per os (1 tablet 100 mg/twice/daily); (b) the patients of 2nd group received fluocytosine (FCT) [150 mg/kg/daily per os (1 tablet 500 mg/twice/daily); (c) the patients of 3rd group received placebo (P) (1 tablet/twice/daily).

In order to evaluate the efficacy of pharmacological therapy, clinical examination was performed every week up to the end of follow-up (3 months); endoscopic examination was performed at the end of pharmacological treatment (5 weeks). All the patients selected for the study provided informed consent.

Results. After 5 weeks of treatment, complete remission of endoscopic lesions was observed in 14 patients of F-group and in 4 patients of FCT-group (p<0.05); partial remission of endoscopic lesions was observed in 6 patients of F-group and in 10 patients of FCT-group (p=n.s.), whereas 2 patients of P-group presented partial remission of esophageal lesions. No response was observed in 2 patients of FCT-group and in 18 patients of P-group, with a difference statistically significant in comparison with F-group (p=0.01 vs FCT-group and p<0.001 vs P-group).

As regards clinical symptomatology, complete remission was observed in 14 patients of F-group in 4 patients of FCT-group (p=n.s.) with a difference statistically significant for both treatments in comparison with P-group (p<0.01). Partial clinical remission was observed in 4 patients of F-group in 6 patients of FCT-group (p=n.s. vs F group) and in 6 patients of P-group. No clinical response was observed in 2 patients of FCT-group and in 14 patients of P-group (p<0.001). No remarkable side-effect has been observed in the patients of both groups of treatment.

Conclusions. The results of this study have demonstrated that both F and FCT are efficacious in the treatment of esophageal candidiasis in AIDS patients with a difference statistically significant in comparison with P. F demonstrated a greater therapeutic efficacy than FCT, with a difference statistically significant, as regards both endoscopic and clinical response. Nevertheless, further controlled investigations are needed to improve our knowledge about the therapeutic action of antifungal drugs in the treatment of Candida esophagitis in HIV disease.


The diagnostic value of colonoscopy was assessed in 88 consecutive patients presenting with first attack of severe haemorrhagic colitis [ShC] (bleeding bowel motions daily, fever and abdominal pain). Blood tests and cultures, stool microscopy, parasitology and culture, abdominal films and sigmoidoscopy were routinely performed on admission. Colonoscopy was performed within 24 hours of admission (no later than 4 days after symptom onset) by a blinded endoscopist and biopsies were taken. Exclusion criteria were age over 65 years, regular use of NSAIDs and acute abdomen. The definite diagnosis of ShC was based on results of histology and stool culture. Acute self limiting colitis (ASLC) was diagnosed in 37, infectious colitis (IC) in 31 (salmonella 20, shigella 3, campylobacter 5, pseudomembranous colitis 4), and bacterial UC in 16 patients. 4 patients with FCT were correctly classified as IC/ASLC or IBD by colonoscopy. Prominent endoscopic features in IC/ASLC were erythema, oedema, telangiectasias, erosions, spontaneous bleeding and small aphthoid ulcers surrounded by a red halo. These lesions were patchily distributed; the sigmoid colon was always severely involved, followed by the rectum and the splenic flexure. The caecum was involved in only 31 IC/ASLC patients. Distal migration of lesions was seen in 15 IC/ASLC patients, who had rectal bleeding on admission but sub-sequently showed severe rectal inflammation on colonoscopy. There were no complications. Repeat colonoscopies and biopsies every 6 months for 18 months was suggested that no IC/ASLC case had been initially mis-diagnosed. Thus, colonoscopy is invaluable in the early diagnosis and appropriate treat ment of ShC.

155 Helicobacter Pylori Associated Gastritis in HIV Infection: Endoscopic and Histological Features in 32 Pts
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Helicobacter pylori (HP) is the major etiologic agent associated with acute or chronic gastritis in immunocompetent patients. Moreover HP presence is demonstrated in 40-70% of biopsies of unslected patients undergoing upper endoscopy. Several recent studies have demonstrated low frequency of HP infection in HIV pts [1]. To verify the HP frequency in Italian HIV infected pts we have performed in the last three years, 220 symptomatic pts e.g. duodenal endoscopy with multiple antral biopsies (mean 6). In 32 pts (14.5%) the Gastro-Enterologist considered as posisitive for HP Endoscopic and histological features are showed in the table.

