- A01 -

REDUCED STAT3 FUNCTION AND INCREASED ANTI-APOPTOTIC SIGNALS IN HCV LIVER CIRRHOSIS. P. Stärkel, C. De Saeger, V. Lebrun, A. Strain, Y. Horsmans. Gastroenterology and liver research laboratories, Université Catholique de Louvain, Brussels, Belgium and University of Birmingham, UK.

Background : In vitro data suggest that hepatitis C virus (HCV) may affect cell proliferation and apoptosis. In particular, HCV core protein seems to interfere with the Jak-Stat signalling pathway. We therefore investigated whether apoptosis is increased and Stat3 signalling is altered in HCV-related liver cirrhosis.
Methods : Normal liver tissue was compared to liver tissue obtained from patients transplanted for HCV end-stage liver disease. Expression of proteins was measured by Western blotting, transcription factor activity was assessed by electrophoretic mobility shift assays, mRNA expression was determined by quantitative PCR.
Results : Compared to normal liver, Stat3 protein expression including both serine and tyrosine phosphorylated forms were significantly increased in liver homogenates and nuclear extracts from cirrhotic livers. Despite increased phosphorylated protein, Stat3 DNA binding was only barely detectable in HCV liver tissue. In parallel, SOCS3 mRNA, a Stat3 regulated gene, was not induced in HCV livers and Stat3 mRNA was significantly decreased. Pro-apoptotic signals including caspase 3 activation and BAX expression were not up-regulated in HCV cirrhosis. Surprisingly, anti-apoptotic signals such as Bcl2 were strongly expressed in HCV tissue compared to normal livers.
Conclusions : Reduction of Stat3 transcription and DNA binding activity in HCV cirrhotic livers could alter hepatic repair mechanisms. Presence of compensatory mechanisms as, for instance, activation of anti-apoptotic pathways does not seem to be sufficient to avoid evolution towards cirrhosis. Studies in less advanced stages should contribute to clarify the role of these pathways in the cirrhotic process.

- A02 -

CYC202 (R-ROSCOVITINE), A CDK2 INHIBITOR, INHIBITS DNA SYNTHESIS AND CELL PROLIFERATION IN RAT LIVER AFTER PARTIAL HEPATECTOMY. P. Stärkel, C. Sempoux, C. De Saeger, Y. Horsmans. Laboratories of Gastroenterology and Pathology, Université Catholique de Louvain, Brussels, Belgium.

Background : Previous work suggests that activation of the cyclin E/CDK2 complex seems to play an important role in driving hepatocytes towards DNA synthesis in the regenerating rat liver.
Aims : We therefore evaluated the effect of CYC202 (R-roscovitine), an inhibitor of CDK2 activity, on liver regeneration after 70% partial hepatectomy (PH) in rats. In addition, several injection schemes were tested in order to optimize the potential anti-proliferative effect of CYC202.
Methods : CYC202 or the vector (DMSO) were injected intra-peritoneally 16 hours before and/or 1, 8, and 20 hours after PH. BrdU incorporation, PCNA, cyclin E and CDK2 expression were assessed 24 hours after PH. CDK2 activity was determined by the histone H2 activity assay.
Results : CYC202 completely abrogated CDK2 activity and blocked BrdU incorporation and PCNA expression 24 hours after PH whereas cyclin E and CDK2 protein expression were not affected. To elicit the inhibitory effect of CYC202 all experimental schemes needed to include at least 2 consecutive injections at 8 and 20 hours after PH closely matching the G1/S phase transition in the regenerating rat liver. Schemes withholding either the injection at 8 hours or the injection at 20 hours, for example, a single injection at 20 hours or 3 consecutive injections at –16, +1 and +8 hours after PH, did not produce any effect on liver regeneration.
Conclusions : Our results confirm an important role for CDK2 in the process of liver regeneration in the rat. They further suggest that the molecular events, including activation of CDK2, occurring between the 8^{th} and 20^{th} hour after PH (G1/S phase transition of the cell cycle) play an important role in determining whether or not DNA synthesis and finally liver regeneration proceed normally after PH in the rat.

- A03 -

CELL ACTIVATION IN ALCOHOLIC (ALD) AND IN NON ALCOHOLIC FATTY LIVER DISEASE (NAFLD) : AN IMMUNOHISTOCHEMICAL AND ULTRASTRUCTURAL STUDY. A. Durnez, R. De Vos, Ch. Verslype*, T. Roskams. KUL, Depts of Morphology and Molecular Pathology and Hepatology*, Leuven, Belgium.

