANOVA to determine the immediate effects of treatment (ie, B1, B2 and P) revealed no significant differences for group ($F=0.74$; $df=10,144$; $p=0.686$), nor a significant interaction ($F=0.87$; $df=20,596$; $p=0.622$). There was however a significant improvement over time ($F=6.78$; $df=10,294$; $p<0.001$). A STEPDOWN analyses revealed significant improvements in BSSS, HAD-A and PCS. Improvements occurred from B1 to B2 and continued to P. A second MANOVA to determine follow-up effects from the 44% of subjects with complete data, revealed similar results with no treatment effects, but a continual improvement over time in all groups.

Conclusions: This study found that CBT, RT and RMC were equally effective in managing IBS. While thoughts may have a role in the continuance of IBS, good routine medical care, with an emphasis on education and reassurance, can be as effective as CBT and relaxation in reducing symptoms of IBS.

173 PUDENDAL LATENCY: AN IMPORTANT PROGNOSTIC INDICATOR IN ANTERIOR SPHINCTER REPAIR

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It has been suggested that pudendal nerve terminal motor latency (PNTML) has little part to play in the prognosis after anterior sphincter repair. By using an artificial neural network we have been able to show that both PNTML and the results of biofeedback are an important part of the prognosis. 30 patients who underwent anterior sphincter repair had 32 preoperative investigations including anorectal physiology, endoanal ultrasound and PNTML measurements. 15 of them also underwent biofeedback therapy. The results of the repair were graded as 1 no change, 2 mildly improved, 3 socially continent, 4 excellent result. The variables were then processed through a neural network and a Spearman correlation between the predicted and actual results was performed. The neural networks were then altered by removing parts of the data (table 1).

Abstract 173, Table 1

	3 Months		6 Months		12 Months	
	Correlation	P value	Correlation	P value	Correlation	P value
Full net	90%	0.0001	74%	0.002	93%	0.0001
No biofeedback	58%	0.025	90%	0.0001	78%	0.001
No PNTML	71%	0.003	56%	0.033	66%	0.013
PNTML only*	48%	0.68	69%	0.05	78%	0.001
Biofeedback & PNTML only*	38%	0.036	37%	0.049	35%	0.09

Also age, functional length, high-pressure zone; Bold=significant.

The results show that the full use of preoperative data is necessary to get the best correlation and that if only PNTML and biofeedback are used then the correlation is poor. It also shows that by removing either has a dramatic effect on the correlation. However if PNTML only is used then the correlation at 12 months is 78%. From these results we can deduce that PNTML is an important factor in the pre operative investigation in patients who may receive an anterior sphincter repair.

Neoplasia Posters: 174-190

174 NON-INVASIVE TESTING FOR *HELICOBACTER PYLORI* MAY BE ASSOCIATED WITH DELAY IN DIAGNOSIS OF UPPER GI MALIGNANCY

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Background: Non-invasive testing for *H. pylori* (serology or radiolabelled ¹⁴C urea breath testing) is increasingly used without upper gastrointestinal endoscopy in selected patients with new onset of dyspepsia (the 'test and treat' strategy).

Aims: To determine whether non-invasive testing was associated with delay in referral and diagnosis in patients with upper GI malignancy.

Patients and methods: Patients diagnosed with gastric or oesophageal malignancy from 1st January 1997- 31st December 1999 were identified from histopathology records. Non-invasive testing for *H. pylori* within 2 years of diagnosis of malignancy was identified from case notes, general practitioners' records and microbiology records.

Results: 152 cases were identified, with mean age 70 years (range 34-91y, 4 patients younger than 45 years). 86 were male. 59 malignancies were oesophageal, 8 junctional, 77 gastric and one duodenal adenocarcinoma; in 7 the precise anatomical origin was undetermined. 22 patients (14.5%) had been tested for *H. pylori* prior to diagnosis (tested group), all by serology (9 oesophageal, 2 junctional and 11 gastric carcinomas); 20/22 were older than 45 years. The median interval between *H. pylori* serology testing and referral for endoscopy was 21 days (range 1-615 days, mean 109 days). There was a delay of more than 12 weeks between serology and referral in 6 patients; 17/22 patients had locally advanced or metastatic disease at diagnosis. Of all patients, median delay between referral to the endoscopy service and diagnosis of malignancy was 9.1 days (range 1-181 days, mean 24.0 days; medians 12 v 9.1 days in tested and untested groups respectively, $p=NS$). Of the patients aged 45 or older, 20/148 (13.3%) had *H. pylori* serology.

