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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 981 patients since 1970, 500 (M:F 238:245) before (Group A) and 518 (M:F 246:255) after (Group B) the establishment of a colonic 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 96%, 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). Deft and wound complications were reduced (p=0.013 and <0.001) but there was more common related sepsis (p<0.01) 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 stoma demonstrate the benefit of the specialist in the surgical treatment of colorectal cancer.

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THE KINETICS OF 5-AMINOLAEVULINIC ACID PHOTOCHEMOSENSITISATION IN THE NORMAL RAT STOMACH.
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3. Imperial College of Science, Technology & Medicine, London.

The synthesis of 5-aminolevulinic 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 more rapidly in the mucosa so that by 6 hr, the level in the mucosa was lower than that in the muscularis propria. On exposure to red light (600nm, 50mW x 100ms), 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.

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).

<table>
<thead>
<tr>
<th>Age</th>
<th>Chr Infl</th>
<th>Activity</th>
<th>H pylori</th>
<th>Atrophy</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>1.59</td>
<td>0.98</td>
<td>1.86</td>
<td>0.39</td>
<td>0.02</td>
</tr>
<tr>
<td>30-39</td>
<td>1.71</td>
<td>1.05</td>
<td>1.68</td>
<td>0.59</td>
<td>0.22</td>
</tr>
<tr>
<td>40-49</td>
<td>1.81</td>
<td>1.20</td>
<td>1.79</td>
<td>0.58</td>
<td>0.19</td>
</tr>
<tr>
<td>50-59</td>
<td>1.75</td>
<td>1.21</td>
<td>1.76</td>
<td>0.74</td>
<td>0.42</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>1.83*</td>
<td>1.27*</td>
<td>1.79</td>
<td>0.81**</td>
<td>0.56**</td>
</tr>
<tr>
<td>Hp pos</td>
<td>1.82</td>
<td>1.22</td>
<td>0.38(n=362)</td>
<td>0.65</td>
<td>0.31</td>
</tr>
<tr>
<td>Hp neg</td>
<td>1.16**</td>
<td>0.68**</td>
<td>0.37(n=37)</td>
<td>0.65</td>
<td>0.46</td>
</tr>
</tbody>
</table>

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.

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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 32p-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.

68 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 32p-postlabelling. Adduct levels ranged from <1 to 29 adducts/106 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.
24-hour intragastric pH monitoring and serum cortisol in shiftworkers, with special reference to eating and working patterns.


Disgeptic complaints are frequent in shiftworkers. The pattern of gastric secretion and food intake may play a role in their aetiology. We examined gastric acidity and cortisol in secretion during changing shifts.

Twelve healthy shiftworkers, 6 male industrial workers and 6 female nurses, aged 22-44, were submitted to three 24-hr gastric pH recordings using antimony electrodes and a Syntec Medical Digitrapper. Starting point of each investigation was at the start of work on the fourth day of the different shifts. The subjects kept their normal lifestyle and completed an "eat/drink" diary. Serum cortisol levels were measured before and after the working period, respectively.

Median 24-hr intragastric pH-values varied from 1.2 to 1.9 (mean 1.6) in the subjects. No overall significant differences in median pH were seen when shifts were divided into three phases (work; leisure time; sleep). This was true for all types of shifts. However, the female shiftworkers had a higher median pH than the men during shift B (1.6 vs 1.4; p < 0.02). Relevant pH-rises (defined as pH > 3 during >30 minutes) were mainly due to food intake (88/118 75%). Spontaneous pH-elevations occurred mainly during sleep, and were more frequent in the women than in the men (26 of 46 pH rises vs 6 of 52; X²-test: p = 0.004). During nightshift, 4 of 6 men showed an unadapted sleep rhythm (i.e. no decrease during work), compared to none of the women.

In conclusion, with respect to gastric acid secretion and gastric pH-rhythm, women seem to be better adapted to shiftwork than men. As pH-elevations during shiftwork are predominantly induced by food intake, dietary advice may be important in shiftworkers, regarding the prevention as well as the therapy of peptic diseases.

A STUDY ON THE EXPRESSION OF MG7 CORRESPONDING ANTIGEN IN GASTROINTESTINAL POLYS AND ITS RELATION WITH CANCER.

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112 cases of polyps of the stomach (64 cases), gallbladder (4 cases), and rectal polyps (48 cases) were studied and followed up by means of immunohistochemical staining with monoclonal antibody (MG7/against gastric cancer and avidin-biotin complex (ABC) technique to identify the expression of MG7 corresponding antigen (MG7-Ag) in gastrointestinal polyps and its relation with histological classification of polyps, atypical hyperplasia (AH) and cancer, to determine "high risk population of cancer".