Human progenitor cell (HPC) activation has been documented in several liver diseases. In ALD and NAFLD however, the activation of HPCs has not been extensively studied. Several studies support an inhibition of the hepatocyte replication in ethanol fed animals and recently in ob/ob mice, models for ALD and NAFLD. We postulated that, in parallel with the well-studied activation of HPCs in rat models of impaired hepatocyte replication, there could be an activation of HPCs in ethanol fed mice, in ob/ob mice and in human ALD and NAFLD. We studied HPCs in human liver biopsies with ALD (n = 25) and NAFLD (n = 13) in different stages of fibrosis and in biopsies of ethanol fed and of ob/ob mice, in cooperation with Prof. Dr. Anna Mae Diehl, Baltimore, using immunohistochemical HPC markers. The number of HPCs was assessed in each biopsy. In addition electron microscopy was performed on selected biopsies. In human fatty liver disease (FLD), we noted an expansion of the HPC compartment (CK7, CK19, OV-6, chrom-A+) mainly in the periportal area, sometimes extending into the parenchymal lobule and the presence of intermediate hepatocyte-like cells (HLCs)(CK7, chrom-A, OV-6+). In normal liver controls, scarce HPCs were found. The number of HPCs and HLCs increased significantly ($p < 0.0001$ and $p = 0.0001$) as fibrosis increased. No significant difference was found in the number of HPCs between ALD and NAFLD. The higher number of HLCs in more advanced stages of disease suggests more differentiation of HPCs towards mature hepatocytes in these stages. Ultrastructurally, a high number of small, immature progenitor cells was seen, characterized by the presence of a basement membrane, junctional complexes with adjacent cells and a full assortment of cytoplasmic organelles and bundles of tonofilaments. In addition, a range of intermediate cell types, showing more hepatocellular differentiation including the presence of a hemicanaliculus and glycogen rosettes, was recognized. A similar expansion of the progenitor cell compartment was seen in both mice models. The observed expansion of the progenitor cell population in human FLD, possibly related to an inhibition of hepatocyte replication, could play a role in the increased prevalence of HCC, which is known for ALD and recently reported in NAFLD. The high prevalence of NAFLD in the western world motivates further research.

- A04 -

ACTIVATION OF PPARALPHA-DEPENDENT PATHWAYS CAUSES RAPID REGRESSION OF FIBROSING STEATOHEPATITIS IN MCD DIET-FED MICE. E. Ip, G. Farrell, G. Robertson, P. Hall*, R Kirsch*, I. Leclercq. Storr Liver Unit, Westmead Millennium Institute, University of Sydney, NSW, Australia ; *Dpt of Anatomical Pathology, Faculty of Health Sciences, University of Cape Town, South Africa.

Pathogenesis of steatohepatitis involves interplay between accumulated hepatic lipid and oxidative stress that generates pro-inflammatory lipoperoxides. We have shown that activation of PPARalpha-dependent pathways clears hepatic lipid, reduces oxidative stress and prevents development of steatohepatitis induced by a methionine and choline deficient (MCD). We have now tested the hypothesis that PPARalpha activation could ameliorate established steatohepatitis. Male C57BL6 mice were fed MCD diet for 8 weeks. During the last 5 days, Wy-14,643 (0.1% w/w), a potent PPARalpha agonist, was added to the diet ; another group (controls) were maintained on the MCD diet. Liver sections were scored for steatosis and necroinflammation ; Sirius red was used to stain collagen and PPARalpha-responsive gene expression was determined (northern blots or RNase protection assay). In MCD-fed mice, ALT levels were elevated and livers exhibited widespread macrovesicular steatosis, necroinflammation and extensive pericellular fibrosis. In mice given Wy-14,643 for 5 days, ALT levels were lower and livers showed less steatosis and minimal inflammation. Consistent with reduced steatosis, Wy-14,643 increased expression of genes involved with fatty acid turnover. Wy-14,643 treatment produced impressive regression of hepatic fibrosis, demonstrated by unweighting of extracellular collagen networks leaving only scattered fibrils.
In conclusion, treatment with Wy-14,643 reverses established fibrosing steatohepatitis in mice. The PPARalpha agonist rapidly depletes the liver of lipid, decreases inflammation and appears to promote collagen degradation caused by the MCD diet. This suggests that increase of intrahepatic lipid oxidation is an efficient therapeutic target for steatohepatitis.

- A05 -

IN VIVO VASCULAR HYPOREACTIVITY IN THE MESENTERIC ARTERY OF RATS WITH CIRRHOSIS AND PORTAL HYPERTENSION. I. Colle, A.S. De Vriese*, H. Van Vlierberghe, N.H. Lameire*, M. DeVos. Departments of Hepato-Gastroenterology and Nephrology*, University Hospital of Ghent, Belgium.