Conclusion: Serological testing for *H. pylori* was used in a significant minority of patients aged 45 years or older who were subsequently diagnosed with upper GI malignancy, and in some it was associated with considerable delay in referral and treatment. Non-invasive testing for *H. pylori* in patients with new onset of dyspepsia should be reserved for patients less than 45 years.

175 AUDIT OF THE "TWO WEEK CANCER RULE" FOR GASTROINTESTINAL MALIGNANCY

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Background: In order to assess resource issues necessary to support a successful "two week cancer" service, the Cornwall Gastrointestinal Unit introduced this service in January 2000.

Aims: To audit the "two week cancer" service for upper and lower GI malignancy.

Methods: A retrospective audit of all GP referrals received over a 9 month period. The main outcome measure was the number of patients who were found to have cancer. The data were also analysed for: (i) time from GP referral to initial assessment, diagnosis and treatment and (ii) the number of referrals that fulfilled the "two week cancer rule" guidelines. Any patient who was referred under the "two week cancer rule" was seen irrespective of whether or not they met the guidelines. The number of patients on the waiting list for endoscopy was measured before and after implementation of the "two week cancer" service.

Results: The audit included 105/146 upper and 264/398 lower GI referrals. GI malignancy was found in 25% of upper and 14% and lower GI referrals. For upper GI compared to lower GI referrals the median time (days) to initial assessment was 16 (range 0-53) vs 12 (1-181); diagnosis 20 (4-77) vs 30 (1-181) and treatment 29 (7-117) vs 34 (2-226). 85% of referrals fulfilled upper GI guidelines whilst 72% fulfilled lower GI guidelines. Cancers were only found in patients who satisfied the guidelines. The number of patients on the waiting list for endoscopy increased by 25% by the end of the study.

Conclusions: The detection rate of GI malignancy was good, with the majority of patients receiving their initial assessment within 2 weeks. The guidelines appear robust, as patients who did not fulfil the referral criteria did not have cancer. Although it is possible to provide a "two week cancer" service within existing resources, patients referred by the more traditional route have to wait longer.

176 IMPROVEMENT IN SURVIVAL IN PATIENTS WITH CANCERS DETECTED BY SCREENING HIGH RISK GROUPS

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Of 1753 patients who attended open access endoscopy between 1984 and 1988, 22 (1.3%) had gastric cancer. 107 (6.1%) had ulcers and 212 (12%) were found to have atrophic gastritis or intestinal metaplasia. Patients with ulcers were re-examined every 2 months until ulcer healing and then offered annual surveillance. 48 accepted. Of the 212 with atrophic gastritis or intestinal metaplasia 104 accepted annual surveillance endoscopy. 14 new cancers were found over ten years, 4 of these in patients undergoing repeat endoscopy for ulcers. These 14 were of an earlier stage than the 22 diagnosed at open access (stage I & II 67% vs 23% $p < 0.05$). Treatment was by D1 or D2 gastrectomy and 5 year survival was significantly better (50% vs 10% $p = 0.006$). The 4 tumours detected on re-endoscopy ulcers that failed to heal may represent missed initial diagnosis rather than true screen detected cancers. Exclusion of these 4 cancers from the analysis improved survival to 60% in true screen detected cancers. For the 10 screen detected cancers both disease stage and survival were influenced by adherence to the original protocol. 2 cases did not attend for more than 4 years and presented with stage IVb and III disease and both have died. 2 cases who did not attend for 2 1/2 years had stage III and II disease. Both are still alive although the patient with stage III disease has liver metastasis. The remaining 6 cases had stage I (n=3), II (n=2) or III (Early gastric cancer with lymph node involvement n=1). 4 are still alive 10 years post diagnosis, one died post operatively and one had a non cancer related death. In patients with atrophic gastritis or intestinal metaplasia 10% of patients will develop gastric cancer over 10 years. Although the numbers involved in this study are small it suggests that in this group annual surveillance can detect tumours at an early and curable stage. The potential benefits of such a surveillance program are large and warrant further investigation in a multi-centre randomised controlled trial.

