Abstracts of papers presented at the Annual Scientific Meeting of Gastroenterological Society of Singapore on 1 December 1991

1. EFFECT OF CAPSAICIN AND CHILLI ON ETHANOL-INDUCED GASTRIC MUCOSAL INJURY.

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One possible explanation for the higher frequency of peptic ulcer in Chinese compared to Malays and Indians is that chilli has a protective effect on gastroduodenal mucosa. We have therefore studied the effect of chilli and its pungent ingredient capsaicin on ethanol-induced gastric mucosal injury. Fasting unanesthesized male Sprague-Dawley rats (n=148) were given by gavage 0.02, 0.2, 0.2, 5.0 mg capsaicin, 100, 200 mg chilli powder, or capsaicin vehicle followed by by 1.8 or 2.0 ml absolute ethanol or normal saline 30 minutes later. After another 60 minutes, animals were sacrificed, mucosal damage assessed by planimetry and the amount of damage expressed as percentages of total glandular mucosal area. Another 20 rats were randomised to receive either powdered rat chow or chow supplemented with 200 mg chilli powder daily for 4 weeks after which gastric mucosal injury was produced by absolute ethanol as before.

No damage occurred when saline was administered following capsaicin or vehicle. With administration of ethanol, pretreatment with 2 mg capsaicin reduced mucosal injury to 3.1 ± 1.7 compared to 19.7 ± 4.6 when capsaicin solvent was used as pretreatment ($p<0.01$). The protection afforded by 0.2 mg and 0.02 mg of capsaicin was not however statistically significant compared to the control group (2 mg : 2.1 +- 0.8[a], 0.2 mg : 5.1 ± 1.7, 0.02 mg : 29.0 ± 7.3, control : 13.9 ± 4.8[b], av b $p < 0.01$). Pretreatment with 100 mg or 200 mg chilli powder reproduced the protective effect of capsaicin (capsaicin 5 mg: 1.7 ± 0.5[c], chilli 100 mg : 6.3 ± 1.4[d], chilli 200 mg: 3.2 ± 1.3[e], control : 34.7 ± 5.7[f]. c,d,e v $fp<0.01$). In the chronic study, the mean lesion score in animals receiving chilli was 11.2 ± 2.9 compared to 32.3 ± 3.9 in the control group ($p<0.002$). Therefore, acute administration of capsaicin and chilli as well as chronic chilli intake protect against ethanol-induced gastric mucosal injury.

2. HELICOBACTER PYLORI AND GASTRITIS IN CHILDREN WITH RECURRENT ABDOMINAL PAIN.

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Recurrent abdominal pain (RAP) is common among children. The association between RAP, the occurrence of *Helicobacter pylori* and historically proven gastritis is unclear. This study aimed to determine the prevalence of *H pylori* in children with RAP and to assess the relation between H *pylori* and histological gastritis.

Thirty-nine children who underwent gastroscopy because of RAP were included. One or more gastric mucosal biopsies were obtained. Histological gastritis was graded according to a modified McNulty system. The presence or absence of *H pylori* was assessed by light microscopic examination of sections stained with Haematoxylin and Eosin (H & E).

Of the 39 patients, 9 had grade 1/4 antral gastritis, 20 had 2/4 antral gastritis, 5 had 3/4 gastritis and the remaining 5 had 4/4 antral gastritis. Of the 5 children with grade 4/4 gastritis, 4 had *H pylori* identified by H & E stain. Ten of the 29 patients with grade 1 and 2 gastritis had normal endoscopic appearance. The 10 patients with grade 3 and 4 gastritis had abnormal mucosal appearance during gastroscopy.

In conclusion, histological gastritis is common in children with RAP. The cause of the gastritis is unknown in the majority of cases. *H pylori* accounts for about 10% of the cases with antral gastritis.