Background : Cirrhosis is complicated by a splanchnic vasodilation leading to and worsening portal hypertension and the hyperdynamic circulation. NO and prostacyclin contribute to this splanchnic vasodilation.
Aim : The *in vivo* response of mesenteric arteries to different vasoactive agents were studied before and after systemic NO-synthase (NOS) and cyclooxygenase (COX) inhibition in experimental animals with cirrhosis and portal hypertension.
Methods : Secondary biliary cirrhosis was induced in male Wistar rats by common bile duct ligation (CBDL, n = 11) and isolated portal hypertension was induced by partial portal vein ligation (PPVL, n = 12). A third group was sham-operated (sham, n = 11). Blood flow in the superior mesenteric artery (MBF) was measured during intramesenteric infusion of the endothelium-dependent vasodilator acetylcholine (1 to 50 ng), the NO donor deta-NONOate (16, 48 and 83 µg), the potassium channel opener pinacidil (25, 75 and 125 µg) and the alpha-1 receptor agonist L-phenylephrine (10, 30 and 50 µg). The measurements were repeated after continuous and combined systemic infusion of L-NAME and indomethacin.
Results : The MBF response to acetylcholine was significantly lower in CBDL than in sham and tended to be lower in PPVL than in sham. L-NAME and indomethacin significantly decreased the MBF response to acetylcholine in all groups. The hyporeactivity to acetylcholine in CBDL and PPVL compared to sham was maintained after L-NAME and indomethacin. The MBF response to pinacidil, deta-NONOate and phenylephrine, both before and after NOS and COX inhibition was lower in CBDL and PPVL than in sham.
Conclusion : This is the first *in vivo* study demonstrating an impaired response to endothelium-dependent and endothelium-independent vasodilators as well as vasoconstrictors in the mesenteric artery of experimental animals with cirrhosis and portal hypertension. This suggests an abnormality in the vascular smooth muscle cells of the mesenteric artery. The hyporeactivity is not only related to an overproduction of NO and prostacyclin. Portal hypertension alone is sufficient to introduce these alterations.

- A06 -

INFLUENCE OF AGE ON RESPONSE TO TREATMENT WITH INTERFERON alphaB AND RIBAVIRIN IN CHRONIC HEPATITIS C PATIENTS INFECTED WITH GENOTYPE 2/3 VIRUS. G. Robaeys (1), H. Van Vlierberghe (2), F. Nevens (3), C. Mathei (3), M. Van Ranst (3), L. Bruckers (4), F. Buntinx (3,5), The members of the BASL (6). (1) ZOL Genk ; (2) RUGent ; (3) KULeuven ; (4) Limburgs Universitair Centrum ; (5) University of Maastricht.

Background : Age unther forty years is an independent predictor of SVR. Patients with genoype 2/3 have a more favourable response on combination therapy with standard IFN than genotype 1 patients. It has been suggested that for those patients only a 6 months treatment is required and that the more expensive PEG IFN is probably not indicated. AIMS : We studied the influence of age on response to treatment in patients infected with genotype 2/3.
Methods : SVR was measured in a subanalysis of a randomised clinical trial evaluating the efficacy of an induction dose of IFN α-2b (daily at 5MU SC, 8 weeks) (group A) as compared to IFN α-2b at 5MU SC thrice weekly (group B), followed by the standard dose of IFN α2b (3MU thrice a week) in previously untreated CHC patients. In both groups, ribavirin was added at week 5. Treatment lasted 48 weeks. We studied the influence of age on the response in a subgroup of patients infected by genotype 2/3 and compared it with patients infected by genotype 1.
Results : Of 406 patients, 59 and 230 were respectively infected by genotype 2/3 and 1 and evaluable for analysis of SVR. There was no difference in SVR between group A and B. Younger patients have a better SVR (26.5%) than patients > 40y (12.6%) (RR = 2.5 ;. 95%CI = 1.42-4.44). Both in genotype 1 and 2/3 younger patients had significantly better SVR than patients with age > 40 (RR = 2.18 ;95%CI = 1.12-4.24 and RR = 1.29 ;95%CI = 0.64-2.59). No interaction between the effect of age and genotype on SVR could be identified (p = 0.28).
Conclusion : Also in CHC patients infected with genoype 2/3 age is a predictive factor associated with response to treatment. Since older patients (> 40y) with genotype 2/3 are less responsive to therapy, probably PEG IFN is also indicated in this subgroup.

- A07 -

PREVALENCE AND DETERMINANTS OF HEPATITIS C IN DRUG USERS IN FLANDERS, BELGIUM : REGIONAL DIFFERENCES. C. Matheï, G. Robaeys, F. Buntinx, P. Van Damme. Department of General Practice, University of Leuven, 3000 Leuven, Belgium.