During 1980 to 1990 112 in-patients with pathologically confirmed type with 268 tissue blocks were collected and sectioned for staining with MG7 using ABC method.

Positive expression of MG7-Ag in villous, mixed and tubular polyps were 98.2%, 95.4% and 60.2% respectively. Other types (inflammatory and hyperplastic) of polyps gave a negative expression. No malignancy was found in all 45 polyps with the negative expression. A close correlation was shown between second grade AH expression of MG7-Ag (p = 0.05). The positive expression of MG7-Ag was closely related with cancer (p = 0.025). 12 of 67 with the positive expression of MG7-Ag developed cancer during 3 to 38 months. Our results show that gastrointestinal (include gallbladder and rectal polyps) with MG7-Ag positive cases may develop cancer. The patients with polyps of positive expression of MG7-Ag are high risk population of the cancer.

SCINTIGRAPHIC ASSESSMENT OF INTESTINAL TRANSIT FOLLOWING ROUX-EN-Y ANASTOMOSIS.

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Delayed gastric emptying has been reported to be a major problem following Roux-en-Y anastomosis despite absence of a mechanical obstruction. The mechanism of this delay is not understood, but there may be a motility problem either in the gastric remnant or Roux loop. This has been investigated in 10 patients after revision Roux-en-Y. Gastric and small bowel transit have been assessed scintigraphically by the technique of compressed image analysis in parallel with gastric emptying measurement. Part of my thesis has been to develop this technique for assessing jejunal motility which has not previously been done.

The gastric remnant was aperistaltic in all of these patients but there was only gastric stasis in one, emptying occurring by gravity through a wide anastomosis into the jejunum. In the jejunal Roux loop peristaltic was absent in all of these subjects and there was stasis in 70% which ultimately slowly emptied with the assistance of gravity. Absent peristalsis in the jejunal Roux loop draining the stomach appears to be the major cause of stasis following Roux en Y anastomosis. Revision gastric surgery is therefore, unlikely to be of any real help. This is the first study to determine the cause of the problems of food stasis in the upper alimentary tract following major gastric surgery.

ASSESSMENT OF LOCAL MICROCIRCULATION BY LASER DOPPLER VELOCIMETRY IN PATIENTS WITH MULTIPLE BULBAR EROSIONS.

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In more than 50% of cases chronic duodenal erosions are not related to reflux oesophagitis or concomitant duodenal ulcer, but represent an autonomous disorder, the pathogenesis of which is still unclear. Acid secretion is normal, while it has been suggested that an impairment of local microcirculation could be involved. We examined 10 patients with multiple autonomous duodenal erosions, 10 patients with duodenal ulcer and 10 healthy controls.

During endoscopy mucosal blood flow in the duodenal bulb was measured by means of a laser Doppler (PP3, Perimed Sweden) through a special probe (PF 3098) introduced in the biopptic channel. Measurements were performed at 4 kHz and the results expressed in Perfusion Units (1 PU = 10 mV).

In duodenal ulcer patients no significant differences in mucosal perfusion were observed compared with healthy controls. In contrast a significant reduction (p < 0.01) of mucosal blood flow was detected in subjects with duodenal erosions. After six weeks of treatment with ranitidin 300 mg hs duodenal blood flow remained unchanged even in patients whose erosions were healed.

Conclusions: a) In autonomous duodenal erosions (but not in duodenal ulcer) mucosal blood supply is significantly impaired; b) the persistence of mucosal ischaemia after endoscopic healing suggests that impaired blood flow is a primitive phenomenon with a possible pathogenetic role.
REDDUCED GASTRIC ACID SECRETION AND RISK OF SALMONELLA INFECTION

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Although a reduction in gastric acid secretion has long been thought to increase susceptibility to Salmonella infections the increase in risk has not been quantified, nor is it known whether taking anti-secretory agents also increases susceptibility. We have used the public health notifications of Salmonella food poisoning and general practice records to carry out a case-control study enquiring about drug usage and history of gastric surgery.