3. LAPAROSCOPIC VAGOTOMY - THE NEW TOOL IN THE MANAGEMENT OF PEPTIC ULCER DISEASE.

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Laparoscopic vagotomy provides a viable alternative to expensive long term treatment with H2 antagonists in patients with intractable peptic ulcer disease. The minimally invasive procedure offers reduced postoperative discomfort and improved cosmesis. We report six cases of posterior truncal and anterior highly selective vagotomy performed laparoscopically between May to Oct 1991. The mean age was 39 years. Five were males and one female. All of them had a long history of H2 antagonist therapy ranging from two to ten years that was characterized by multiple relapses. Preoperative BAO and PAO levels were all high.

The average duration of surgery was two and a half hours. Postoperatively, diet was resumed on the 3rd day and patient discharged on the 4th or 5th day. There were no complications from the procedure. Postoperative BAO and PAO done in three patients so far revealed a dramatic decrease in acid output.

We recommend this operation as an innovative option to conventional open highly selective vagotomy in patients who have failed to respond to long term medical therapy.

4. EXPERIENCE WITH THE NEEDLE KNIFE AS A PRECUT TOOL IN ERCP.

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Access to the biliary system is not always easily obtained using conventional ERCP cannulation methods. We present our experience with the Huibregtse-Katon needle knife (NK) for precut sphincterotomy and present its efficacy and safety. Between Jan 1990 and May 91, a total of 542 ERCP's were performed at our Dept. Of these, sphincterotomy was performed in 338 cases. NK was used in a total of 59 cases (11%). NK exposed the common bile duct in the first attempt in 39 cases while 5 cases succeeded at a second ERCP. In 12 cases, NK was performed for deep insertion of a stentard papillotome while 8 were prior to endoscopic biliary stenting. 4 cases were for Billroth II situations.

All successful NK precuts were followed by conventional complete sphincterotomy. In only 1 case was NK used for diagnostic purpose. A total of 15 cases were unsuccessful (2 were due to stones, 9 had malignancy and 4 were of unknown etiology). Hemorrhage occurred in 3 cases, submucosal injection of contrast in 3 and perforation in 1 case. Our overall success rate in deep bile duct cannulation with the help of NK was 97.2%. We recommend NK as useful precut tool for sclective bile duct cannulation, but only by experienced endoscopists.

5. COMPLEMENT DEFICIENCY IN LIVER CIRRHOSIS - OBSERVATIONS & APPLICATIONS.

SML Lim, KK Heng, LH Poh, A Rauff, Dept of Surgery, National University of Singapore

Life-sustaining liver allografts are not easily obtained particularly in Asean countries. For patients in liver failure, there are currently no other methods of liver dialysis that can effectively prolong life. Xenografts are a potential source of live-saving donor organs. Here, we investigate the feasibility of xenotransplantation of livers in cirrhotic patients. This study is divided into two parts: (1) an analysis of the importance of complement depletion in preventing the hyperacute rejection of liver xenografts; (2) an analysis of the levels of complement deficiency in cirrhotic patients.

Experimental design

(1) An ex vivo liver perfusion circuit was used to study the role of complement in the hyperacute rejection of liver xenografts. Porcine livers were perfused for 2-5 hours with: (a) complement-rich human fresh frozen plasma (FFP) with packed red cells (n=6), and (b) xenogeneic decomplemented human FFP with packed red cells (n=6). The survival of these livers was determined by biochemical and histological methods.

(2) An analysis of the degree of complement deficiency in a small group of local cirrhotic patients was performed. C3, C4 and CH50 levels of 14 cirrhotic patients and 23 normal healthy individuals were assayed.

Results

(1) Hyperacute destruction of liver xenografts at 2 hrs was observed following ex vivo perfusion with complement-rich human FFP. This was confirmed histologically, and biochemically by the rapid elevation of serum potassium to a mean of 15.6 ± 6.5 mmol/L and aspartate transaminase to a mean of 1262.3 ± 203.3 U/L. Perfusion of porcine livers with heat-inactivated FFP (complement-poor) resulted in prolonged survival of liver xenografts which remained morphologically and histologically normal at 5 hrs. Serum biochemistry was within normal range in this group of xenografts.