A considerable variability of the prevalence of hepatitis C among injecting drug users within western European countries has been documented, with rates varying between 37 and 98%. No conclusive explanation could be given for this geographic variability. Therefore a cross-sectional study was undertaken to compare the prevalence of HCV and related risk factors in two distinct geographic areas in Belgium, the city of Antwerp and the mixed urban-rural area of Limburg. Patients in a methadone maintenance programme were recruited in 2 low-threshold centres. All participants were interviewed by means of a standardized questionnaire with respect to their socio-demographic status, mental health, drug use history, drug use related and sexual risk behaviour. Blood specimens were collected for hepatitis B, hepatitis C and HIV screening. In Antwerp 205 and in Limburg 105 drug users participated. Demographics were comparable in both populations, except for the distribution of foreign nationalities. Socio-economic situation was significantly better for drug users in Limburg while drug-related and sexual risk behaviour was significantly more prevalent in Antwerp drug users. The prevalence rates of anti-HCV, anti-HBc and anti-HIV were respectively 71%, 62% and 4% in Antwerp and 46%, 21% and 0% in Limburg. Multivariate analysis indicated injecting drug use, duration of injecting drug use, ever worked as a commercial sex worker, originating from the Middle East or Northern Africa, marginalization and anti-HBc reactivity as related independently to a positive hepatitis C serology. This study shows an important difference of HCV prevalence among drug users across 2 geographic regions in Belgium. The higher prevalence rate of HCV in the city of Antwerp was related to a higher prevalence of risk factors/behaviour. We identified marginalization and originating from a country in the Middle East or Northern Africa as independent predictors for HCV. However, further research is wanted to identify the underlying mechanisms.

- A08 -

COMPLIANCE AND EFFECT OF TREATMENT FOR CHRONIC HEPATITIS C (CHC) IN INTRAVENOUS DRUG USERS (IVDUS). G. Robaeys (1), H. Van Vlierberghe (2)., M. Van Ranst (3). C. Matheï (3), L. Bruckers (4)., F. Buntinx (3,5), The members of the BASL (6) Steering Committee, and the Benelux Study Group. (1) ZOL Genk ; (2) RUGent ; (3) KULeuven ; (4) Limburgs Universitair Centrum ; (5) University of Maastricht ; (6) Belgian Association for the Study of the Liver.

Background : There is reluctance to treat IVDUs infected with CHC because of presumed lower compliance and response to antiviral therapy.
Aims : We studied if the compliance and response were lower in IVDUs compared to non-IVDUs.
Methods : Complete response (CR), compliance and SVR were measured in a subanalysis of a randomised clinical trial evaluating the efficacy of an induction dose of IFN ?-2b (daily at 5MU SC ; 8 weeks) (group A) as compared to IFN ?-2b at 5MU SC thrice weekly (group B), followed by the standard dose of IFN ?-2b (3MU thrice a week) in previously untreated CHC patients. Ribavirin was added at week 5. Treatment lasted 48 weeks. CR was defined as : an ALT within normal limits and serum PCR negative at the end of therapy. Compliance was determined as presentation for PCR determination at the end of treatment. SVR was defined as an undetectable HCV RNA level at the end of a 6 month follow-up period.
Results : Of 406 patients, 98 (24%) were IVDUs (49.0% included in arm A). Noncompliance in IVDUs was not different from non-IVDUs (resp 12.7 and 10.2% RR = 1.24 ; 95%CI = 0.64-2.39). CR was better in IVDUs than in non-IVDUs (50.6 and 36.2% RR = 0.72 ; 95%CI = 0.55-0.93). However, when controlling for genotype the CR was not different (RR = 0.89 ; 95%CI = 0.68-1.16). Controlling for treatment arm, age, sex, presence of cirrhosis, viral load didn't change these results. There was no difference in SVR between IVDUs and non-IVDUs (28.8 and 20.4% RR = 1.2 ; 95%CI = 0.68-1.16).
Conclusions : IVDUs showed the same compliance and response to treatment with IFN and ribavirin compared to other patients with CHC viral infection after adjusting for genotype. Therefore, it is not longer justifiable to withhold treatment to chronic hepatitis C patients who use intravenous drugs.

- A09 -

EPIDEMIOLOGICAL EVALUATION OF 1680 HCV PATIENTS IN LIEGE AND SUBURBS. C. Gérard (1), J. Delwaide (1), B. Bastens (2), B. Servais (3), D. Vaira (1,4). (1) CHU Sart Tilman, Liège ; (2) Saint Joseph, Liège ; (3) Bois de l'Abbaye, Liège ; (4) Le Groupe Liégeois d'Etude des Virus Hépatotropes (GLEVHE).