Endoscopic Features
Gastric Ulcer (13%) Antral gastritis (15/47%) Duodenitis (8/25%) Normal (17/53)

Histologic Features
Total (32 pts) HIV (18 pts) AIDS (14 pts)
Superficial gastritis 3/15(5%) 2/11(15%) 1(7%)
Chronic gastritis 6/13(46%) 7/10(50%) 5/7(71%)
Chronic active gastritis 16(50%) 10(50%) 5(36%)

Our data confirm the low frequency of HP infection in HIV infected pts even if symptomatic for epigastric pain, dyspepsia and vomiting. In all pts we observed various degrees of histologic gastritis even if endoscopic features were macroscopically normal. Not significant difference was registered in frequency and type of gastritis between HIV and AIDS pts. This low frequency of HP infection in HIV pts can be explained by hypochlorhydria typical of AIDS patients. Further investigations are necessary to verify the endoscopic hypothesis even if this suggestion requires subsequent studies to be confirmed [3].

156 The Enteropathogenic E. coli Strain RDEC-1 produces a new enterotoxin active on rabbit ileum in vitro Francesco Raimondi 1-3, Stefano Guadagni, 2, James B. Kaper 3, Alessio Fasano 3-1, 1 Division of Pediatric Gastroenterology and Nutrition University of Maryland, Baltimore, Md; 2 Istituto di Scienze Pediatriche e Ginecologiche, Opesdale "Pugliese", Catanzaro, Italy; 3 Center for Vaccine Development, University of Maryland, Baltimore, Md

RDEC-1 is known to possess biological features similar to human EPEC strains and to be diarrhoegenic in the rabbit. We have found that RDEC-1 elaborates an enterotoxin inducing intestinal secretion in the small bowel in vitro.

Rabbit distal ileum and colon, stripped of the serosal and muscular layers were mounted in Ussing chambers where they were bathed by a Ringer solution at 37°C and gassed with 95% O2/5% CO2.

Both ileum and colon from RDEC-1 and the supernatant from RDEC-1 induced a significant increase in potential difference (Delta PD) and short-circuit current (Delta ISc) that was abolished by substituting the chloride ion with sulphate in the bathing solution, by treatment with proteinase K and by heating the supernatant at 90°C for 15 minutes. After fractionating the supernatant, the activity could be demonstrated in the 30-100 kDa fraction.

Curing RDEC-1 of a 42 MDa conjugative plasmid of previously unknown function (which we named pSR) eliminated the enterotoxic activity. Transforming pSR into E. coli HB101 conferred enterotoxigenic activity to native strain. This strongly suggests that the gene encoding for the toxin is located on pSR. Preliminary attempts to establish the second messenger mediating the action of this new toxin showed no additive effect with maximal stimulation by theophylline, BBrGMP and calcium ionophore A23187.

In conclusion, our data suggest that RDEC-1 elaborates a new plasmid-encoded enterotoxin that we named RET for RDEC Enterotoxin.


The goal of this study was to evaluate the potential role of retinoic acid (RA) in the treatment of human pancreatic adenocarcinoma. Six different human pancreatic adenocarcinoma cell lines were characterized by cytochrome phenotype and found to express cytochrome 8, 18 and 19 that are typically expressed in ductal pancreatic carcinomas. RA resulted in a time- and dose-dependent decrease of anchorage-dependent and -independent growth of all cell lines. In addition to growth inhibition, all cell lines demonstrated increased cellular differentiation as demonstrated by increased protein synthesis, decreased saturation density, decreased expression of protein kinase C, increased expression of ductal specific marker genes as well as morphological criteria. All-trans, 9-cis and 13-cis retinoic acid were found to be the most potent retinoids regarding growth inhibition and induction of differentiation. To evaluate the molecular basis of the RA action we used a combined approach of Western and Northern Blotting, immunoprecipitation and R-PCR. In all cell lines tested we found a homogenous expression pattern of the intracellular RA effector molecules. All cell lines expressed the retinoic acid receptors (RAR) alpha, beta and gamma. These retinoid binding proteins were shown to be localized to the nuclei of pancreatocytic cells. In contrast, retinoic X receptor isoforms (RXR) could not be detected. Of the cellular retinoid binding proteins we demonstrated the expression of CRABP and CRBP I but not CRBP II. To verify the expression of RAR in human pancreatic cancer we performed in situ hybridization of 25 human pancreatic carci-
Abstract: GP-3: A Newly Characterized Glycoprotein on the Inner Surface of the Zymogen Granule Membrane Undergoes Regulated Secretion

