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CHARACTERISATION OF CYTOTOXIN-ASSOCIATED PROTEINS OF HELICOBACTER PYLORI

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Helicobacter pylori (HP) is not a clonal pathogen. Only certain strains are able to produce a toxic substance, a protein of ca. 130 kDa, which induces intracytoplasmic vacuolization on cells in culture. The aim of this study was to further characterise this cytotoxin-associated protein (p130) in concentrated broth culture filtrates (CBCF) and in whole cell suspension sonicates (WCSS) of HP strains by verifying whether p130 is shared by the HP strains tested and by determining its isoelectric point (pI).

CBCF and WCSS of 10 cytotoxic HP strains (CTHP) and 7 non-cytotoxic organisms (NCTHP) were separated by electrophoresis in 8% SDS-PAGE. Proteins transferred to nitrocellulose sheets were immunoblotted with sera from patients infected by CT and NCT HP strains and with a mouse polyclonal antibody raised against electroeluted p130 of a CTHP strain (CCUG 17874). CBCF and WCSS of this strain and of non-cytotoxic strain G21 were affinity purified on Affigel Blue. The most vacuolating fractions of the CTHP strain and the corresponding ones of G21 were analysed under NEPHGE conditions and incubated with the above mentioned sera. The reaction was visualised with anti-human and anti-mouse IgG conjugated with peroxidase.

p130 was only recognised by sera from patients infected by CTHP organisms and by the mouse anti-p130 antibody in CBCF and WCSS of cytotoxic HP strains alone. In addition, the mouse antibody neutralised intracytoplasmic vacuolization caused by CBCF and by live HP homologous strain. The average pI of p130 was 7.3. p130 was not present in CBCF and WCSS of non-cytotoxic organisms.

In conclusion, cytotoxic HP strains share an antigenically similar polypeptide of 130 kDa which is associated with intracytoplasmic vacuolization, and is mostly retained by HP organisms. The determination of the isoelectric point of p130 is a useful step in the purification of the toxic factor.

F270

ROLE OF HELICOBACTER PYLORI SEROLOGY IN SCREENING PRIOR TO DIRECT ACCESS ENDOSCOPY.

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Background H. pylori is associated with 95% of duodenal ulcers and 80% of gastric ulcers, with most of the remainder being associated with NSAID use. A non-invasive means of diagnosing infection could be useful in screening subjects under the age of 45 (where the risk of gastric cancer is low) prior to endoscopy. Aims To assess the value of serology in screening prior to endoscopy. Methods The use of H. pylori serology in screening prior to endoscopy was assessed prospectively on 301 subjects directly referred by their primary care physician, following validation of the serology on 295 clinic referred subjects. The serology used was based on an acid glycine extract of H. pylori and is manufactured by Porton, Cambridge. It was validated against histology and biopsy urease (CLO) test. Results A cut-off point of 6.3, giving a sensitivity and specificity of 98% and 75% in the 295 clinic subjects, was selected as the most appropriate for screening. A screening policy of not endoscoping subjects under the age of 45 who were not taking NSAIDs or who had a serology titre of less than 6.3 units/ml was assessed prospectively on the 301 directly referred subjects. This would have missed only only one duodenal ulcer out of 19 peptic ulcers in the under 45s and would have saved 62/148(42%) of endoscopies in this age group. It would have been necessary to lower the cut-off point to 5.5 to pick up all pathology with a 35% saving in endoscopies. Conclusion H. pylori serology is valuable as a screening method prior to endoscopy.

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ACTIVATION OF HUMAN PERIPHERAL BLOOD NEUTROPHILS BY HELICOBACTER PYLORI IN VITRO.

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H.pylori (HP) infection causes chronic gastritis with neutrophil infiltration, and is associated with duodenal ulceration: the pathogenic mechanisms linking these events are unclear. We have previously shown enhanced reactive oxygen metabolite (ROM) production in HP-infected gastric biopsies using 75μM luminol-amplified chemiluminescence (CL), and have now investigated the possibility that stimulation of neutrophil ROM production by HP might explain this observation.