Aim of the study : to present the epidemiological profile of 1680 patients who have been found to be HCV carriers by PCR-RNA between 1993 and 2002 in Liège and suburbs.
Methods : the search for viral RNA was realized by using the RT-PCR Amplicor version 2.0 from Roche (sensitivity = 50 UI/ml). The HCV genotype was determined by using the LIPA-HCV from Innogenetics. Age and sex of patients were always known ; for some of them the most probable mode of contamination could also be documented.
Results : Number of new diagnosis per year : from 1993 to 2002, 1680 patients have been diagnosed by PCR as carriers of hepatitis C virus, with a mean of 177 new diagnoses per year (222 per year during the last 6 years).
The age and sex distribution of HCV patients indicate a bimodal distribution. Indeed, HCV patients are divided in two distinct age groups : the first group, representing 57.9% of the global distribution, is "young" (under 50 years old) and contains a majority of males (M/F = 1.44) ; the second group (42.1%) is "older" (more than 50 years old) and presents a majority of females (M/F = 0.86).
The genotype distribution is as follows : genotype 1 (60.5%) ; 2 (13.6%), 3 (13.4%), 4 (10.8%), 5 (1.4%) and 6 (0.3%). Half of the patients (50.1%) are infected with genotype 1b, which is known to be among the most resistant to therapy. Between 1993 and 2002, the proportion of patients infected with genotype 1 became significantly lower.
Risk factors for HCV infection reported by the patients were distributed as follows : transfusion of blood products (37%), IV drug use (27%), invasive medical examination (13%), dialysis (4%), sexual (2%), other or unknown (17%). Genotype 3 was significantly more frequent in the young age group than in the older one ($p < 0.00001$). Similarly, IV drug use as risk factor was significantly associated with young age. The evolution with time of the probable modes of contamination indicates an increase in the IVDU group. More surprisingly, transfusion of blood products remains quite constantly reported by newly diagnosed patients.
Conclusion : Since 1993, the number of HCV carriers diagnosed by our laboratory in Liège and suburbs has been increasing linearly of about 200 new cases per year. Whereas drug users are more and more diagnosed, it appears that twelve years after discovery of hepatitis C virus, newly discovered infections in past-transfused patients remain quite stable. This last point suggests that HCV infection in Belgium continues to be underestimated by the public.

- A10 -

IMPACT OF OBESITY AND WEIGHT LOSS ON THE LIVER AFTER BARIATRIC SURGERY. C. Assene (1), J. Closset (1), A. Mehdi (1), M. Barea (1), J.-J. Houben (2), Ph. Thiry (1), E. Lebrun (3), J. Bruyns (4), N. Nagy (5), F. Fery (6), M. Adler (1). (1) Medico-Surgical Dpt of Gastroenterology, Hôpital Erasme, Dpts of Surgery ; (2) CHIREC ; (3) Ambroise Paré ; (4) Hôpital St Pierre ; (5) Dpt of Pathology, Hôpital Erasme ; (6) Dpt of Endocrinology, Erasme Hospital, 1070 Brussels, Belgium.

Non-alcoholic fatty liver disease (NAFLD) is a frequent lesion associated with obesity with a growing incidence in Western world countries. The aim of our study was to evaluate the prevalence and risk factors for NAFLD and non-alcoholic steatohepatitis (NASH) – an entity associated with a progressive course – in patients undergoing bariatric surgery as well as postoperative evolution of the liver injury. After informed consent, 68 consecutive patients between November 2001 and February 2002 in 4 affiliated hospitals were recruited. Extensive clinico-demographic (n = 5), biochemical (n = 10) and imaging (hepatic density and subcutaneous fat deposit measured by CT scan) variables were obtained preoperatively. Preoperative liver biopsy was scored according to Brunt. The same preoperative parameters were reevaluated 6 months after surgery. Mean (± SD) was 37 (± 10) years and 40.9 ± 6.2 kg/m^2 for age and BMI. ALT was in the normal range in 90% (61/68) of the patients. Histology was normal in 15 (28%) of the 54 liver biopsies. Steatosis, severe (> 33%) steatosis, NASH and fibrosis were present in 53.7% (n = 29), 11% (n = 6), 38.8% (n = 21) and 27.7% (n = 15) respectively. Univariate analysis revealed association between liver steatosis (> 10%) and lower liver density ($p = 0.0004$), high subcutaneous fat ($p = 0.021$), high ALT ($p = 0.026$), glucose ($p = 0.023$), C peptide (p 0.005) and low HDL-cholesterol ($p = 0.04$) levels. A relation was seen between NASH and lower liver density ($p = 0.001$), higher C-peptide ($p = 0.008$), higher triglycerides ($p = 0.03$) and lower HDL-cholesterol ($p = 0.009$) levels as well as between lower liver density ($p = 0.009$), lower HDL-cholesterol ($p = 0.03$), higher triglycerides ($p = 0.01$) levels and liver fibrosis. Surgical treatment, regardless of the methods, was associated with a significant improvement in BMI (mean+-SD : -10.24 ± 3.6, $p = 0.0001$), AST (median, p25-75 : -6.5, 2 to 8, $p = 0.01$), triglycerides (median, p25-75 :-38, 6.7 to 75, $p = 0.02$) and glycemia (mean ± SD :-10.2 ± 9.5, $p = 0.01$).
Conclusion : Isolated steatosis, NASH and liver fibrosis were frequently observed in obese patients even though they disclosed normal ALT. Liver density, triglyceride, C-peptide and HDL-cholesterol levels are non invasive predictors of severe liver injury, which may help in deciding the need for liver biopsy.