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We have recently reported the cloning of the rat zymogen granule membrane glycoprotein GP-3 and the related pancreatic secretory lipase (Wishart, M. J. et al. 1993, Gastroenterology 105, 639-646). We have now generated specific anti-peptide antibodies against both GP-3 and secretory lipase and used these antibodies for the biochemical and physiological characterization of GP-3. Western blotting confirmed that GP-3 was found exclusively in zymogen granule membranes and was absent from zymogen granule content which contains the majority of secretory lipase. Extraction of zymogen granule membranes with Triton X-114 showed GP-3 to be significantly more hydrophobic than lipase. The GP-3 amino acid sequence contains one potential N-linked glycosylation site at Asn 336. The loss of concanavalin A labeling after both chemical deglycosylation with TFMS and enzymatic deglycosylation with N-glycanase showed GP-3 to possess a small N-linked oligosaccharide side chain. Digestion of intact and permeabilized zymogen granules with the nonspecific protease pronase further localized GP-3 to the inner surface of zymogen granule membranes. Since GP-3 is resident on the inner surface of the zymogen granule membrane, it should appear on the outer cellular surface after exocytosis. Although membrane attachment of GP-3 was resistant to treatment with phosphatidylinositol-specific phospholipase C, we observed that GP-3 is released into the pancreatic juice and that secretion of GP-3 was greatly enhanced by CCK.

Progression to High Grade Pancreatic Duct Adenocarcinomas Could Be Related to P53 Tumor Suppressor Gene Alteration

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K-ras gene activation by point mutation has been reported in 90% of human pancreatic duct cell adenocarcinomas (PDACs) Similar activating mutations in K-Ras genes have been found in Syrian Golden Hamster induced PDACs and related preneoplastic duct lesions suggesting that they act as an early event. Wild-type P53 gene is rate limiting for cellular proliferation, negatively regulating the cell cycle via the P53 protein and has been shown to inhibit oncogene-mediated transformation. Mutated protein cannot arrest the cell cycle in G1 phase to allow DNA repair. This suggest that lack of functioning P53 protein implies a genetic instability and rapid selection of neoplastic clones.

To confirm this model in pancreatic tumors we studied 98 PDACs by immunohistochemical technique using P53 antibody. In addition 35 cases have been studied by the PCR and DGGE sequencing techniques. P53 hyperexpression was found in 66/98 PDACs and P53 gene mutation in 18/98 PDACs. According to the histologic grade we found immunoreactivity in 5/14 (30%) G1, in 11/40 (27%) G2, in 30/44 (68%) G3 PDACs; P53 gene mutation: in 4/13 (30%) G1, in 7/15 (46%) G2 and in 7/100 (7%) G3 PDACs. In the 64 (48%) tumors with P53 alterations we found 9 (14%) G1, 18 (28%) G2 and 37 (57%) G3; in the 65 (51%) with no P53 alteration we found 18 (29%) G1, 37 (53%) G2 and 14 (20%) G3. No immunoreactivity was found in metastatic and dysplastic pancreatic duct lesions we searched. In conclusion our data suggest that P53 alteration is a late event not involved in the genesis of PDACs but it seems to be implicated in tumor evolution from low grade to higher grade. This might be due to neoplastic cells inability to adequately repair damaged DNA, leading to genetic instability and to clonal expansion of P53 mutant cells because P53 mutated cells could have a selective advantage in the proliferation compared with cells without P53 mutations.

Medium-Chain Triglycerides are not as Well Absorbed in the Presence ofPancreatic Insufficiency as Many Would Believe

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Medium-chain triglycerides (MCT) are used in pancreatic insufficiency because they are more readily hydrolyzed than long-chain triglycerides (LCT) and can be absorbed as triglycerides. These assumptions are based on outdated reports. Moreover the decrease of steatorrhea using MCT could be an analytical error if it was measured by the Van De Kamer’s method which fails to extract completely MCT from feces. Aim of this study was to evaluate the absorption of MCT in the presence of pancreatic insufficiency using an accurate method for faecal fats.