Methods Neutrophils were isolated from citrated venous blood of 8 healthy volunteers by dextran-sedimentation of erythrocytes, density gradient centrifugation of buffy coat and osmotic lysis of contaminating erythrocytes. HP was cultured in brucella broth + 1% calf serum, centrifuged and resuspended in PBS. Neutrophils (5 x 10^4/ml) were incubated with 1ml of luminol in a liquid scintillation counter for 5 minutes, or until a steady baseline CL response obtained. Washed, live or sonicated HP (10-100μL from stock containing 10^9 CFU/ml), or HP culture supernatant was then added. CL response was measured for a further 5 minutes and compared with buffer control or neutrophils stimulated with N-formyl-met-leu-phe (FMLP) ($5x10^{-9}$ to $5x10^{-7}$M) or phorbol 12-myristate 13-acetate (PMA) (5-100ng/ml).

Results ("CL index" = [stimulated CL - baseline CL] / baseline CL) Resting CL of neutrophils was increased by HP live organisms (median "CL index" 2.6 (quartile range 1.0 to 9.3), p = 0.002 compared to buffer control); HP sonicated organisms (2.1(0.9 to 3.5), p^2= 0.04); and HP culture supernatant (1.0(0.3 to 2.8), p = 0.01). The HP-induced CL response was biphasic and calcium-dependent. Preincubation with HP increased CL stimulated with FMLP (mean 20%, n=3) and PMA (35%, n=3). Bismuth subcitrate (1.2μg/ml) inhibited HP- and FMLP-stimulated neutrophil CL (-67%, -63% respectively, n=4); metronidazole (10μg/ml) inhibited HP-stimulated neutrophil CL (-41%, n = 3).

Conclusions i) H.pylori and its soluble products stimulate neutrophil ROM production *in vitro:* this phenomenon may be of pathogenic relevance *in vivo.* ii) The H.pylori-stimulated neutrophil response is similar to that produced by the chemotactic peptide FMLP. iii) Antioxidant properties may contribute to the effectiveness of metronidazole and bismuth in H.pylori-related human disease.

Colorectal neoplasia F272–F281

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FAECAL ALPHA-1-ANTITRYPSIN CONCENTRATION IN PATIENTS WITH COLORECTAL CANCER OR ADENOMATOUS POLYPS

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Improvements in screening tests for colorectal cancer (CRC) are required. Alpha-1-antitrypsin (A1AT) measurement in faeces has been used as a test for protein losing enteropathy, but its value has not been examined in patients with colorectal neoplasia.

Using an improved extraction technique, faecal A1AT concentration in 24 patients with CRC, 10 patients with adenomatous polyps and 21 symptomatic controls (including patients with diverticular disease and peptic ulcer disease) was compared. All subjects underwent rigid sigmoidoscopy and double-contrast barium enema or colonoscopy before carrying out a 5 day faecal collection at home and without dietary restriction. Pooled samples were homogenised and lyophillized, A1AT was extracted from faeces with a cationic detergent and measured by radial immunodiffusion.

Patients with CRC had a higher dry weight concentration of faecal A1AT (3.4, 0.5-12.05 (median, range) vs 1.85, 0.5-3.4 mg g^{-1}; p=0.009 (Mann Whitney) and wet weight concentration (0.67, 0.1-2.21 vs 0.34, 0.07-0.71 mg g^{-1}; p=0.036) when compared with control subjects. There was no difference in dry or wet weight concentrations in the polyp group (2.3, 0.5-4.5 and 0.26, 0.11-0.88 mg g^{-1} respectively) compared with controls. 54% of CRC patients had a faecal A1AT concentration >3.4 mg g^{-1} dry weight and 46% >0.71 mg g^{-1} wet weight.

Preliminary results suggest that faecal A1AT excretion in patients with CRC requires further investigation, particularly with respect to a possible role in population screening.

F273

BILIARY AND FAECAL BILE ACIDS IN PATIENTS WITH COLORECTAL CANCER OR POLYPS

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Using gas liquid chromatography, faecal bile acids were determined in patients with cancer (n=14), polyps (n=9) and controls (n=10) and biliary bile acids in similar groups of patients: cancers (n=11), polyps (n=11) and controls (n=11). Patients were controlled for such confounding variables as cholecystectomy, gallstones, hepatic function and age.

Patients with adenomatous polyps had a higher concentration of faecal bile acids (5.23 μmol g^{-1}, 2.16-13.67 (median, range) vs 1.96, 0.91-6.97; p=0.016) and total secondary bile acids (5.23, 2.16-13.4 vs 1.96, 0.73-6.63; p=0.02) compared with control subjects. Patients with colorectal cancer had an increased (p=0.029) proportion of secondary faecal bile acids (mol%) compared with controls (100, 96.5-100 vs 95.19, 81.73-100).

