56 Laparoscopic Transcystic Cholangioscopy (LTC) for the Removal of the Common Bile Duct Stones

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Sixty five of 700 patients had combined CBD stones. For the four patients in the initial stage who had laparoscopic transcystic cholangioscopy the operation was directly performed followed by open surgery. In the subsequent 49 patients, LTC lithotripsy was applied. Endoscopic nasobiliary drainage tube was inserted before LTC lithotripsy. Out of the 49 patients with LTC lithotripsy, 37 patients (75.5%) completely treated only by LTC lithotripsy. The stones were pushed out into the duodenum or removed with the tip of the cholangioscope in eleven cases. The stones were crushed into pieces by EHL probe in twelve cases, and the cholangioscope could not be inserted into the CBD via the cystic duct in two cases, because of the complete obstruction of the cystic duct due to acute cholecystitis. The average hospital stay was 9.0 days (range, 6-18) in LTC lithotripsy (n = 37), not significantly different from 8.4 days (range, 4-19) (p = 0.535) of the group LCE alone. The patients returned to normal activities usually on the next day of discharge. This modality of laparoscopic transcystic cholangioscopy has the great advantage over endoscopic sphincterotomy of a short term treatment and the preservation of a normal functioning sphincter Oddi. The instrument used in the present cases did function well because the scope (Pentax PCN-J, Olympus XCH-PR2R) was designed for this specific purpose.

57 Enteral Diet High in Glutamine Increases Renal Arginine Production

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Glutamine (GLN) and arginine (ARG) are important in the host response to injury. ARG is generated in the kidney from citrulline (CIT). It has been suggested that intestinal GLN metabolism provides CIT for renal ARG synthesis. This has never been conclusively demonstrated. This study investigates the effect of a GLN enriched enteral diet on renal ARG production. Male Fischer 344 rats (weights 260-270 g) received a glutamine enriched diet (n = 12, 12.5% W/W) or a balanced control diet (n = 12, CONTR) for 14 days. On day 15 renal plasma flow (RPF) was measured using radioabelated microspheres and blood was drawn from the left renal vein (RV) and aorta (A). Plasma concentrations (nmol/ml) of GLN, ARG and CIT were determined. Amino acid fluxes (nmol/min) were calculated by the product of A-RV differences and RPF to both kidneys, a minus sign indicates release. Results showed no differences in RPF between the groups. Compared to CONTR, GLN fed rats had significantly increased arterial concentrations of ARG (86.8 ± 4.4 vs 113.7 ± 4.8; p < 0.0005), CIT (48.1 ± 1.3 vs 62.7 ± 2.1; p < 0.0001) and GLN (688.5 ± 25.1 vs 788.4 ± 22.6; p < 0.005). Compared to CONTR, kidney fluxes in the GLN group showed significantly higher release of ARG (~131.3 ± 18.0 vs ~181.6 ± 18.2; p < 0.05) and a closely related higher uptake of CIT (128.9 ± 14.8 vs 180.7 ± 16.3; p < 0.05). No differences in RPF were measured between the groups. GLN enrichment significantly increased arterial levels of GLN, ARG and CIT. Kidney uptake of CIT in the GLN enriched group was enhanced and resulted in an increased stoichiometric production of ARG.

Conclusions: Enteral glutamine stimulates renal arginine production by providing increased amounts of citruline that is converted to arginine in an equimolar fashion. The effects of glutamine might in part be explained by increased arginine production.

58 Pre-Trauma Growth Hormone Treatment Decreased Glucose Turnover and Net Hepatic Release and Maintained Gut Glucose Uptake

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Growth hormone (GH) treatment appears to influence trauma metabolism favourably by reducing nitrogen losses. We have earlier found decreased carbohydrate oxidation postoperatively after GH treatment. Our objective was to study effects of pre-trauma GH treatment on hepatic and intestinal glucose metabolism in a trauma model in pigs.

Twenty-four pigs were randomized to three treatment groups; GH-3 was pretreated with GH 24 IU daily three days before the experiment, GH-1 was treated with growth hormone 24 IE at the start of the surgical procedure and CON served as untreated controls. A standardized abdominal surgical procedure in general anesthesia was performed. Primed constant infusions 3-3H-glucose were given and rates of appearance (Ra) and disappearance (Rd) calculated. Substrate fluxes for glucose, lactate, pyruvate and alanine over the liver and the intestinal tract and whole body nitrogen balances were calculated.