OPTIMIZED VIROLOGICAL RESPONSE IN PATIENTS WITH GENOTYPE 4 CHRONIC HEPATITIS C TREATED WITH PEGINTERFERON ALFA-2A (PEGASYS®) IN COMBINATION WITH RIBAVIRIN. M. Diago, General Universitario,Valencia Spain ; S. Hadziyannis, H. Dunant, Hospital, Athens, Greece ; H. Bodenheimer Jr, Beth Israel Medical Center, New York, USA ; T. Hassanein, University of California, San Diego, La Jolla, USA ; S. Uchman, Attleboro Gastroenterology, Attleboro, USA ; P. Marcellin, Hôpital Beaujon, Clichy, France ; G. Ramadori, Georg-August Universität Göttingen, Germany ; J. Delwaide, CHU Sart Tilman, Liège, Belgium ; F. Sedarati, Hoffmann-La Roche, Nutley, USA, for the PEGASYS International Study Group.

Background : Patients with chronic hepatitis C (CHC) infected with HCV genotype 4 have traditionally been described as “difficult-to-treat”. Recently, we showed that the poor sustained virologic response (SVR) of these patients to therapy with standard interferon (SVR 0-5%) *(Zylberberg et al. Ann Intern Med 2000* ; *132* : *845-846)* can be overcome by treatment with peginterferon alfa-2a alone (SVR 45%) *(Sherman Ann Intern Med 2001 ;135* : *927)* or in combination with ribavirin (RBV) (SVR 77%) *(Rhodes et al.t :8th International Symposium on Hepatitis C and Related Viruses* : *2001)*.

Objectives : To study the efficacy and safety of 24 or 48 weeks of treatment with peginterferon alfa-2a combined with an 800 or 1000/1200 mg daily dose of RBV and to determine an optimal treatment regimen in CHC patients infected with genotype 4.

Methods : A total of 49 CHC patients infected with HCV genotype 4 identified in two phase III studies (NV15801 and NV15942) were included in these analyses. Patients in the NV15801 trial (n = 13) were treated with peginterferon alfa-2a 180 µg sc qw plus RBV 1000/1200 mg qd for 48 weeks. Patients in NV15942 trial (n = 36) were treated in one of four groups : peginterferon alfa-2a 180 µg sc qw plus RBV 800 mg qd or RBV 1000/1200 mg qd for 24 weeks or 48 weeks based on body weight. Efficacy assessments consisted of undetectable HCV RNA and normalisation of ALT at the end of a 24-week posttreatment follow-up period. Safety was assessed by evaluation of adverse events and laboratory tests.

Results : The majority of patients were from Europe (n = 34) and USA (n = 13). Patients were predominantly male (69%) with baseline viral load ranging from 0.05 to 8.18 million copies/mL (13 patients (26%) had a viral load > 2 million copies/mL). Twelve patients (24%) had cirrhosis. Among patients treated with peginterferon alf-2a plus 1000/1200 mg RBV for 48 weeks in both studies, 19 (79%) achieved an SVR. Patients treated with RBV 800 mg for 48 weeks or RBV 1000/1200 mg for 24 weeks achieved lower SVRs of 63% and 67%, respectively. No SVR was achieved in patients treated with RBV 800mg for 24 weeks. The majority of patients who were sustained virological responders were also sustained biochemical responders as measured by normalization of their serum ALT concentrations. The treatments were well tolerated and only four patients discontinued therapy for adverse events (n = 3) or laboratory abnormality (n = 1), all in the group treated with RBV 1000/1200 mg dose for 48 weeks.

Conclusion : Our results indicate that both treatment duration and RBV dose affect treatment outcome and that the optimal treatment regimen in this patient population appears to be peginterferon alfa-2a qw plus RBV 1000/1200 mg qd given for 48 weeks. Although genotype 4 CHC patients, like those infected with genotype 1, need to be treated aggressively for optimal response, they seem to be able to achieve SVRs similar to the very high SVRs reported for patients with genotype 2/3 infection *(Hadziyannis et al. EASL 2002* ; *Shiffman et al., unpublished data, 2002).* Therefore, it may no longer be appropriate to categorize infection with HCV genotype 4 as a “difficult-to-treat” disease.

THE OUTCOME OF STEATOTIC LIVERS ON THE LONG TERM AFTER TRANSPLANTATION. S. Francque (1,2), F. Durand (1), D. Cazals-Hatem (1), P. Michielsen (2), B. De Winter (3), G. Verpooten (4), C. Degott (1), J. Belghiti (1), D. Valla (1). (1) Dpt of Hepatology, Hôpital Beaujon, Clichy, France ; (2) Dpt of Gastro-enterology and Hepatology, University Hospital Antwerp, Belgium ; (3) Laboratory of Gastro-enterology, University of Antwerp, Belgium ; (4) Dpt of Nephrology, University Hopsital Antwerp, Belgium.