177 EXCHANGE OF DIGITAL IMAGES VIA E-MAIL IS NO SUBSTITUTE FOR SLIDE REVIEW IN DOUBLE REPORTING OF UPPER GASTROINTESTINAL DYSPLASIA

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Introduction: It is current practice to seek a second opinion in the biopsy diagnosis of upper gastrointestinal neoplasia before definitive treatment is planned as it is accepted that there will be disagreement in a proportion of cases. This audit was undertaken to assess the level of agreement between two pathologists on light microscopy (LM) and also to evaluate the potential usefulness of e-mailed digital images (static telepathology) as a possible method for rapid exchange of diagnostic opinion.

Methods: 52 biopsies from 32 patients were assessed by each pathologist and classified according to the Vienna classification of dysplasia: Negative, indefinite, low grade dysplasia, high grade dysplasia or carcinoma. In 23 cases digital images were taken by one pathologist and sent via e-mail to the other who graded them independently from the LM.

Results: In 43 of the 52 cases there was complete agreement between the two pathologists on LM assessment. In the 9 cases with disagreement this was by only 1 grade on the Vienna scale. The pathologist assessing digital images (23 cases) showed concordance between LM and digital diagnoses in only 7 cases. Where there was disagreement this was by 1 grade in 13 cases and by 2 grades in 3 cases. There was a marked tendency to under grade on the digital image assessment. Where there was disagreement by LM in this group the second pathologist tended to agree with the first on the digital image implying the introduction of bias by field selection.

Conclusions: There was good agreement between the two pathologists by LM, 82%. However, analysis of digital images showed only 30% agreement with the LM diagnosis. The exchange of digital images cannot therefore be recommended for obtaining a second opinion in upper gastrointestinal neoplasia.

178 HIGH TUMOUR TELOMERASE ACTIVITY CORRELATES WITH SHORTENED PATIENT SURVIVAL AND MORE ADVANCED TUMOUR STAGE IN GASTRIC BUT NOT IN OESOPHAGEAL ADENOCARCINOMA

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Background: The ribonucleoprotein telomerase extends telomeres in cancer cells and has been proposed as a prognostic marker for cancer. We measured telomerase expression in gastric adenocarcinomas and those arising in the lower oesophagus/gastro-oesophageal junction (GOJ), and correlated telomerase with pathological stage and post-operative survival.

Methods: Samples of cancer tissue were obtained at time of surgical resection. Telomerase activity of protein extracts derived from cancer specimens was determined using the Telomeric Repeat Amplification Protocol. A single pathologist blinded to the results of the telomerase assays reviewed all slides of cancers to assign T and N stages.

Results: Cancers exhibited a wide range of telomerase expression. There was no significant difference between telomerase activity (median in arbitrary units, 95% CI) of oesophageal/GOJ (551, 154-2394, n=26) and gastric (703, 139-1618, n=20) adenocarcinomas. In gastric adenocarcinomas however, high telomerase activity (>median levels) was associated with poor patient survival (median 3.0 months) compared to low telomerase activity (median survival 22.4 months, $p = 0.01$, log rank test). Cancers expressing high telomerase activity were significantly more advanced with regard to T stage than cancers expressing low telomerase levels ($p = 0.03$, Mann Whitney U test). No such differences were observed for adenocarcinomas of the oesophagus/GOJ.

Conclusions: There is a difference between gastric and oesophageal/GOJ adenocarcinomas in terms of the relationship of telomerase expression and clinico-pathological variables. Among patients with gastric adenocarcinoma, telomerase activity correlates with markers of advanced disease, whereas this relationship does not hold true in oesophageal adenocarcinomas. Telomerase activation may occur at different stages of the formation of the malignant phenotype in these two cancers and may reflect differences in their pathogenesis. Telomerase could be a prognostic marker in gastric but not in oesophageal adenocarcinoma.

179 THE ROLE OF THALIDOMIDE IN REVERSING CACHEXIA IN PATIENTS WITH INOPERABLE OESOPHAGEAL CANCER

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Background: More than 80% of cancer patients will develop cachexia before death. Thalidomide, which is an anti-TNF agent, has shown weight gain and lean tissue anabolism in patients with HIV disease even when caloric intake was kept constant.

Aim: To evaluate the role of thalidomide in reversing cancer induced cachexia in patients with oesophageal cancer.

Design: Preliminary report on five patients in a before and after design where patients were used as their own controls.

Methods: Five inoperable oesophageal cancer patients were included in the study. Patients were established on an isocaloric diet over a 10-day period after which baseline Body weight, Body Composition, REE (resting energy expenditure) and 24 hour urinary nitrogen/urea values were estimated. At the end of 2 weeks on diet alone both metabolic and body composition studies were repeated and patients were started on 200mg/day of thalidomide for a fortnight 3- Similar measurements were repeated after being on diet and thalidomide for 2 weeks.