We studied 7 patients (1 protein-calorie malnutrition, 6 chronic pancreatitis; 5 with >20 g/day steatorrhea) on a low fat diet. For periods of 5 days butter (60 g/day) or MCT (55 g/day) without or with pancreatin (LCT or MCT, LCT + P or MCT + P respectively) were added to the diet. In the last 3 days of each period, faeces were collected, weighed and assayed for fat and nitrogen contents by the Jeebejoby’s method and the Kjeldahl’s one respectively. Results: A) Faecal weight, fat and nitrogen outputs of the patients with severe steatorrhea are shown in the table (x ± SE). Faecal weight, fat and nitrogen losses were significantly decreased using LCT with pancreatin (LCT vs LCT + P; P = 0.009, 0.034 test of P13 respectively). Most of these data were obtained with pancreatin (LCT vs MCT + P = 0.072). B) The 2 patients with mild steatorrhea passed much more feces using MCT (LCT vs MCT + P: 125.30 ± 50 vs 355 ± 102.2, NS). Faecal fats were also increased with MCT (LCT vs MCT + P: 8.1 ± 1.5 vs 10.3 ± 2.3 vs 15.2 ± 2.8, NS). In conclusions, pancreatic extracts are necessary for an optimal absorption of MCT or MC fatty acids can determine a cathartic effect.

Octreotide in Acute Necrotizing Pancreatitis: Results of a Prospective Case-Controlled Study

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Background: Acute severe necrotizing pancreatitis is associated with a significant mortality. To date no successful treatment is established. The purpose of our prospective open case-controlled study was to assess the efficiency of high doses of octreotide in the treatment of patients with acute severe necrotizing pancreatitis.

Methods: 77 patients with severe acute necrotizing pancreatitis were studied. In all of them surgical intervention had been necessary and local (ab- scess, necrosis) or systemic (sepsis, pulmonary or renal failure, shock) complications developed under conservative treatment. 31 patients received 100 µg octreotide tid intravenously for 10 days in addition to the standard intensive care therapy. The outcome was compared with that of 48 case-controlled matched patients with acute pancreatitis who had not been treated with octreotide. Patients and controls were followed up until death or discharge from the hospital (maximum 70 days).

Results: The groups (Octreotide-group, control-group) were highly comparable with regard to age (mean age: 53, 49 years), sex, severity of illness (APACHE II-score: 26.4, 27), etiology of pancreatitis, and pretreatment at the time of admission to the intensive care unit. Mortality within 70 days was 30% (9 of 31) in the octreotide group and 50% (25 of 46) in the control group (p < 0.05).

Conclusion: The results of our case-control study showed a beneficial effect of octreotide in patients with severe acute necrotizing pancreatitis. Based on these data a prospective, double-blind, placebo controlled study should be performed to reconsider these results.

Signal Transduction of Acidic Fibroblast Growth Factor in Rat Pancreatic Acinar Cells

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Fibroblast growth factor (FGF) receptors contain an intrinsic tyrosine kinase domain that is activated upon receptor occupation and phosphorylates target proteins such as the y-isoenzyme of phospholipase C. By contrast, heparin-binding receptors like the CCK receptor activate y-isoenzymes of phospholipase...
pase C in a G-protein-dependent fashion. In the present study we investigated acidal fibroblast growth factor (aFGF)-induced inositol 1,4,5-triphosphate (IP-
3)-production and amylase secretion in isolated pancreatic acini and the role of G-proteins in this process. Methods: Pancreatic acini from rat pancreas by collagenase digestion and were permeabilized with 10 μg/ml of digitonin. IP3-production and amylase release were measured using a radiote-
ceptor assay and a colorimetric assay, respectively. Pertussis toxin-induced ADP-ribosylation was performed in isolated membranes from aFGF- or CCK-
prestimulated acini and unstimulated control acini. Results: Incubation of the acini with aFGF caused a biphasic increase of both amylase release and IP3-
production. The maxima were observed at a growth factor concentration of 0.1 μM. The dose-response curve for CCK-stimulated amylase release was also biphasic with a maximum at 0.1 nM. However, different from aFGF, the dose-of CCK induced IP3-production at supramaximal CCK concentrations. These re-
tions was accompanied by a further increase in IP3-production. In digitonin-
permeabilized cells, guanosine 5'-O-(3-thiotriphosphate) (GTP[S]) shifted the dose-response curve for aFGF-induced IP3-production and amylase to higher growth factor concentrations. Pertussis toxin-catalyzed ADP-ribosylation of isolated membranes led to a specific labeling of a 43 kDa band, representing a-subunits of the G-proteins G1, G2 and G3. In membranes from aFGF- or CCK-preincubated acini ADP-ribosylation of this band was decreased by 53% and 45% as compared to control membranes. Conclu-
Con: In pancreatic acini aFGF is a potent stimulator of amylase secretion. In this study, we used a previously developed method to measure IP3-production and amylase release with aFGF-induced ADP-ribosylation. Further studies are needed to confirm our results.