Cancer patients had a higher proportion of secondary biliary bile acids (37.23%, 22.2-49.87 mol% vs 25.39, 9.6-53.2; p=0.057) when compared to controls and also when compared with polyps (25.19, 9.34-41.1; p=0.015. No such differences were seen in the polyp group.

Conclusions:

1. Supports theory that increased faecal bile acid excretion may lead to the development of colorectal polyps.
2. The increased secondary biliary bile acids in cancer patients reflects findings in their faeces and may result from increased colonic absorption in these patients.

F274

SCREENING FOR COLORECTAL CANCER USING AN IMMUNOLOGICAL FAECAL OCCULT BLOOD TEST

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There is concern about the low sensitivity of the chemical (guaiac based) Haemoccult (Rohm Pharma) test in mass population faecal occult blood (FOB) screening for the early detection of colorectal carcinoma. Hemeselect (SmithKline Diagnostics), an immunological FOB test, has been shown to be more sensitive for symptomatic colorectal cancer and may prove to be a more reliable screening test. However little is known of its sensitivity and, in particular, specificity for neoplasia in asymptomatic subjects.

To date 2000 asymptomatic subjects aged 50-75 years have been offered screening with both Haemoccult and Hemeselect tests. 777 (38.9%) completed both tests, of which 8 (1.0%) were Haemoccult positive and 74 (9.5%) Hemeselect positive. All but 4 (95%) have undergone large bowel investigation revealing 2 rectal cancers and 32 patients with 43 adenomas (22 greater than 1cm). Neither cancer was detected by Haemoccult. Specificity for neoplasia is 99.6% and 94.6% for Haemoccult and Hemeselect respectively. Positive predictive values for (a) all neoplasia and for (b) neoplasms >1cm are (a) 62.5% and (b) 50% for Haemoccult; and (a) 43.2% and (b) 29.7% for Hemeselect. Sensitivity cannot yet be evaluated.

Although the Hemeselect positive rate is high, its substantial positive predictive value for larger neoplasms warrants continuing evaluation.

F275

HUMAN FAECAL ALBUMIN AN - INDICATOR OF ASYMPTOMATIC COLORECTAL NEOPLASIA.

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The detection of human albumin in faecal samples has been investigated as a means of identifying subjects with asymptomatic colorectal carcinoma.

A total of 385 faecal samples were collected over 3 days from 144 asymptomatic subjects identified as having positive faecal occult blood tests in an ongoing screening study, all subjects subsequently underwent colonoscopy: 38 were shown to have an asymptomatic carcinoma, 60 to have single or multiple adenomas and 8 an active colitis; 38 subjects had healthy colons. Faecal albumin levels were determined by a Radial Immunodiffusion technique utilizing rabbit anti-human albumin antibodies.

Mean albumin levels in those with carcinoma (407.0, range 0.0 - 8400.0 μg/gm), adenomas (227.6, 0.0 - 4099.0 μg/gm) and colitis 200.5, 0.0 - 1806.8μg/gm) were higher than those in healthy subjects (138.9, 0.0 - 415.0 μg/gm), Mann Whitney $p < 0.0001$, $p = 0.001$ and 0.01 respectively.

Of those completing 3 days of tests, levels of over 150 μg/gm were detected in 24 (65%) of the cancer patients and 21 (50%) of those with adenomas compared with 5 (14%) of the healthy subjects (x^2 $p < 0.0001$ and $p = 0.001$ respectively).

This is the first report of elevated faecal albumin levels in subjects with asymptomatic colorectal neoplasia. Work to improve the sensitivity and specificity of the test is being undertaken.

F276

INFLUENCE OF INTRA-ABDOMINAL SEPSIS ON COLORECTAL CANCER SURVIVAL

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Post-operative sepsis as an immunomodulator has been implicated in the long term survival after colorectal cancer surgery, but the few reported results are conflicting. We, therefore, investigated 393 consecutive patients who underwent left colonic and sphincter saving resections for colorectal cancer from 1970-1989, divided into 59 (Group A) who developed intra-abdominal sepsis and 334 (Group B) who did not. Only 361 patients were available for analysis as 15 (25.4%) and 17 (5.0%) respectively died postoperatively. The groups were matched for age (p>.005), sex (p=0.51), Dukes stage (p=0.59), tumour differentiation (p=0.65), site of tumour (p-=0.13) and timing of operation (p=0.52). There were more anastomotic leaks in Group A (30/44 vs 5/317, p<001) and longer hospital stay (median 34 vs 22 days, p<0.001).