Results: 1 female and 4 male patients with mean age 69 years (61-77yrs) lost weight on diet alone from a mean baseline weight of 73.9kg to 72.6kg in 2 weeks. After therapy with thalidomide for 14 days all patients experienced weight gain from a mean weight of 72.6kg to 74.3kg. Similar trend was shown in lean body mass in all these patients. There was an increase in REE in kcal/kg/day in 4 out of 5 patients on thalidomide therapy.

Conclusions: Thalidomide treatment is effective in causing weight gain mainly in the lean body mass in patients with inoperable oesophageal cancer. Its promising role as an anticachectic treatment in cancer needs further evaluation.

180 ASCORBIC ACID IS PRO-PROLIFERATIVE BUT REDUCES PROSTAGLANDIN PRODUCTION IN GASTRIC CARCINOMA CELLS IN CULTURE IN RESPONSE TO *HELICOBACTER PYLORI*

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Introduction: Ascorbic acid (vitamin C) is an antioxidant vitamin that is actively secreted into the gastric lumen. The presence of *Helicobacter pylori* infection reduces intra-luminal ascorbic acid. A diet low in vitamin C is said to defer an increased the risk of gastric adenocarcinoma.

Methods: Gastric cancer cell lines AGS, MKN-7 and MKN-45 were grown to confluence in RPMI / 10% serum, serum starved, then co-incubated with ascorbic acid in the presence or absence of *Helicobacter pylori* NCTC 11637 for 8 hours. PGE2 was measured using ELISA (R&D systems) and proliferation by measurement of conversion of MTT to a blue formazan dye, a reaction catalysed by mitochondrial succinate dehydrogenase. COX-1 and COX-2 expression were assessed by western blotting using monoclonal antibodies (Cayman Chemicals, USA).

Results: Ascorbic acid alone resulted in a dose dependent proliferation of all three cell lines and down regulation of PGE2 production. There was no down regulation of COX-1 or COX-2 production as assessed by western blotting. *Helicobacter pylori* induced an increase in PGE2 production, accompanied by an increase in COX-2 expression. Ascorbic acid co-incubation resulted in a reversal of the increased PGE2 expression, but there was no change in the COX-2 expression. The table shows PGE2 production (pg/ml) with Hp and increasing concentrations of ascorbic acid (μM). n=5 in each group.

Abstract 180, Table 1

	Con	Hp+	0.01	0.1	1	10
AGS	56	321	11	12	54	66
MKN-7	286	835	94	32	56	140
MKN-45	838	1595	948	746	661	592

Conclusions: Ascorbic acid induces a dose dependent proliferation of gastric cancer cells in vitro, but down regulates PGE2 production in both unstimulated and Hp stimulated cells. However there was no down-regulation of COX-1 or COX-2 production.

181 THE CARDIA IS EXPOSED TO HIGH CONCENTRATIONS OF NITRIC OXIDE GENERATED FROM SALIVARY NITRITE

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Introduction: 30% of ingested nitrate is resecreted in saliva and 25% of this converted to nitrite by oral bacteria. The swallowed nitrite reacts with gastric acid containing ascorbic acid forming nitric oxide (NO).

Aim: To investigate luminal concentrations of NO in different regions of the stomach.

Methods: 15 healthy *H. pylori* negative volunteers were studied. A novel, custom made probe incorporating two miniature NO sensors mounted on a 4 channel pH electrode was passed per orally into the distal stomach. Following X-ray confirmation of its position, the probe was withdrawn at 1cm increments every 2min with real time measurement of NO and pH. This was repeated after ingesting 2mmol nitrate, equivalent to that in a salad meal. Plasma nitrate and salivary nitrite were also monitored.

Results: Mean salivary nitrite concentration was 48 μmol/l and this rose to 388 μmol/L after the nitrate meal. Under fasting conditions, intragastric NO concentration ranged from 1–10 μmol/l and following the nitrate meal increased to 2.5–48 μmol/l (p<0.05). The highest concentrations of NO were observed in the cardia region where the swallowed nitrite first encountered acidic gastric juice (figure).

Conclusion: Nitrite in swallowed saliva generates high concentrations of NO in the most proximal cardia region of the stomach. High levels of NO are mutagenic and carcinogenic and its localised production may be an important factor in the development of intestinal metaplasia and cancer of the gastric cardia.