163 A Simple 13C2O2 Breath-Test for Assessing Pancreatic Exocrine Insufficiency
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A noninvasive test for assessment of fat digestion has been developed, which is based on the intraluminal hydrolysis of cholesteryl[1,13C2]octanoate by pan-
creatic cholesterol esterase. We performed this test in 10 patients with chronic pancreatitis and in 10 healthy volunteers. The test was performed on volunteers (500 mg of cholesteryl[1,13C2]octanoate) administered in a liquid meal together with 5 g of xylose to exclude any influence of gastric emptying. Breath samples were taken prior to ingestion of the meal and thereafter every 15 min for 6 hours. The 13C2O2 was measured using an automated mass spec-
trometer (European Scientific, GB). Results: Gastric emptying time of the test meal did not differ significantly among the 3 groups. In healthy subjects the median cumulative recovery of 13C2O2 at 6 hours was 32% (range 20-49). The median cumulative recovery in patients with complete pancreatic duct obstruction was widely; the pattern was similar to that of controls in 2 patients, but excretion was delayed in 5, and was virtually absent in the remaining 3 patients. The median cumulative recovery at 6 hours was 13% (range 1-37). Statistically significant differences (p < 0.05) in hourly recovery of 13C2O2 were found between these patients and controls. In patients with complete pancreatic duct obstruction, the median cumulative recovery of 13C2O2 at 6 hours was 17% (range 9-34), this was statistically significant (p < 0.05) when compared with controls. The 1-hr recovery of 13C2O2 was less than normal in 6 patients with pancreatic disease and in 2 patients with pancreatic duct obstruction. The 3 patients with severe exocrine injury had the lowest 13C2O2 excretion in 2 of these, the test was repeated after pancreatic enzyme supplementation, which produced a significant rise in 13C2O2 recovery. There was a significant correlation (p < 0.05) between 13C2O2 excretion and the results of the fluorescein diluate test. Conclusions: A, this study indicates that severe pancreatic exocrine im-

164 Inhibition of CCK-Induced Pancreatic Growth by Dexoxi
glumide, A New CCK-A Receptor Antagonist
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Dexoxi
glumide (Dex; compound coded CR-217) is a new selective CCK-
A receptor antagonist which has been carefully characterized by in vitro and in vivo investigations. Previous studies from our laboratory have shown Dex to be capable of inhibiting CCK-induced pancreatic secretion in a supramaximal manner. In the present investigation the effect of Dex (gift of Dr. D. Rovati, Rotta Research Laboratory, Monza, Italy) on gastric and pancreatic adaptation in response to both exogenous and endogenous CCK was studied in rats. Caerulein (1 μg/kg, s.c., three times daily) was used as CCK agonist whereas carcino
tostat (200 μg/kg, i.g., once daily), a potent trypan inhibitor was employed as endogenous CCK releaser. These compounds were admin-
istered to rats alone or in combination with Dex (25 mg/kg s.c., 20 min before each stimulation) for one week. Rats were then sacrificed, gastric corpus and antrum, as well as pancreas were excised, weighted and analyzed for tissue DNA and protein content.

Neither exogenous nor endogenous CCK affected growth of the corpus and the antrum of the stomach but both caerulein and carcino
tostat treatment resulted in pancreatic hypertrophy and hyperplasia. Dex suppressed both caerulein- and carcino
tostat-induced increases in pancreatic weight, DNA and protein contents (Table).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>pancreas weight</th>
<th>pancreas DNA</th>
<th>pancreas protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>caerulein</td>
<td>125 ± 4*</td>
<td>124 ± 6*</td>
<td>151 ± 9*</td>
</tr>
<tr>
<td>caerulein + Dex</td>
<td>101 ± 8*</td>
<td>108 ± 7</td>
<td>108 ± 5</td>
</tr>
</tbody>
</table>
| carcino
tostat | 159 ± 4*      | 128 ± 9*     | 173 ± 7*        |
| carcino
tostat + Dex | 112 ± 6* | 109 ± 9 | 128 ± 6* |

% of control; * < 0.01 versus control (ANOVA test)

These results demonstrate the ability of Dex to antagonize the growth-
proliferating effects of both endogenous and endogenous CCK on the pancreas, and confirm that CCK induces pancreatic growth through activation of CCK-A receptors.