(2) Sera from patients with established liver cirrhosis demonstrated that complement levels were significantly lower for C3, C4, CH50, compared to sera of normal healthy individuals. The mean levels for C3, C4, and CH50 in normal individuals were 128.2 ± 42.6 mg/dL, 27.0 ± 12.9mg/dl and 32.1 ± 10.1u/ml, and in cirrhotic patients were 69.0±36.5mg/dL, 16.8±9.5mg/dL and 22.5 ± 18.8u/ml respectively.

Conclusions

These studies confirm the importance of complement in the hyperacute destruction of livers in an ex vivo model and demonstrate that removal of complement abrogates this effect. We also confirm the existence of a complement deficiency state in patients with established liver cirrhosis. It is interesting to speculate that the population of cirrhotic patients with complement deficiency may well tolerate in the short term, a life-sustaining xenograft as a bridge prior to the availability of a suitable human allograft.

6. DIETARY ASSESSMENT OF IRRITABLE BOWEL SYNDROME (IBS) PATIENTS.

CK Yap, M Cheong, KM Fock. Department of Medicine, Toa Payoh Hospital, Singapore.

Epidemiological evidence has promoted the hypothesis that dietary fibre deficiency may predispose the gut to colonic-motility disorders. However, other evidence point to fibre manipulation having a placebo effect. If fibre deficiency is implicated, then there should be deficiency in patients with IBS when compared to normal controls. We conducted a dietary assessment using the method of a dietary recall in 31 patients with IBS. 8 patients were excluded due to prior dietary manipulation, presence of diabetes mellitus or were on medications for concomitant illness. 23 patients who satisfied 3 or more of Manning's criteria (12) or had painless diarrhoea (11) were studied. The IBS group (female : male 1.8, mean age 35 years, mean Body Mass Index 21.9) was compared to 21 healthy controls (female : male 1.3, mean age 28 years, mean Body Mass Index 21.4). One dietitian interviewed all subjects and the levels of fibre and lactose intake were estimated using standard nutritional reference values. The mean dietary intake of fibre and lactose intake for normals were 16.22 ± 10.7g (median 16.9g) and 2.59 ± 5.5g (median 1g) respectively. The corresponding mean dietary intake for IBS patients were 12.13 ± 5.5g (median 10.6g) and 3.26 ± 6.22g (median 2g) respectively. Statistical analysis was done using the Wilcoxan Rank Sum test. There was a statistically significant difference ($p<0.01$) in the fibre intake between IBS and normals but none was found for lactose intake ($p=0.35$). The relative deficiency in fibre intake points to its possible role in patients with symptoms of colonic dysmotility.

7. THE COLONIC AIR INSUFFLATION TEST - AN AID TO THE POSITIVE DIAGNOSIS OF IRRITABLE BOWEL SYNDROME.

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Irritable colon syndrome presents as altered bowel habit often associated with abdominal pain. The diagnosis is classically one of exclusion of structural pathology. Manning et al proposed six symptoms which were more common in patients with irritable colon compared to those with structural disease. These criteria therefore help in the positive diagnosis of irritable bowel syndrome. Reproduction of typical abdominal pain with colonic air insufflation at sigmoidoscopy has been mentioned by several authors as a feature of irritable colon syndrome. However, the diagnostic value of this test has not to our knowledge been formally evaluated. From February to December 1990, 84 patients presenting with abdominal pain had colonic air insufflation test performed after diagnostic sigmoidoscopy. All nine patients with known structural causes of abdominal pain (Group A) had negative tests. Of 75 patients with functional abdominal pain, 28 of 37 (76%) with irritable bowel (Group B) had positive tests compared to 20 of 38 (53%) with functional abdominal pain not due to irritable bowel (Group C). (A v B $p<0.0001$; B v C $p<0.05$; A v C $p<0.005$). We conclude that the colonic insufflation test is a useful adjunct for the positive diagnosis of irritable bowel syndrome and is particularly useful in differentiating the latter from non-colonic structural causes of abdominal pain.