Objectives : Moderately steatotic livers (≥ 30%) are mostly rejected for transplantation because of the increased risk of primary graft non-function and other peri- and postoperative problems. Little is known, however, about the outcome of steatotic grafts on the long term. We analysed the outcome of steatotic grafts, the evolution of steatosis and the risk factors for steatosis at 1 year after transplantation.
Methods : Of the 289 liver transplantations performed between November 1989 and March 2000, 32 patients received a steatotic liver, 25 had a follow-up biopsy at 1 year after transplantation and were included for analysis. 42 patients who received a liver with 0% of steatosis and had a biopsy at 1 year constituted a control group. Data for both donor and recipient at the time of transplantation and at 1 year after transplantation were collected and statistically analysed with independent samples T-test, Chi Square test, correlation and logistic regression analysis and univariate analysis in forward conditional when appropriate.
Results : except for donor and recipient BMI there were no statistically significant differences in group characteristics. The difference in donor and recipient BMI is believed to be a reflection of the role of the BMI as a risk factor for steatosis, and the donor-acceptor matching for body weight and length in donor organ allocation. There were no differences between the 2 groups at 1 year after transplantation in terms of % of steatosis, levels of transaminases and liver function parameters. There were even so no differences in the number of episodes of acute rejection and the need for corticosteroids. Steatosis after transplantation is associated with the presence of diabetes before transplantation ($p = 0.003$), donor ($p = 0.008$) and recipient age ($p = 0.013$), alcohol use ($p = 0.020$), donor and recipient BMI ($p = 0.032$) and corticosteroid use ($p = 0.03$). Recurrence of Hepatitis C did not reach statistical significance ($p = 0.08$). The % of steatosis correlates with BMI ($h^2 = 0.13$) and triglyceridemia ($h^2 = 0.22$). A male patient receiving a steatotic graft has a significantly higher % of steatosis at 1 year after transplantation (32.59 ± 6.89) then a male patient receiving a non-steatotic graft (4.02 ± 2.85) or a female patient (1.23 ± 5.00 and 1.44 ± 4.44). The presence of steatosis had no functional impact on the graft at 1 year.
Conclusions : Steatotic and non-steatotic grafts do equally well on the long term after liver transplantation, indicating that the donor pool can be safely expanded to moderately steatotic livers if the per- and postoperative problems of steatotic donor livers can be dealt with.

- B01 -

FŒTAL LIVER SYNGENIC TRANSPLANTATION (FIRST REPORT). V. Coulic, P. Delrée, C. DePrez, S. Bakari, L. Lasser, E. Dekoster (CHU Brugmann, ULB), Brussels ; GPI, Loverval, Belgium.

Previous works have proved the capacity of several syngenic fœtal digestive organs to develop in ectopic conditions and give growth to morphologically differentiated and physiologically functional adult-like formations. Fœtal liver hemopoietic tissue was already used for the treatment of leukaemia in children. Up to now the possibility of ectopic development of fœtal hepatocytes in an adult recipient seems to remain unexplored . The aim of the present work was to test the ectopic developmental pattern of fœtal liver implanted into syngenic adult organisms : is fœtal liver graft able to give growth to adult liver tissue and could it be proposed for liver insufficiency supply.
Material and methods : 15 Wistar rats were used for this experiment. Donors were foeti aged either 15 or 21 days i.u.(respectively 0,33 gr and 2,5 gr BW). Recipients were adult males and females aged 4-6 months. Under anaesthesy, the fœtal liver as a whole or as a lobe (in every case no more than 2x2x1 mm) was introduced in a subcutanean pouch of the recipient ear. Visual observation with measurement of the graft, biopsies for histological investigation (haematoxylin eosin staining) were performed from day 0 to day 90. Results. During the first week p.o. all the grafts lost their structure. At 1 month p.o. in all examined histological preparations some hepatocytes and bile ducts were identified in the implantation site. This was confirmed in 3 months p.o observations. Nevertheless rejection picture (lymphocytic, macrophageal and fibroblastic infiltration of the graft with alterations of its structure) was revealed in one case at 2 months p.o.
Conclusion : Fœtal liver ectopic implants seems to follow the same rules of development as other fœtal digestive organs with a first phase of destruction followed by a regeneration phase. They are able to give growth to specific hepatic tissues and cells. The observation of «rejection» after 2 months p.o . may be due to an imperfect syngenic matching of donor and recipient that is possible with Wistar rats or to trauma of the graft. Control of this experiment is necessary and has already started in Fischer rats. It seems, nevertheless, that in appropriate conditions fœtal liver implantation may have perspectives of use for help in therapy of liver insufficiency before adult liver transplantation or when the last is impossible. Taking into account the peculiarities of the first phase of the graft development, the model may also present interest for the study of stem and precursor cells culture in vivo.

- B02 -

SPECIFIC RADIOIMMUNOASSAY FOR THE DETECTION OF THE BIOLOGICAL ACTIVE FORM OF GHRELIN. C. De Vriese, M.D. Martin-Martinez, F. Grégoire, P. De Neef, P. Robberecht, C. Delporte. Dpt of Biochemistry, Université Libre de Bruxelles, B-1070 Brussels, Belgium.