182 ALOE VERA GEL INHIBITS GASTRIC CARCINOMA CELL PROLIFERATION IN VITRO

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Background: Aloe vera gel (AV) is the mucilaginous aqueous extract of the leaf of *Aloe barbadensis miller*. It is a widely used herbal remedy for inflammatory and digestive disorders and is also claimed to have anti-cancer effects. *Helicobacter pylori* (Hp) causes an inflammatory gastritis and is implicated in gastric carcinogenesis.

Aims: To determine if aloe vera inhibits gastric adenocarcinoma cell proliferation *in vitro*.

Methods: AGS, MKN 7 and MKN 45 gastric epithelial carcinoma cell lines were cultured in RPMI medium/10% serum. Cells were then serum starved and co-incubated with varying concentrations of AV. Cell proliferation was assessed by measuring the conversion of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) to an insoluble blue formazan dye. This reaction is catalysed by mitochondrial succinate dehydrogenase and correlates with the number of viable cells present. Proliferation is expressed as the OD at 550nm as a percentage of control. Experiments were repeated with a co-incubation of Hp 100 cfu per cell. Finally, paper disks soaked in AV were placed on blood agar plates inoculated with Hp.

Results: AV showed a dose-dependent significant inhibition of proliferation at AV dilutions 1 in 10 to 1 in 10⁵. Results are expressed as the median (interquartile range) percentage of control activity. p<0.05 for each concentration compared to control (table 1).

Abstract 182, Table 1

	AV dilution				
	1:10 ¹	1:10 ²	1:10 ³	1:10 ⁴	1:10 ⁵
AGS	52 (37–56)	78 (71–89)	69 (68–75)	77 (75–78)	76 (74–81)
MKN 7	53 (49–58)	84 (73–97)	85 (79–90)	90 (87–96)	95 (94–97)
MKN 45	61 (61–69)	83 (70–101)	83 (73–95)	84 (72–97)	86 (84–88)

There was no change in proliferation from control in cells co-incubated with AV and Hp. Hp growth on blood agar was not inhibited by AV.

Conclusion: Aloe vera gel inhibits cell proliferation in uninfected gastric carcinoma cells but has no effect in the presence of Hp infection. If AV has an anti-cancer action on gastric carcinoma cells, this appears to be negated by H pylori.

183 DOES THE DURATION OF SYMPTOMS AFFECT RESECTABILITY OF GASTRO-OESOPHAGEAL MALIGNANCIES?

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Aim: Since the new government initiative requires urgent (2-week rule –TWR) assessment of suspected GI cancer, we analysed the relationship between duration of symptoms prior to presentation to hospital and resectability of gastro-oesophageal malignancies.

Methods: Patients diagnosed to have gastro-oesophageal malignancy at St George's Hospital over a two year period (May 1998-May 2000) were identified using a combination of coding and endoscopy records. Information about duration of symptoms, time from referral

Abstract 183, Table 1

	Resectable (N=17)	Unresectable (N=37)	p value
Mean age (range) years	71(42-85)	78(52-95)	NS
Median duration symptoms	14 weeks	11 weeks	NS
Time to assessment (days)	21.8 (SE 6.2)	27.1 (SE 5.1)	NS
Presentation to diagnosis (days)	36.5 (SE 8.1)	32.5 (SE 4.8)	NS
Diagnosis to treatment (days)	41 (SE 7.8)	26.7 (SE 4.6)	NS
Ca stomach	10	17	
Ca oesophagus	6	15	
Ca gastro-oesophageal junction	1	5	

to clinic assessment, histological diagnosis, time to treatment and outcome were recorded. Stage of tumour at diagnosis was categorised as resectable or unresectable based on clinical and imaging information.

Results: 54 patients were identified for the study. 76% had adenocarcinoma and the remainder squamous cell cancers. 37 patients were deemed inoperable of which 22 had locally invasive disease while 15 had hepatic and/or pulmonary metastases (table 1).

Conclusion: There was no difference in symptom duration, time from referral to assessment, diagnosis and treatment between patients with resectable and unresectable tumours. Therefore, the recent TWR to expedite investigation of patients with alarm symptoms may not affect outcome.