In the long term treatment group, GH decreased nitrogen excretion (GH-3: 30.7 ± 16.4 mg/kg, GH-1: 37.7 ± 16.4 mg/kg, CON: 55.2 ± 8.37 mg/kg, p = 0.001), glucose Re (GH-3: 14.68 ± 1.24 µmol/kg/min at 5 hours (5 h) after surgery, CON: 27.3 ± 1.27 µmol/kg/min (5 h, p = 0.003), hepatic net glucose release (GH-3: 4.54 ± 0.44 µmol/kg/min, CON: 599.2 ± 46.06 µmol/min, p = 0.03). Glucose uptake in the gut was unchanged.

Thus, long term pre-trauma growth hormone treatment decreased nitrogen excretion, glucose turnover and hepatic glucose output. Glucose supply to the gut was maintained.

59 Pancreaticobiliary Responses to Elemental and Polymeric Protein: Importance of Proteolytic Activity

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Little is known about pancreaticobiliary responses to polymeric or elemental protein and the importance of intraduodenal (id.) proteolytic enzymes. We therefore studied pancreaticobiliary responses to meals containing intact and elemental protein in the absence of proteolytic activity from the gut. Methods: Three experiments were performed in 6 healthy male subjects (25 ± 1 years). After a one hour basal period, saline (300 ml/h) was perfused id. with the synthetic protease inhibitor camostate, CAM, 0.6 g/h. In the second hour of SAL and CAM perfusion, 15 g albumin (ALB) or 15 g (nmol acetic acids) (ALB), in the same composition as ALB was perfused id. In addition, on a separate day 15 g of ALB was perfused id. without CAM. At 15 min intervals plasma CAK and PP were determined by RIA; bilirubin (BO) and amylase output (AO) by spot sampling of duodenal juice using PEG-4000 as a recovery marker. Results: CAM abolished id. trypsin and chymotrypsin activity CAM did not influence basal CAK, PP, BO but tended to increase AO. Perfusion of AA with CAM increased AO from 4.3 ± 0.7 to 8.2 ± 0.7 kU/h, BO from 10 ± 4 to 66 ± 13 µmol/h, CAK from 6 ± 26 to 8 P3600 min and PP from 92 ± 56 to 1056 ± 100 pM (p < 0.05). Perfusion of ALB with CAM failed to significantly increase AO (7.5 ± 1.5 vs 6.2 ± 1.1, BO (20 ± 7 vs 17 ± 6 µmol/h), CAK (39 ± 14 vs 22 ± 9 pM 60 min) and PP (<21 ± 11 vs 83 ± 60 pM 60 min). Differences between AA and ALB were significant (p < 0.05) for all parameters. Perfusion of ALB without CAM increased BO from 13 ± 4 to 44 ± 9 g/mol/h (p < 0.05), CAK from 18 ± 8 to 10 ± 9 pM 60 min (p < 0.05), AO from 4.5 ± 1.0 to 7.8 ± 1.3 kU/h and PP from 36 ± 58 to 140 ± 48 pM 60 min when compared to SAL. Conclusion: In the absence of proteolytic activity, amino acids, but not albumin stimulate exocrine pancreatic secretion and gallbladder emptying. These data may have implications for dietary management of patients with exocrine pancreatic insufficiency.

60 Nitric Oxide Synthase Inhibitor (L-NAME) Markedly Reduces Hepatic Perfusion and Oxygen Delivery in Endotoxemia


NO inhibitors have been applied in the treatment of septic shock due to their strong vasocostrictor property. Recent reports have suggested that such treatment may cause serious organ damage. In the present report circulatory and metabolic changes in the liver were studied during endotoxemia and treatment with the NO synthase inhibitor L-nitro-L-arginin-methyl-ester (L-NAME).

Methods: Juvenile pigs were randomized to one of the following groups (1) Endotoxin + L-NAME, (2) Endotoxin + Saline, (3) Saline + L-NAME, (4) Saline. Results from group 1 (n = 7) and 2 (n = 8) are presented. Blood pressure was measured in the aorta, pulmonary artery, hepatic and portal veins. Flow was measured in the hepatic artery (HAF) and the portal vein (PFV). Endothelin (1.7 µg/kg) was given continuously as portal infusion during 8 hours of observation. L-NAME (25 mg/kg) was given as a bolus after 3 h of observation.