Records of 101 cases of Salmonella infection (66 S.enteritidis, 16 S.typhimurium, 19 others) all aged >45 years and 202 age, sex and practice matched control subjects were examined. Overall, cases (80%) were slightly more likely than controls (74%) to have had at least one prescribed drug in the year prior to infection (χ²=1.0, p<0.05). 16 (16%) cases and 14 (7%) contacts had been prescribed an H₂ antagonist sometime previously (relative risk [RR] 2.5, 95% confidence limits [CL] 1.2-5.3). In the month prior to a case's infection 8 cases and 6 controls were prescribed an H₂ antagonist (RR -2.8, CL -0.9-0.0); adjusting for the confounding effect of other drugs had little effect (adj. RR 2.4, CL 0.9-6.9). Only 1 case and no controls were being prescribed Neocytam and he was prescribed cimetidine simultaneously. Previous gastric surgery was noted in the records of 5 cases and 1 control. Thus a total of 12 (12%) cases and 7 (3.5%) contacts were being prescribed H₂ antagonists at the time of infection or had previous gastric surgery (RR associated with reduced acid secretion 3.8, CL 1.5-9.3). In conclusion H₂ antagonists appear to be associated with a small increase in risk of Salmonella infection, a risk which is probably less than that associated with gastric surgery.

EFFECT OF CYTOCHALASIN B ON IN VITRO RAT GASTRIC MUCOSA

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Previous studies have suggested that Cytochalasin B prevents the rapid repair of gastric mucosa in vitro by selectively disrupting cell migration. We have investigated the effect of Cytochalasin B on in vitro rat gastric mucosa.

Using chambered gastric mucosa taken from male Wistar rats was mounted in a gas lift apparatus and allowed to reach its maximum transmucosal potential difference (P.D.) in the presence of standard luminal and nutrient solutions. The mucosa was then incubated with Cytochalasin B (1.2x10⁻⁴M) in the nutrient solution for 90 minutes. A further group of tissues was allowed to recover for 90 minutes in the presence of Cytochalasin B after a 10 minute luminal challenge with 0.75M NaCl. Controls were incubated with standard luminal and nutrient solutions. Continuous measurement of P.D. and intermittent measurement of tissue resistance (R) was undertaken. After 90 minutes the tissues were fixed in formal saline and subjected to histological analysis.

Results

Saline challenge (n=5) produced a fall of mean P.D.(mV)±SEM from -18.00±2.05 to +1.80±0.41 after 10 minutes (p<0.05 compared to controls) and subsequent recovery in the presence of cytochalasin at -4.90±1.21 was significantly inhibited (p<0.05). Mean R(ohm/cm²)SEM fell from 66.00±8.17 to 135.85±83 and recovered to 49.00±6.59 (p<0.06). The mean P.D. of uninjured tissues (n=5) exposed to cytochalasin fell from -17.30±1.54(SEM) to -6.55±1.45 after 90 minutes (p<0.05 compared to controls). Mean R(ohm/cm²)SEM fell from 77.00±6.63 to 57.00±7.35 (p<0.05). Histological analysis of both sets of tissues revealed similar damage throughout the mucosa. Controls remained intact.

Cytochalasin B prevents the recovery of in vitro gastric mucosa after saline challenge but it appears that this action is mediated by direct interference with the tissue rather than by interference with repair mechanisms.
GASTRIN AND SOMATOSTATIN mRNA IN HUMAN ENDOSCOPIC GASTRIC BIOPSIES.
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Regulatory peptides which act locally within gastrointestinal epithelia cannot be adequately studied by measuring plasma peptide concentrations. Alterations in gene expression have been measured in animals by observing changes in specific peptide mRNA. In man, however, such approaches have been limited by the quantity of fresh tissue available. To address this problem we have analysed peptide hormone mRNAs from endoscopic biopsies.

Gastric antral biopsies were taken at endoscopy and snap frozen in liquid nitrogen. The tissue was ground under liquid nitrogen and then hand-homogenised in acid guanidinium isothiocyanate in a 1.5 ml microfuge tube. Total RNA was extracted with phenol/chloroform and precipitated with isopropranol.

10μg of RNA was run on 1% agarose formaldehyde gels and the RNA transferred to nylon filters. The filters were hybridised with human 32P-labelled cDNA probes, washed at high stringency and exposed to film. Filters were subsequently washed and reprobed with a ribosomal oligonucleotide to correct for loading differences.

Total RNA yields of up to 40μg have been obtained from five Smg biopsies. The RNA was undegraded, with distinct 28S and 18S ribosomal bands. We have successfully identified gastrin and somatostatin mRNA with appropriate human cDNA probes and are quantitating changes in response to physiological and pathological stimuli.

Conclusion: This technique allows mRNA encoding regulatory peptides to be detected in endoscopic biopsies, and should permit studies of intra-epithelial control mechanisms in man.