184 EFFECTS OF EPIDERMAL GROWTH FACTOR ON GASTROINTESTINAL EPITHELIAL CELL PROLIFERATION, CRYPT BRANCHING AND THE DEVELOPMENT OF GASTROINTESTINAL TUMOURS IN THE *MIN* MOUSE

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Background/Aims: Gastrointestinal growth can occur through two mechanisms, namely increased crypt cell production and increased crypt number, which occurs through the process of crypt fission, manifested as crypt branching. Epidermal growth factor (EGF) is a potent stimulant of cell proliferation both *in-vitro* and *in-vivo*, and can alter both intestinal proliferation and crypt fission. Multiple intestinal neoplasia (*Min*) mice have a mutation in the murine adenomatous polyposis coli (*Apc*) gene and develop multiple intestinal adenomas, as in the familial adenomatous polyposis syndrome of humans. We have examined the effects of EGF on polyp development and proliferation in the *Min* mouse.

Methods: 25 *Min* mice (C57BK/6J-Apc^{Min}) and 25 wild type littermates, 4 weeks old, were divided into 2 groups, half received saline while half received EGF by means of a mini-osmotic pump implanted subcutaneously in the back of the animal. After 4 weeks of treatment, the number of polyps in the small and large intestines were scored, as was the number of metaphase arrested cells and the percentage of branching crypts.

Results: There was no difference in the number of polyps between treatment groups. The saline group had a mean of 78.8±12.1 & 3.9±0.6 polyps for the small intestine and colon respectively while the EGF treated group had 68.5±11.2 & 3.0±0.09. There was also no significant difference in the diameters of any of the polyps found in the colons from either the EGF or saline treated groups, however proliferation was significantly increased in the small intestine and colon of the *Min* mice (p<0.01).

Conclusion: EGF had little effect upon the numbers of polyps in the small intestine and colon, despite increasing proliferation, suggesting that this is not a marker of neoplastic change in this model.

185 USE OF LOW ACTIVITY I-131 MIBG IN THE TREATMENT OF NEUROENDOCRINE TUMOURS

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Patients with disseminated neuroendocrine tumours (NETs) are not normally suitable for surgery and often do not respond to chemotherapy. These patients may be polysymptomatic and require palliative treatment for many months or years. It has been reported

that Iodine-131 meta iodobenzyl guanidine (I-131 mIBG) can have significant anti-tumour activity in NETs. The normal dosing regimen is expensive and difficult to administer.

Aim: The aim of this study was to determine the safety and efficacy of a low activity regimen in patients with disseminated NETs.

Methods: A total of 14 patients with histologically confirmed NET (13 carcinoid and one gastrinoma) with disseminated disease were treated. All had good uptake on I-123 mIBG scintigraphic imaging. Patients were selected if tumour related symptoms were not controlled or there was radiological evidence of progressive disease. Patients were treated with 1-6 cycles, 3 monthly 2.7-3.7GBq, I-131 mIBG. Assessment of response was determined by change of measurable tumour size by CT imaging.

Results: Immediate side effects of the treatment included mild nausea and occasional tumour pain. There was no other significant toxicity from the treatment. Continued progression of disease was seen in 4 patients. In 7 patients there was stability of previously progressive diseases with stability continuing for a minimum 6 months after treatment. In 3 patients there was disease regression (25-50%). Tumour regression was often delayed and could lag behind the therapy by as much as 18 months although most of these patients had symptomatic relief before they had a reduction in tumour size.

Conclusions: Treatment with low activity I-131 mIBG resulted in tumour stability or reduction in tumour size in 10/14 (70%) of NET patients. Treatment with low activity I-131 mIBG may be useful in patients with NETs.

186 SOMATOSTATIN RECEPTOR SCINTIGRAPHY IN NEUROENDOCRINE TUMOURS—IS SINGLE PHOTON EMISSION TOMOGRAPHY (SPECT) REQUIRED?

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Introduction: Somatostatin receptor scintigraphy (SRS) with Indium-111 (In-111) octreotide has become an accepted standard in imaging patients with known or suspected neuroendocrine tumours (NETs). However many of these tumours may be small and hidden by radioactivity in overlying tissues. This is particularly true in the upper abdomen where there is physiological activity of In-111 octreotide in the liver, spleen and kidneys. In this situation single photon emission tomography (SPECT) may be useful in identifying small volume NETs.

Aim: The aim of this study was to determine (i) the number of additional patients and (ii) additional tumours in patients with NETs who can be identified as somatostatin receptor positive using SPECT imaging.