Results: Endotoxin transiently reduced PVF by 25% and HAF by 45% (P < 0.05), while L-NAME caused a further and lasting reduction in flow (PVF 78%, HAF 90%, P < 0.05). Transhepatic (portal/hepatic vein) vascular resistance increased to 3 times baseline value during endotoxemia, while L-NAME caused a further marked increase in resistance to 12 times initial value (P < 0.05). Endotoxin caused a 27% reduction in cardiac output (CO), while addition of L-NAME reduced CO by a total of 71% (P < 0.05). Portal oxygen saturation (SO2) increased by 60% in group 1 and 87% in group 2. Arterial SO2 was unchanged in both groups. Hepatic O2 uptake was not changed in group 1, but markedly reduced in group 2.
Conclusion. L-NMATE treatment during endotoxia markedly reduces liver perfusion and oxygen supply. This may explain the liver damage reported in previous studies.

61 Interactions of Endotoxin with Blood Components
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Endotoxin (lipopolysaccharide, LPS) interacts with several plasma protein systems and blood cells, causing release of a multitude of endogenous mediators that contribute to the pathophysiological process of septic shock. Plasma is also known to be a potent LPS inhibitor. Although many serum proteins and blood cells may bind LPS it is difficult to evaluate the relative importance of such interactions.

Methods and results: Binding of radiolabelled 125I-LPS to human blood cells were investigated in the following sets of experiments: 125I-LPS (0.1-10 µg/ml) were incubated with whole blood (heparinized) for 2-12 hours at 37°C. Plasma and formed blood elements were isolated and the major part (80%) of the 125I-LPS was recovered in plasma, 6-7% was associated with the blood platelets, whereas only small amounts (<2%) were retained in granulocytes, erythrocytes, monocytes and lymphocytes. Incubation of freshly isolated blood cells with either 125I-LPS or FITC-LPS and subsequent analysis by radioactive counting, autoradiography, flow cytometry and immunofluorescence microscopy showed that monocytes were by far the most effective blood cell binding LPS. Purified lipoprotein fractions incubated with 1 µg/ml 125I-LPS for 2 h at 37°C were subjected to lipoprotein electrophoresis and staining and subsequent autoradiography. 125I-LPS bound to all lipoprotein fractions (HDL, LDL, VLDL). The same result was obtained when heparinized plasma or whole blood were incubated with 0.1-10 µg/ml 125I-LPS. Superose 12 chromatography of 125I-LPS incubated plasma showed 2 marked peaks; one coeluting with the macromolecular plasma proteins in the void volume and the other in the IgG/alumunin region.

Conclusion: In vitro, radiolabeled LPS were able to bind both to HDL, LDL and VLDL as well as to several other serum constituents. Monocytes represent the most important target blood cell for LPS binding and are also the most important mediator cell of LPS effects in the body.

62 Catheter-Related Sepsis in Patients on Home Parenteral Nutrition

In the period from 1980 to 1993, 78 patients received HPN for 1 to 198, median 33 months, corresponding to a total treatment period of 344 patient years.

The patients had a Broviac silicone rubber catheter placed on the chest or in the arm. The exit site of the catheter was covered with a sterile dressing twice a week until 1988, and hereafter with a transparent dressing (Tecaderm) once a week. The exit site of the catheter and the connections of the infusion line was painted with Povidone-iodine 10% (Iosbetadine) until 1985, and hereafter with 0.5% chlorhexidine in 70% ethyl alcohol. Since 1987 most of the patients received their nutrition from 3-litre bags. The patients were trained to administer parenteral nutrition by a special nursing team during a 2-4 week period before they were discharged from the ward.

Results: 108 episodes of catheter sepsis occurred in 35 (45%) of the patients, corresponding to one episode of catheter sepsis per 3.2 catheter treatment years.

The sepsis incidence (number of episodes of catheter sepsis per catheter treatment year) from 1980-1993 was:

<table>
<thead>
<tr>
<th>Year</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980-82</td>
<td>0.61</td>
</tr>
<tr>
<td>1983-84</td>
<td>0.52</td>
</tr>
<tr>
<td>1985-86</td>
<td>0.47</td>
</tr>
<tr>
<td>1987-88</td>
<td>0.23</td>
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<tr>
<td>1989-90</td>
<td>0.22</td>
</tr>
<tr>
<td>1991-92</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Conclusion: A significant reduction in sepsis incidence was observed, which could be related to the change of disinfectant in 1985 and the introduction of 3-litre bags in 1987. The change in transparent dressings in 1988 did not result in increased frequency of sepsis.