165 Ultrasound Guided Extracorporeal Shock Wave Lithotripsy (ESWL) of Pancreatic Duct Stones
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Introduction: Forstones in the pancreatic duct can lead to obstruct-
ion and maintain obstructive chronic pancreatitis. It is known that removal of the obstruction in the pancreatic duct produces immediate pain relief. We re-
port our experience with ultrasound guided ESWL of symptomatic pancreatic duct stones, which were not primarily extractable by endoscopy.

Method: In 23 patients suffering from chronic calcifying pancreatitis ESWL of symptomatic duct stones was performed in combination with end-
osscopic sphincterotomy. Only 5 patients had solitary stones. The average diameter of the largest stone in each case was 11 (5-18) mm. The dilated pancreatic duct measured on average 8 (5-10) mm. Strictures of the pan-
creatic duct were present in 11 patients. For fragmentation of the pancreatic duct stones up to 2000 ECG-triggered shock waves (MFL 9000, Dormir/Munich) were delivered per session. Average shock wave energy was 18 (14-22) kJ. After ESWL the fragments were extracted and/or their spontaneous passage documented.

Results. Disintegration of obstructive calculi was possible in all cases. Complete stone free ducts were achieved in 7 patients, some stone ma-
terial remained in 16; pancreatic obstruction, however, could be resolved in all cases. 8 patients became completely asymptomatic, 11 reported a marked reduction of their pain. No major complications were observed.

Discussion. ESWL combined with endoscopic sphincterotomy is a suc-
cessful, non-operative new treatment for pancreatic duct stone disease. It should be performed as soon as possible after manifestation of clinically rele-
vant symptoms in order to prevent parenchymal atrophy and consecutive exocrine and endocrine dysfunction.

166 Clinical Interest of Identification of Ki-ras Mutations in Pure Pancreatic Juice
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Most human pancreatic adenocarcinoma are associated with mutational acti-

192013 another two cases were performed by PCR-mediated RFLP analysis. For cells or brush cytology were performed to 87 patients who underwent ERCP for diagnostic or therapeutic reasons. Seventy nine samples could be amplified (91%), the 79 corresponding patients were classified in 3 groups according to standard tests: group 1 n = 37; patients free of any pan-
creatic diseases or presenting non tumoral pancreatic disease (acute or chronic pancreatitis); group 2 n = 23 pancreatic tumor; group 3 n = 19 pancreatic diseases with unknown etiology by standard tests. Methods: ERCP samples were subjected to polymerase chain reaction (PCR) amplification of Ki-ras gene and codon 12 analysis was performed by PCR mediated restriction fragment length polymorphism (RFLP) analysis. As a complementary analysis, the DNA fragment was sequenced. Results: Results of the molecular blind study were evaluated by comparison with the clinical follow-up of patients. In group 1, 35 patients, were normal by PCR-mediated RFLP and direct sequencing. Two false positive cases by PCR-mediated RFLP in group 1 were invalidated.

Gut: first published as 10.1136/gut.35.4_Suppl.A35 on 1 January 1994. Downloaded from http://gut.bmj.com/ on September 15, 2023 by guest. Protected by copyright.
by direct sequencing showing a normal Ki-ras 12th codon. In group 2, 11/14 patients with pancreatic carcinoma, 2/2 cystadenocarcinoma, 2/3 ampullary tumors, 1/3 cholangiocarcinoma, and 0/3 islet cell tumors showed punctual mutation of Ki-ras. In group 3, 4/16 showed a mutation of Ki-ras at the 12th codon. Conclusion: Endoscopic retrograde intraduodenal catheter aspiration is a simple technique to analyse cell samples. Specificity of PCR mediated RFLP was 94.5%, and sensitivity for pancreatic carcinoma was 81%. Identification of Ki-ras mutation could distinguish pancreatic carcinoma from islet cell tumors, but not from ampullary tumors. Clinical follow-up patients from group 3 will find out the real value of this early diagnostic test.