Methods: The SRS imaging was reviewed in 66 patients imaged over 2 years with proven NET. All patients had whole body and SPECT In-111 octreotide imaging performed up to 24 hours after injection of up to 200 MBq of tracer using a twin headed Gamma camera fitted with medium energy collimators. The identification of known lesions using both methods was compared with the results of both planar and SPECT imaging.

Results: A total of 52 (78%) patients had a positive SRS on planar imaging alone. SPECT was able to identify tumour in 59 (89%) patients. Also many more additional lesions were found on SPECT. Most of the sites of tumour seen on SPECT but not planar imaging were in the liver or upper abdomen.

Conclusions: SPECT (especially of the liver and upper abdomen) should become an integral part of SRS, so that an additional 11% of patient's tumours will be found

187 SYMPTOMATIC NEUROENDOCRINE TUMOURS: BRITISH SOCIETY OF GASTROENTEROLOGY (BSG) SURVEILLANCE 1998-2000

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Neuroendocrine tumours can secrete hormones that have an effect on the gastrointestinal tract, producing classical syndromes. Clinical series have demonstrated the rarity of these tumours yet they present a considerable diagnostic challenge. The BSG research unit surveillance scheme offered the opportunity to identify a large representative series of such cases. Incident cases diagnosed from June

1998 to June 2000 were notified on the monthly report card distributed to all consultant gastroenterologists and gastrointestinal surgeons. The reporting doctor then completed a questionnaire detailing the age and clinical presentation of the patients, tumour site, hormone assay level, and method of treatment. Survival data were obtained at the end of the study period. 244 cases were reported, including 32 prevalent cases and 2 inappropriate tumours. 57% of these cases had questionnaires completed, producing 106 cases for analysis. 64 had symptoms attributable to the hormonal effects of the tumours, such as peptic ulceration or diarrhoea, and 42 had non-hormonal symptoms such as bowel obstruction, or extra-gastrointestinal symptoms such as rash or confusion. The commonest tumours producing hormonal GI symptoms were carcinoids (n=44, 69%), presenting with diarrhoea as the main symptom in 83%. Other symptoms included flushing, weight loss or abdominal pain. 80% had liver metastases demonstrated at presentation. Gastrinomas accounted for 20% (n=13) of the tumours, presenting with peptic ulceration in 77%, and diarrhoea in 62%. Other tumours identified were VIPomas, pheochromocytomas, thyroid medullary tumours, insulinomas, glucagonomas, somatostatinomas, hyperparathyroid tumours, and spindle cell tumours. 78% of all patients were alive at the end of the study period. Carcinoid syndrome was the commonest neuroendocrine condition causing gastrointestinal symptoms. Diarrhoea appears to be a more common presenting symptom of gastrinomas than has previously been appreciated. With a series of tumours as large as in any previous UK survey, the BSG monthly surveillance system shows promising potential.

188 T CELL RECEPTOR ZETA (CD3/TCR- ζ) CHAIN EXPRESSION IN TUMOUR INFILTRATING LYMPHOCYTES IN COLORECTAL CANCER

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Background: CD3 lymphocytes co-express TCR- ζ chain, and ζ chain expression is essential for signal transduction and activation of CD3 lymphocytes. Alterations in CD3/TCR- ζ chain expression might disrupt internal signal transduction, resulting in deficient T cell activation. This might be a novel mechanism by which cancers escape from immune control despite the presence of tumour infiltrating lymphocytes (TILs). However, whether ζ chain is downregulated in cancer patients remains controversial.

Aim: To examine CD3- ϵ chain and ζ chain expression in TILs in colorectal cancer (CRC) and in adjacent unaffected mucosa from patients with CRC.

Methods: Paraffin sections from 30 colorectal cancer specimens (7 Dukes's A, 10 Dukes's B, 12 Dukes's C and 1 Dukes's D) and unaffected adjacent colon were studied. Immunohistochemical staining was performed on consecutive sections with antibodies specific for CD3- ϵ chain or ζ chain. Positively stained areas were quantified using image analyser (in μm^2) in ten fields for each specimen. Pilot experiment confirmed that this method was as accurate as individual cell counting but simpler. Statistical differences were calculated using the Mann-Whitney test.

Results: Loss of ζ chain expression was observed in only one patient. In all other cases expression of ζ chain correlated with CD3- ϵ chain, and the number of CD3- ϵ^+ and ζ^+ lymphocytes were almost equal. In addition, CD3- ϵ^+ and ζ^+ lymphocytes were seen more frequently in non-cancerous tissue than in tumours. The median areas of CD3 and ζ chain positive staining (μm^2 /10 fields) in different Dukes' stages are shown in the table.