The median follow-up was 84 months for both groups. There was no significant difference in the 5 year actuarial (43% vs 57%, p=0.25) and disease free survival (51% vs 54%, p=0.23) between the two groups. There was no independent effect of perioperative blood transfusion on 5 year actuarial survival in both groups. Stepwise regression analysis of prognostic variables using Cox's proportional hazard model identified Dukes' stage, differentiation and age as independent determinent factors for survival but not sepsis.

These results suggest that post-operative sepsis does not influence the long term survival in colorectal cancer as has been reported.

F277

A PROSPECTIVE STUDY ON THE INFLUENCE OF BLOOD TRANSFUSIONS ON INFECTIOUS COMPLICATIONS AFTER COLORECTAL CANCER SURGERY

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Many retrospective studies have indicated an adverse effect of allogeneic blood transfusions on the recurrence rate of neoplasias and the rate of postoperative infectious complications. A prospective randomized study was performed in 424 patients with colorectal carcinoma to investigate these putative allogeneic blood transfusion effects. Patients randomized to the autologous group donated two units of blood prior to surgery. Transfusion rules were standardized.

In the allogeneic group 118/212 (56%) patients needed transfusions, against 158/212 (75%) in the autologous group, of which only 59/212 (28%) patients needed additional allogeneic transfusions. In this group exposure to allogeneic blood was reduced by 50%.

Infectious complications were seen in 111 patients (26%). Wound infection occurred in 8%, urinary tract infection in 7.3%, pneumonia in 3.2% and intra-abdominal infections in 6.6%. In the allogeneic group 51 (24%) patients had infectious complications compared to 60 (28%) patients in the autologous group (n.s.). Significantly more blood loss was measured in the group of infected patients ($p<0.005$). Of the 276 patients who received blood transfusions 82 (30%) developed infectious complications compared to 29 (20%) of the 148 untransfused patients ($p<0.05$). The infected patients received a higher mean number of blood transfusions compared to the uninfected group (3.0 versus 1.6, $p<0.0005$).

In conclusion: 1. Blood loss and blood transfusions are important risk factors for postoperative infectious complications. 2. These factors cannot be overcome by replacing allogeneic blood transfusions by autologous blood transfusions.

F278

PRE-OPERATIVE RADIOTHERAPY ENHANCES EXPERIMENTAL CARCINOGENESIS AT COLONIC ANASTOMOSES

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Adjuvant radiotherapy for rectal carcinoma has become widely used although the long term consequences of irradiation on unstable mucosa around anastomoses are unknown. The influence of pre-operative irradiation on colonic anastomoses in rats was explored.

Method

72 adults male F344 rats were used. The lower descending colon and rectum was exposed to 16 Gy orthovoltage x-rays, via anterior and posterior portals, through a 2x1cm aperture in a 4mm lead sheet. One week later animals underwent a 5mm transverse colotomy within the radiation field, which was repaired with 1) 4 interrupted 5/0 sutures of silk, stainless steel or polyglactin 910 (Vicryl) or 2) a "sutureless" closure. Post-operatively 24 rats were killed at 1,3 and 6 months.

Results

23 tumours (of which 16 were carcinomas) developed at anastomoses and just 3 (all adenomas) in the adjacent irradiated colon (Contingency table analysis of observed *versus* expected: Tumours; $X^2=15.4, p<0.001$ Carcinomas; $X^2=16.0$, $p<0.005$). No significant difference in tumour yield was noted between the anastomotic techniques.

Conclusions

Radiation carcinogenesis is greatly enhanced at colonic anastomoses. These findings should sound a note of caution to the widespread use of radiotherapy in rectal carcinoma, certainly until significant survival benefit has been shown.

F279

NUTRIENT ANTIOXIDANTS HAVE AN EFFECT ON THE COLONIC CRYPT CELL PROLIFERATION IN PATIENTS WITH ADENOMATOUS POLYPS.

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Epidemiological studies have shown an inverse relationship between the nutrient antioxidants (B-carotene, vitamin E, vitamin C and selenium) and the incidence of colorectal carcinoma. The risk of colorectal cancer can be assessed using colonic crypt cell proliferation.

Aim: To assess the effect of B-carotene, vitamin E vitamin C and selenium supplementation on the colonic crypt cell proliferation in patients with adenomatous polyps.