### 167 Endogenous Nitric Oxide in the Control of Esophageal Motility in Humans

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Recent animal studies have suggested that nitric oxide (NO) plays an important role in the regulation of esophageal motility, being partly responsible for latency period and latency gradient between the onset of a swallow and contractions of the circular smooth muscles. The aim of this study was to evaluate whether endogenous NO is responsible for physiological timing of the forthcoming contractions in the human esophageal body after swallowing. Five male volunteers (age 21–25 years, weight 67–72 kg) were investigated in the study. The effects of increasing doses of the NO synthase blocker, Nω-monomethyl-L-arginine (L-NMMA 1.0–4.0 μmol/min i.v.) and L-arginine (L-arg) (30 μmol/kg.min i.v.) on the peristals of esophageal body in response to wet swallows (5 ml of water) and lower esophageal sphincter (LES) resting pressure. The esophageal motor activity was determined manometrically using 4-channel Konigsberg catheter (Physiologische Praxis, USA) and Microtip Recorder (Synectics, Stockholm, Sweden). The motility patterns and statistics were analysed using specially developed software (Gastrosoft, Irvine, USA). Significance was accepted with p values less than 0.05. Additionally, during all examinations arterial blood pressure (BP) was measured every 5 min. L-NMMA resulted in a significant and dose dependent reduction of the latency period between the swallows and the onset of contractions which was mostly pronounced in the distal esophagus (control: 7.0 ± 0.7 s vs. L-NMMA 4.0 μmol/min: 5.87 ± 0.57 s), and this effect was partially reversed after addition of L-arg to the L-NMMA infusion (6.91 ± 0.62 s). The overall duration (4.07 ± 0.15 s) and the onset propagation (3.93 ± 0.82 cm/s) of esophageal contractions were significantly reduced (3.63 ± 0.21 s and 3.37 ± 0.40 cm/s) while the amplitude remained unchanged during L-NMMA infusion and again, those effects were reversed during simultaneous infusion of L-arg. The resting tone of LES increased significantly during infusion of L-NMMA (control: 111.6 ± 3.3 mm Hg) and this was reversed by addition of L-arg. The mean BP significantly increased during infusion of L-NMMA (control 97.0 ± 5.7 vs. L-NMMA 4.0 μmol/min: 116.4 ± 3.1 mm Hg) and this was reversed by L-arg. We conclude that in humans endogenous NO is involved, at least in part, in the physiological regulation of motility pattern of distal portion of the esophageal body and LES.

### 168 High Dose Effects of Dietary Fat on Postprandial Gastrointestinal Motility are Reversed by a Specific Choleysteokinin (CCK)-A Antagonist

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Dietary fats evoke a dose-dependent inhibitory effect on postprandial antral motor activity. CCK is potentially involved in mediating nutrient-induced changes in gastrointestinal (GI) motility. CCK effects can be specifically blocked by the CCK-A antagonist loxigulamide (L). This study was designed to evaluate whether L affects the response of GI motility to fat during the postprandial period. A total of 16 manometric tests were performed in 4 healthy controls (2 M, 2 F; 19–25 yrs). Each subject was studied in 4 separate occasions, at least one week apart. Manometry was carried out by using a low compliance perfusion system attached to an 8-lumen probe which was positioned with the side-openings across the antroduodenal junction (5·1 cm apart) and in the proximal small bowel (3·10 cm apart). Motility was recorded for 3 hours after ingestion of a low-fat mixed meal (513 KCal, 9% fat). Twenty minutes before meal ingestion each subject received an i.v. infusion of octanoic acid (S) as placebo or L 5 mg/kg·min bolus followed by 10 mg/kg·min × 180 min). Ten minutes after the beginning of meal ingestion different emulsions were infused in the stomach via a 9 catheter assembled with the manometric probe: control emulsion (CE; bovine albumin 3 g in S up to 150 cc) or fat emulsion (FE; bovine albumin 3 g and 80 g corn oil in S up to 150 cc). The effects of the two emulsions were separately tested in the presence of S and L i.v. infusion. Fat emulsions and i.v. infusions were randomly administered. Antral (A) and descending duodenum (D) postprandial motility were analysed and the results expressed as mean motility index (MMI) (±SD) at 10 min intervals for 180 min.