8. HELICOBACTER PYLORI AND GASTRIC CANCER : CORRELATION WITH GASTRITIS, INTESTINAL METAPLASIA AND TUMOUR HISTOLOGY.

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It has been hypothesized that Helicobacter pylori (H pylori) may be causally related to atrophic gastritis and intestinal metaplasia with subsequent development of the intestinal but not the diffuse type of gastric carcinoma. The aim of this study was to examine the association between H pylori, histological gastritis and intestinal metaplasia in gastric cancers of different histological types. 169 gastrectomy specimens received in one Pathology Department were studied. 156 were adenocarcinomas (intestinal type 87, diffuse type 50, mixed type 19). Subjects with intestinal-type carcinoma were older and more likely to be males when compared to those with tumours of the diffuse type. Gastritis occurred in 137 of 163 body specimens (84%) and 126 of 131 antral specimens (96%). The frequency of gastritis was unrelated to tumour histology. Atrophic gastritis was commoner in both body and antral mucosa in intestinal-type carcinoma compared to the diffuse type. This was also the case with intestinal metaplasia for body, although not for antral mucosa. H pylori was present in 101 of 163 cases (62%) in the body and 56 of 131 cases (43%) in the antrum. In intestinal-type carcinoma H pylori occurred in 52/84 (62%) of body mucosa and 24/70 (34%) of antral mucosa while the corresponding figures for diffuse type carcinoma were 29/48 (60%) and 17/38 (45%) respectively. Tumour histology therefore had no influence on the occurrence of H pylori. Tumour site had no effect on the presence/absence of gastritis, atrophic changes, intestinal metaplasia or H pylori. While both H pylori and gastritis are associated with gastric cancer the association is unrelated to tumour histology and may not be a causal one.

9. GASTRIC REDUCTION SURGERY FOR MORBID OBESITY IN SINGAPORE.

TK Ti. Department of Surgery, National University Hospital

This is a preliminary report of a personal series of 8 patients who have had gastric reduction surgery for morbid obesity in Singapore.

The patients (5 women and 3 men) were at least 60% overweight and had all tried conventional methods of weight loss without success. The main reasons for seeking surgery were a feeling of social rejection, tiredness, decreased activity and diffieulty in breathing. Other symptoms were obstruetive sleep apnoea, backstrain and obesity related illness - hypertension, cholelithiasis and venous stasis in lower limbs.

The surgical techniques used were gastric bypass with roux-en-Y gastrojejunostomy in 5 patients and vertical banded gastroplasty in 3 patients. All 8 patients recovered from the surgery with little morbidity. Weight loss averaged 50-60% of excess weight, occurring mainly in the first 6 months after surgery and stabilising at about 2 years.

As has been the experience in the West, patients with morbid obesity in Singapore can be successfully treated by gastric reduction surgery.

10. PEPTIC ULCER DISEASE IN THE ELDERLY.

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A retrospective study of peptic ulcer patients aged 60 years and above seen by the Medical Unit, Gastroenterology Division of Toa Payoh Hospital from January 1990 to end of September 1991 was carried out with the following objectives:

(1) To assess the magnitude and demography of the problem.

(2) To analyse the clinical presentations, complications, and outcome.

A total of 116 patients 60 years of age and older with endoscopically proven peptic ulcer were seen, constituting 38% of all ulcer patients over the same period. The age varied from 60 to 91 years with a mean age of 71.6 years. There were 70 men and 46 women with a male to female ratio of 1.5:1. Gastric ulcer patients outnumbered duodenal ulcer patients by ratio of 2.2:1.