Abstract 188, Table 1

		Dukes' stage		
		A	B	C
Normal	CD3	3878	2794	3541
	Zeta	3829	2712	3486
Tumour	CD3	2825	1581	2593
	Zeta	2711	1524	2523
Significance level (normal v tumour)	CD3	0.34	0.09	0.04
	Zeta	0.34	0.09	0.04

Conclusion: Loss of ζ chain expression is uncommon in TILs from patients with colorectal cancer and is unlikely to be a mechanism for immune escape in all CRC patients.

189 BUTYRATE: FOOD FOR COLONIC CANCER CELLS ?

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Background: In vivo, colonocytes have a local energy source in the form of butyrate (a short chain fatty acid produced by bacterial fermentation in the colonic lumen) and receive glucose and glutamine from the vasculature. The preferred fuel source for these colonocytes is butyrate. In vitro, colonic tumor cell lines preferred energy source is debatable, as most tissue culture media do not contain butyrate but a variety of other energy sources. We investigated the metabolism of butyrate, glucose and glutamine in 5 different colonic cell lines and 2 cell lines originating from outside the colon. Two of the 5 colonic cell lines (HT29 and CaCO-2) were established from a primary tumour whereas COLO-205, LoVo, SW620 are established from metastatic deposits.

Aim: To compare butyrate metabolism in colonic epithelial cancer cell lines derived from primary cancer and metastases.

Method/Results: Cell lines were maintained in serum-free media and incubated with either [^{14}C (U)]-glutamine, [^{14}C (U)]-glucose or n- ^{14}C butyrate. Oxidation was measured by trapping ^{14}C released on sodium hydroxide-saturated filter paper and counted. Results of butyrate metabolism are shown in the table.

Abstract 189, Table 1

Cell line	$\mu\text{mol CO}_2/\text{mg protein} \pm \text{S.E.M.}$
HT29 colon	40.2 $\pm$ 1.2
CaCO-2 colon	37 $\pm$ 6.8
COLO-20 colon	8.7 $\pm$ 0.2
LoVo colon	7.7 $\pm$ 0.9
SW620 colon	4.5 $\pm$ 0.5
Oe33 oesop	0
Hep-G2 liver	399 $\pm$ 52

Conclusion: Colonic cell lines from a primary tumour origin showed a greater ability to metabolise butyrate when compared to those from a secondary source. All colonic cell lines preferred butyrate as an energy source rather than glucose or glutamine.

190 PLASMA BIG ET-1 - A TUMOUR MARKER FOR UPPER GASTRO-INTESTINAL TRACT CANCERS

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Introduction: Endothelin-1 (ET-1), the most potent vasoactive peptide has been associated with the development of various cancers. This study was performed to assess whether plasma big endothelin levels (big ET-1), a stable precursor of ET-1 could be used as a tumour marker in upper gastro-intestinal tract cancers.

Patients and methods: Plasma concentration of big ET-1 was measured in 26 patients with proven upper gastro-intestinal cancers prior to any treatment from February 2000 to August 2000 and in 20 age/sex matched controls. Plasma samples were analysed within 2 months of collection using sandwich enzyme linked immuno-assay (Biomedica, Austria).

Results: Median plasma levels of big ET-1 in patients with gastro-oesophageal cancer 3.6 pg/ml [range 1.3–30.2 pg/ml] (gastric cancer n=9, oesophageal cancer n=5) were significantly elevated compared to median plasma levels of big ET-1 in controls 2.1 pg/ml [range 1.2–13.4 pg/ml] p=0.005 (Mann-Whitney). However, median plasma levels of big ET-1 in patients with pancreatic cancer (n=12) 3.1 pg/ml [range 1.5–8.1] were not significantly elevated compared to controls (table 1).

Abstract 190, Table 1

Groups	Median plasma levels (pg/ml)	Range (pg/ml)	Mann-Whitney
1 Controls	2.1	1.2–13.4	
2 Gastro-oesophageal cancer	3.6	1.3–30.2	p=0.005
3 Pancreas	3.1	1.5–8.1	ns

Conclusion: Plasma big ET-1 levels were significantly elevated in gastro-oesophageal cancer patients but not in pancreatic cancer patients. Plasma big ET-1 levels could be used as a tumour marker to detect the presence of gastro-oesophageal cancers.