63 IgA Antigliadin Antibodies: A Further Improvement in Childhood and Adult Coeliac Disease Screening
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IgA antigliadin antibodies (JAB) were identified some years ago, but only a few studies have been produced on their utility in coeliac disease (CD) screening. Our aim was to establish if IgA JAB improve the sensitivity and specificity of IgA antidiemysial (EMA) and antigliadin antibodies (AGA) for CD. IgA JAB were searched for by indirect immunofluorescence (IFL) on cryptic sections of monkey jejunum in the sera of 81 patients with untreated adult and children CD and, as controls, in the sera of 95 patients with various gastroenterological diseases and of 60 blood donors. IgA JAB were positive in 96% of the untreated coeliacs in comparison with a positivity of 93% and 72% for EMA and AGA respectively. Like EMA, IgA JAB persisted at low titre in 7 (14%) of 50 coeliacs tested after 1 year of gluten free diet (GFD) in spite of the regrowth of jejunal villi, whereas IgA AGA disappeared in all these patients. IgA JAB and EMA reappearance was close to 100% in the 13 children with CD studied after 6 months of gluten challenge, while IgA AGA reached their highest prevalence (about 70%) after 1 month of gluten ingestion. All disease and healthy controls were negative for the 3 IgA antibodies. The search for IgG JAB was unreliable not only for the high number of "false positives" in control sera, as already described for IgG EMA, but even for a cross-reactivity between IgG, normally present in primate tissues, and FITC-anti human IgG.

Our results prove that IgA JAB and EMA are the best screening tests for CD, but it must be underlined that JAB display a slightly higher sensitivity than EMA. Moreover, the routine use of IgA JAB instead of IgA EMA could also be advantageous in terms of cost/benefit ratio, as for the former we have the whole primate jejunum available, whereas for the latter the only small portion of the lower part of primate oesophagus. IgA AGA, instead, must be preferred to IgA JAB and EMA for monitoring the answer to GFD in treated coeliacs.

64 Rapid Increase of Bone Mineral Density with Diet in Adult Coeliac Disease
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Purpose: In order to evaluate the effect on the bone mass of gluten free diet, we investigated prospectively the bone mineral density in consecutive adult patients with newly diagnosed coeliac disease.

Methods: Sixty-six patients with untreated coeliac disease (aged 17-79 years) were examined at diagnosis and 43 of them one year after dietary recommendation. Bone mineral density was measured in the forearm using Single Photon Absorptiometry and in the lumbar spine, femoral neck and trochanter using Dual Energy X-ray Absorptiometry. The values were compared with those in healthy controls, matched for age, sex and menopausal state.

Results: Bone mineral density was reduced at all sites in patients with untreated coeliac disease (p < 0.001). Bone mineral density increased within one year after dietary recommendation in the lumbar spine, femoral neck and trochanter (p < 0.01). In the forearm the increase of bone mineral density was non-significant (p = 0.0504).

Conclusion: Bone mineral density in patients with untreated coeliac disease increases rapidly after treatment with gluten free diet is started, emphasising the importance of early diagnosis and treatment.

65 Coeliac Disease in Adult Diabetes – A Common Association
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The purpose of this study was to determine the prevalence of coeliac disease (CD) among adults with diabetes mellitus. The measurement of serum IgA antigliadin antibody (IgA-AGA) concentration was used as a screening test for CD, followed by small bowel biopsy in those patients with a value >90 U/L.

Of 1785 patients with insulin dependent (IDDM, 43%) and non insulin dependent (NIDDM, 57%) diabetes mellitus, 73 had raised IgA-AGA, while 8 had IgA deficiency. Duodenal biopsies were obtained from 57 subjects (49 with raised IgA-AGA and 8 with IgA deficiency) of whom 11 had total villous atrophy (1 with IgA deficiency) and 3 had severe partial villous atrophy, characteristic of CD. Eight of these 14 had symptoms compatible with CD which resolved on a gluten free diet (GFD). Significant reductions in haemoglobin, ferritin and red cell folate were found and corrected by the diet and supplements. In 7 patients who were adhering strictly to a GFD, a repeat biopsy showed morphological improvement.

Included in the 1785 patients screened were an additional 4 with known CD. Thus the overall prevalence of coeliac disease in this diabetic population is 1 in 100. In IDDM it is 1 in 52 and in NIDDM 1 in 340.

The use of CD is common among adults with diabetes and is an additional cause of ill health which can be corrected by a GFD. The measurement of IgA-AGA is a useful screening test to identify those who require small bowel biopsy.