Sixty-four percent of the patients had one or more co-existing chronic illnesses, of which cardiovascular disease was the most frequently encountered medical problem (60%). Thirty-three patients (28%) had history of NSAID or aspirin ingestion Fifty-two percent presented with abdominal pain. Abdominal pain was absent in 22% and 17% had melena or hemeternesis at presentation. 9% who were admitted for unrelated illnesses developed upper gastrointestinal bleeding while in the ward. The commonest complication was bleeding occurring in 56 patients (48%). NSAID or aspirin ingestion was documented in 41% of the bleeders. 60% of the bleeders did not complain of abdominal pain. The median hemoglobin was 8.5% and median blood transfusion requirement was 695ml. Only 3 patients underwent surgery. The mortality for patients with hemorrhage was 7%. The overall mortality was 3%.

Conclusions :

(1) The elderly constituted about one third of our ulcer patients.

(2) There were more gastric than duodenal ulcers.

(3) Presentation is often atypical and more variable.

(4) 95% of the bleeders can be managed by medical treatment alone.

(5) Contributing factors for mortality were co-existing illnesses.

11. SMALL BOWEL TRANSPLANTATION - A RESEARCH MODEL.

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The clinical application of small bowel transplantation is limited by various problems which include immunological reactions, nutritional function and surgical technique. This paper addresses methods to overcome these problems, using a simple technique of heterotopic transplanatation of an exteriorised loop of small bowel in rats.

DA donors and PVG recipients representing a complete MHC-mismatch, weighing 150-250g were used. The donor procedure involved the mobilisation and resection of a 6-8cm segment of mid-jejunum isolated on the superior mesenteric pedicle. The resected bowel was preserved at 4°C until required for implantation. The superior mesenteric vessels of the donor graft were anastomosed end-to-end with the recipient femoral vessels using 10-0 nylon. Cold ischaemia time ranged from 45-60 minutes. Both the proximal and distal ends of the bowel were exteriorised as jejunostomies.

CyA immunosuppression was commenced immediately following surgery for 6 weeks at 3 different doses (15,20,25 mg/kg body weight). The dose schedule included daily intramuscular injections for two weeks, twice weekly injections for two weeks, and once weekly injections for two weeks. Functional integrity of the grafts was measured using the maltose absorption test. Animals were fasted overnight and 300 mg/kg maltose in 1 ml of 0.45% saline solution was injected into the small bowel allografts. Blood glucose levels were anaylsed at 0,15,30,45,60,90,120,150,180 minutes after instillation.

Results

There were no technical failures. In group 1 (25mg/kg CyA), all 6 animals died with intact grafts between 1-4 weeks due to infection, probably related to the high dose of CyA. In group 2 (20mg/kg CyA), survival was prolonged to a mean of 54.3 d (n=6), with one long term survivor at 14 weeks. Again all animals died of infection. However, all intestinal grafts were noted to be intact at the time of death. In group 3 (15mg/kg CyA) (n=8), long term survival beyond 100 d was achieved in 5 out of 8 animals (62.5%). The remaining 3 animals died with intact grafts between 7-13 weeks from infection. In those animals with functioning allografts at 100 d, the absorption of maltose was comparable to control animals with autografts.

This study demonstrated that long term survival of small bowel transplants between MHC-mismatched rodents was achieved with CyA immunosuppression in 62.5% of cases at a dose of 15mg/kg CyA. In these animals, structural and functional integrity of the allografts was maintained.

12. WHEN CAN COLORECTAL CANCER BE CURED BY SURGERY? TK Ti, Department of Surgery, National University Hospital

A personal series of 53 patients operated between 1984 and 1986 is analysed to ascertain the factors determining long term survival in coloretal cancer.
There were 23, five year survivors. 5 years survivors occurred in all 4 patients with Duke's A Stage of disease. 10 of 11 patients with Duke's B disease and 9 of 17 patients with Duke's C disease. None of the patients who presented with Duke's D disease survived 5 years.