Methods: Fifty patients with adenomatous polyps were recruited. These were randomised into five equal groups. Group 1: no supplementation, Group 2: 9mg of B-carotene daily, Group 3: 160mg of vitamin E per day, Group 4: 750mg of vitamin C daily, Group 5: 100ug of selenium per day. Four pinch biopsies were taken before and at the end of supplementation and colonic crypt cell proliferation was assessed using the bromodeoxyuridine immunohistochemical technique. The labelling index percent (LI%) is calculated as the percentage ratio of the mean number of proliferating cells to the total number of cells per crypt

Results: TOTAL LI%

	Pre-supplement	Post-supplement
Normals	2.9	
No supplement	7.1	6.6
B-carotene	7.0	3.9* $p<0.01$
Vitamin E	5.4	5.7
Selenium	7.6	2.6* $p<0.0001$
Vitamin C	5.7	5.1* $p<0.0005$

Conclusion: Polyp patients had a significantly higher total LI% when compared to normals. Vitamin E had no effect on LI%. Vitamin C, B-carotene and selenium supplementation significantly reduced the colonic crypt cell proliferation in patients with adenomatous polyps

F280

RECTAL TUMOURS - DOES ENDOSCOPIC TRANSANAL RESECTION COMPROMISE SURVIVAL?

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Endoscopic transanal resection (ETAR) provides effective local therapy for low rectal tumours but may adversely affect long term survival. We have assessed the outcome and survival rate of patients treated with ETAR since 1982.

Three groups were defined: patients with tubulovillous adenoma, patients with carcinoma who could have had a "curative" procedure but for age or intercurrent disease and patients who had a palliative resection because of local fixity or distant metastases. Analysis was by Kaplan-Meier lifetable analysis.

A total of 178 resections were performed on 100 patients whose median age was 78 years (range 44-93) and whose median follow up was 36 months (range 0-111). The 30 day post-operative mortality rate was 5%; a further 7% of patients died later from unrelated diseases and 32% died from malignancy. Rectal bleeding was abolished or reduced in 80%, bowel habit returned to normal or improved in 77%, and tenesmus and pain were improved for 4 out of 10 patients with this symptom. The survival rates are shown in the table.

	n	%Survival 12 months	60 months
Tubulovillous adenomas	32	96	77
"Curative" ETAR	29	92	43
"Palliative" ETAR	39	37	19

The 5 year survival rate for curative ETAR for rectal cancer was similar to that of conventional surgery. ETAR effectively palliated patients with locally extensive or metastatic disease and was also associated with a 19% 5 year survival. Transanal resection may not substantially compromise overall survival in this elderly group of patients.

F281

COLORECTAL CANCER AND SURGICAL SPECIALISATION - HOPE FOR A BETTER OUTCOME?

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Surgery for colorectal cancer formerly the domain of general surgeons has come under scrutiny. Studies have identified inter- surgeon variation in outcome. The impact of a specialised service has not been addressed.

We have, therefore, compared the immediate and late results of 1018 resections performed in 982 patients since 1970, 500 (M:F 238:245) before (Group A) and 518 (M:F 246:253) after (Group B) the establishment of a colorectal service unit in 1981, whose median ages were 66 (27-94) and 70 (26-94) respectively ($p<0.01$). The groups were similar in Dukes' staging; Group A: Stage A 9%, B 49%, C 42% and Group B: Stage A 10%, B 53% and C 37% respectively. There were more patients with liver metastases at operation in Group A (80 vs 62, $p=0.003$). there was no difference in the number of emergency (Group A 66 vs Group B 57) and curative operations (Group A 387 vs Group B 422). There was a significant increase in Group B in the proportion of anterior resections to abdominoperineal excisions of rectum compared to Group A (130/52 vs 99/101, $p=<0.001$).

The median hospital stay (27 vs 22 days, $p<0.01$) and mortality (11.2% and 7.3%, $p=0.031$) were significantly less in Group B although the population was older ($p<0.01$). DVT and wound complications were reduced ($p= 0.013$ and < 0.001) but there was more catheter related sepsis ($p<0.001$) in Group B. The 5 year actuarial survival ($p=0.002$) and disease free survival ($p=0.003$) was better in Group B than in Group A.

Improved early outcome and long term survival with avoidance of stomas demonstrate the benefit of the specialist in the surgical treatment of colorectal cancer.

F283

AN INVESTIGATION INTO THE NATURAL HISTORY OF CHRONIC GASTRITIS USING THE SYDNEY CLASSIFICATION SYSTEM .