<table>
<thead>
<tr>
<th></th>
<th>CE ± S</th>
<th>FE ± S</th>
<th>CE ± L</th>
<th>FE ± L</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Ml</td>
<td>39.9 ± 18.9</td>
<td>20.3 ± 20.1*</td>
<td>31.6 ± 20.8</td>
<td>32.5 ± 13.4*</td>
</tr>
<tr>
<td>D Ml</td>
<td>131.2 ± 87.7</td>
<td>186.0 ± 85.0</td>
<td>32.4 ± 31.6#</td>
<td>30.9 ± 47.9#</td>
</tr>
</tbody>
</table>

In conclusion, L reverses the inhibitory effect exerted by dietary fat on antral motility. L reverses the intestinal motor response to meal ingestion regarding the amount of fat.

### 169 Electrogastrography (EGG) in Chronic Pseudo-obstruction (CIP): A Noninvasive Test which Correlates with Pathology


CIP is a pancreatic disorder of intestinal motor function which may be caused by primary disease of enteric nerves (visceral neuropathy) or enteric smooth muscle (visceral myopathy). Intestinal motility studies may be technically difficult because of hypomotility and patients often need laparotomy for a tissue diagnosis. This study aimed to determine if surface EGG would accurately diagnose the presence and type of pathologically proven CIP.

After an overnight fast we assessed gastric electrical control activity for 1 hour in the fasting and fed state by cutaneous surface EGG in 14 adults (range 20–63 years) with proven CIP. Electrical activity was recorded from four pairs of silver/silver chloride bipolar electrodes, the captured signal, amplified and digitalised and running spectral analysis performed. The dominant frequency and power of spectrum were calculated using a sequence of computerised algorithms and displayed as a pseudo three dimensional plot. Results were correlated with the known pathological diagnoses (visceral myopathy (NM) n = 7, visceral neuropathy (N) n = 4, undifferentiated (U) n = 3).

Dysrhythmias were present in 13 of 14 patients (1) A neuropathic pattern of tachygastria (electrical control activity frequency >5 cycles/minute) was documented in 5 patients (N = 4, U = 1). (2) Myopathic patterns of irregular continuous activity (no dominant frequency) or broad arrhythmia were found in 6 patients (M = 5, U = 1). In all 6 patients there was abnormal electrical response activity (ERA) to food. (3) Mixed abnormalities were noted in 2 patients (M = 1, U = 1) and normal activity with a clear dominant frequency of 3 cycles/minute was present in only one patient (M = 1).

This non-invasive technique is both sensitive and specific in providing evidence of a dysrhythmia in patients with CIP and discriminates between primary pathologies. EGG should prove diagnostically valuable, in addition to providing insights about the disturbance of electrical control activity.

### 170 Continuous In-Vivo Manometry of the Human Gallbladder

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Continuous in-vivo manometry of the gallbladder was conducted in 6 patients who had undergone percutaneous cholecystolithotomy for symptomatic gallbladder stones ten days previously and had a Foley catheter inserted into the gallbladder after the procedure. A solid state transducer was inserted into the lumen of the foely catheter and connected to a portable 24-hour data logger which constantly recorded intrahepatic pressure. Patients were asked to note the type and timing of any oral intake during the recording and these were correlated with gallbladder activity. The gallbladder pressure response to intravenous CCK was also recorded.

Results:

<table>
<thead>
<tr>
<th>Event/stimulus</th>
<th>Gallbladder pressure (mmHg) (mean ± SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal (Nocturnal)</td>
<td>18.4 ± 1.6</td>
</tr>
<tr>
<td>Basal (Durnal)</td>
<td>17.4 ± 1.3</td>
</tr>
<tr>
<td>Cup of tea</td>
<td>35.2 ± 1.5*</td>
</tr>
<tr>
<td>Breakfast</td>
<td>29.9 ± 2.0</td>
</tr>
<tr>
<td>Lunch</td>
<td>26.2 ± 1.7</td>
</tr>
<tr>
<td>Dinner</td>
<td>38.7 ± 2.0*</td>
</tr>
<tr>
<td>Intravenous infusion of CCK (0.02 mcg/kg)</td>
<td>39.9 ± 1.4*</td>
</tr>
</tbody>
</table>

*p < 0.05 vs Basal (Nocturnal) pressure: Wilcoxon signed rank test

Our early experience has shown that continuous direct in-vivo gallbladder manometry in humans is possible and the validity of the technique may be confirmed by recording pressure rise after intravenous infusion of CCK. This new technique may help to elucidate patterns of gallbladder activity and clarify the role of various diets in gallbladder emptying.