One of the patients with Duke's B disease developed metastatic disease to the liver 1 1/2 years after sigmoid colectomy; right hepatic lobectomy was performed and she is now apparently cured 5 1/2 years after hapatic lobectomy.

These survival figures compare favourably with larger international series. Apart from stage of disease, meticulous surgical technique to ensure clear surgical margins and complete lymphadenectomy minimises local recurrence. In rectal cancer appropriate use of anterior resection and Abdomino-perineal resection reduces the need for permanent colostomy without increasing the risk of local recurrence.

13. LAPAROSCOPIC APPENDECTOMY: IS IT WORTHWHILE? Kum CK, Peter Goh, Department of Surgery, National University Hospital

This was a prospective controlled pilot study to compare conventional appendectomy with laparoscopic appendectomy. The aim was to determine whether laparoscopic appendectomy should be recommended as a routine procedure for acute appendicitis. Within a two-month period, 15 cases diagnosed to have acute appendicitis in one of three surgical teams underwent laparoscopic appendectomy. Thirty-seven cases in the other teams, who underwent conventional appendectomies, served as controls. Laparoscopic appendectomies did not take longer than conventional appendectomies as suggested by some critics. The doses and frequency of both intramuscular and oral analgesia required postop were significantly less in the laparoscopy group. There was no significant difference in the delay before feeds, diet and discharge between the two groups. There were three (7.9%) wound infections in the conventional group compared to none in the laparoscopy group. Patients who had laparoscopic appendectomies pay, on the average, Sin$400 more in their hospital bills. The additional cost was from the use of disposable laparoscopic instruments. Although laparoscopic appendectomy costs more than open appendectomy, the advantages of a shorter postoperative recovery, earlier return to economic activity, better cosmesis, lower risk of wound infection, minimal adhesions and reduced chance of incisional hernia make it worth the additional cost. Laparoscopic appendectomy is thus a good alternative that should be offered to patients with information on additional cost that will be incurred.

14. DOES HAEMORRHOIDECTOMY TREAT THE ANORECTAL PHYSIOLOGICAL ABNORMALITIES IN PROLAPSED PILES? Ho Yik Hong, Seow Choen, Goh Hak Su, Department of Colorectal Surgery, S'pore Gen. Hospital.

Does surgical excision cure the physiological abnormalities in prolapsed haemorrhoids? These factors (high anal pressures, impaired anal sensation and impaired rectal compliance) may contribute importantly to the aetiology by perpetuating regional vascular engorgement. Twenty-four patients (mean age 39.1 SEM 2.4 yrs; 12 males, 12 females) with satisfactory post operative results were compared with thirteen normal controls (mean age 52 SEM 5.3 yrs; 8 males, 5 females). All patients had prolapsed haemorrhoids for a mean duration of 7.2 SEM 1.3 yrs. Clinical assessment and anorectal physiological studies were performed pre-, 6 and 12 weeks post operatively.

The significant abnormalities in haemorrhoids were higher mean resting anal pressures (MRP: mean 82.5 SEM 5.3 mmHg vs controls 60.9 SEM 4.5 mmHg; $p<0.005$), impaired rectal compliance (COM: mean 3.3 SEM 0.7 ml/mmHg vs controls 9.8 SEM 3.1 ml/mmHg; $p<0.05$) and abnormal perineal descent (mean 1.5 SEM 0.2 cm vs controls 2.1 SEM 0.1 cm; $p<0.005$). The anal electrosensation (AE) was significantly ($p<0.05$) impaired at 6 weeks. At 12 weeks, the MRP (mean 57.3 SEM 6.7 mmHg), COMP (mean 15.3 SEM 6.2 mmHg) and AE had become not different from the normals.

The MRP and COM abnormalities in prolapsed haemorrhoids were reversed by haemorrhoidectomy. A transient AE loss at 6 weeks post operation was compatible with incomplete regeneration of the wound mucosa. It is important to fully document the pattern of change after successful haemorrhoidectomy so that complications of anorectal function, when they occur, may be understood.