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In order to investigate the natural history of chronic gastritis, paired antral biopsies from 399 dyspeptic patients with this condition were assessed for the five histological features (chronic inflammation, polymorph activity, Helicobacter density, glandular atrophy and intestinal metaplasia) advocated in the Sydney classification system. The five features were scored on a four point scale ranging from 0 to 3 by a single pathologist. The results were analysed according to patient age and Helicobacter status using the Chi-square test for trend. Mean scores are shown in the table below (* = $p<0.05$; ** = $p<0.001$).

Age	Chr Infl	Activity	H pylori	Atrophy	IM
<30	1.59	0.98	1.86	0.39	0.02
30-39	1.71	1.05	1.68	0.59	0.22
40-49	1.81	1.20	1.79	0.58	0.19
50-59	1.75	1.21	1.76	0.74	0.42
> =60	1.83*	1.27*	1.79	0.81**	0.56**
Hp pos	1.82	1.22	n=362	0.65	0.31
Hp neg	1.16**	0.68**	n=37	0.65	0.46

The age related data suggest that atrophy and intestinal metaplasia occur as a result of prolonged exposure to either H pylori infection itself or other factors synergistic with it.

It can be assumed that most patients with H pylori-negative chronic gastritis have spontaneously cleared the organism as they have an immune response against the bacteria. We therefore further conclude that H pylori clearance leads to marked reduction in inflammation and PMN activity but not atrophy and intestinal metaplasia. These latter changes may be irreversible.

Stomach and duodenum F282–F293

F282

THE KINETICS OF 5-AMINOLAEVULINIC ACID PHOTOSENSITISATION IN THE NORMAL RAT STOMACH.

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The synthesis of 5-aminolaevulinic acid (ALA) is the first committed step leading to the formation of porphyrin and eventually haem. This synthesis is tightly regulated by feedback inhibition but administration of excessive exogenous ALA will lead to accumulation of porphyrin precursors especially protoporphyrin IX (PP9), a potent photosensitiser for photodynamic therapy (PDT). ALA was administered intravenously to normal rats in various doses and the resultant PP9 accumulation in the gastric wall was studied using photometric fluorescence microscopy. A rapid build up of PP9 fluorescence was seen in the mucosa which reached a peak at 1, 2 and 3 hr after administration of 20, 100 and 200 mg/kg of ALA respectively followed by a rapid fall off to background level by 24 hr. Fluorescence distribution was intracellular. Very little accumulation was seen in the submucosal and muscular layers and a mucosa : muscularis propria PP9 fluorescence ratio in excess of 10 was obtained at the time of peak fluorescence with all 3 doses. The intensity of fluorescence increased with dose but not linearly. Fluorescence fell off much more rapidly in the mucosa so that by 6 hours, the level in the mucosa was lower than that in the muscularis propria. On exposure to red light (630nm, 50mW x 1000sec), a marked mucosal necrosis resulted with minimal damage to the underlying layers. With lower doses, this selective effect was more marked with preservation of even the muscularis mucosae without reducing the size of the damage produced. A very selective photosensitisation of the gastric mucosa can be achieved with low dose ALA making possible photodynamic ablation of diseased gastric type mucosa such as dysplastic gastric or Barrett's epithelia. ALA photosensitisation does not carry prolonged cutaneous phototoxicity thus enhancing its safe use in PDT of the upper gastrointestinal tract.

F284

DNA ADDUCTS IN THE POST-VAGOTOMY STOMACH

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Carcinogenic chemicals can bind covalently to intracellular DNA, the resulting complex being known as a DNA adduct and correlations have been found between the number of DNA adducts found in a tissue and the risk of developing cancer in that tissue. Recently use of the ^{32}p-postlabelling procedure has enabled DNA adducts to be quantified in human tissues and we have used this technique to quantify adducts in the gastric mucosa of a group of vagotomised patients in an attempt to identify any increased risk of cancer following this operation.

88 patients were entered into the study, 59 having had a prior truncal vagotomy and drainage and 29 a highly selective vagotomy (HSV). Samples of gastric mucosa were obtained by endoscopic biopsy, DNA purified by solvent extraction and adduct levels quantitated by ^{32}p-postlabelling.

Adduct levels ranged from <1 to 29 adducts/10^8 nucleotides. Adduct levels were significantly higher after truncal vagotomy and drainage than after HSV ($p<0.01$) but did not correlated with intragastric bile levels.

We conclude that gastric mucosal DNA damage is greater after truncal vagotomy and drainage than after HSV and would suggest that this provides further evidence that HSV should be the operation of choice for peptic ulcer.