Background : Ghrelin is a new growth hormone releasing peptide of 28 amino acids, isolated from the stomach, which also stimulates food intake and reduces fat metabolism. The unique octanoylation of ghrelin in position 3 is critical for its biological activity.
Objectives : Design a specific radioimmunoassay (RIA) to detect the biological active forms of ghrelin. Monitor the degradation of ghrelin in serum by RIA and identify the products by HPLC.
Methods : [Cys^{12}]-human ghrelin [1-11] conjugated to keyhole limpet hemocyanin was emulsified with Freund's adjuvant and used to immunize a rabbit. [Tyr^{24}]-human ghrelin [1-23] was radioiodinated on the terminal tyrosine by the iodogen method and purified on a C18 Sep-Pak. Radioimmunoassays were performed in duplicate at 4°C in a 300 µl final volume containing 100 µl of standard ghrelin or unknown sample, 100 µl of antiserum and 100 µl of ^{125}I-labeled tracer. The antigen and the antibody were preincubated overnight, then ^{125}I-labeled tracer was added. After a further 18h incubation, 1ml of 4% polyethyleneglycol 6000 containing 1% sheep antirabbit serum was added. After 30 min incubation at room temperature, free and bound tracers were separated by centrifugation. Rat serum was incubated for variable times in the presence of octanoylated ghrelin. The samples were purified on a C18 Sep-Pak, lyophilized, then analyzed by HPLC on a C18 Vydac column using a 3-80% acetonitrile gradient in 50 min and a 226nm UV detector. HPLC fractions were collected and submitted to RIA.
Results : The rabbit polyclonal antibodies directed against a synthetic peptide corresponding to the N-terminal sequence of ghrelin recognized specifically the octanoylated ghrelin, and not the des-octanoylated ghrelin. In the RIA, the limit of detection for ghrelin was 3 fmoles/assay. In the presence of serum, octanoylated ghrelin was rapidly degraded into des-octanoylated ghrelin, the biologically inactive ghrelin without evidence of proteolysis. This reaction was inhibited by the esterase inhibitor PMSF.
Conclusions : A specific and sensitive RIA detecting the biological active form of ghrelin was designed. Since ghrelin is rapidly desoctanoylated by serum, the RIA should be very useful to assess the biological active concentrations of ghrelin in the plasma, and other tissues.

- B03 -

THE GHRELIN RECEPTOR : STRUCTURE FUNCTION RELATIONSHIP OF SHORTENED PEPTIDES AND ANALOGUES. M. Van Craenenbroeck, F. Grégoire, P. De Neef, J. Perret and P. Robberecht. Laboratory of Biological Chemistry and Nutrition, School of Medicine, Université Libre de Bruxelles, 808 route de Lennik, CP611, B-1070 Brussels, Belgium.

The 28 amino acid octanoylated peptide Ghrelin is the natural ligand of the Growth Hormone Secretagogue receptor. Although Ghrelin has only limited homology with Motilin, Ghrelin and Motilin receptors have 56% similarities.
The purpose of the work is to precise the structural requirements of Ghrelin for efficient interaction with its receptor. CHO cells expressing stably the recombinant human receptor were used for functional studies (IP an $[Ca^{2+}]_i$ determination) and HEK 293 expressing transiently the receptor for binding studies.
We confirm that octanoylation of Ser^3 is absolutely required for receptor recognition. We established that Ghrelin (1-23) and (1-14) were 5 and 10 fold less potent as Ghrelin (1-28) respectively. The three peptides were equally efficient. The systematic substitution of each residue (except the octanoylated Ser^3) by an alanine residue (Ala-scan) reveals the importance of the phenylalanine residue in position 4. [Ala^4]-Ghrelin (1-14) is 200 fold less potent than Ghrelin (1-14). The acylation of the aminoterminus reduced 20 fold the peptide potency and markedly reduced the peptide efficacy.
In conclusion : the aminoterminal moiety of Ghrelin is sufficient for full biological activity and high affinity recognition. A triad consisting in the positively charged aminoterminus, the octanoyl group in position 3 and the Phe residue in position 4 is absolutely required for receptor recognition.

- B04 -

ACTIVATION OF MYENTERIC NEURONS BY GHRELIN AND GHRP-6 IN THE GUINEA-PIG SMALL INTESTINE. R. Bisschops, P. Vanden Berghe, I. Depoortere, T. Peeters, J. Janssens, J. Tack. Center for gastroenterological Research, 3000 Leuven, Belgium.

Background : Ghrelin, the natural ligand for the growth hormone secretatogue receptor first isolated from rat stomach, may play a role in gastric motility (Masuda, 2000). Both Ghrelin and its receptor are present in the guinea-pig small intestine (Xu, DDW 2002). The aim of the present study was to investigate the effect of Ghrelin and its synthetic analogue, GHRP-6, on activation of myenteric neurones in the guinea-pig small intestine.
Methods : Longitudinal muscle myenteric plexus preparations of guinea-pig jejunum were incubated with the calcium indicator fluo-4. Confocal calcium imaging (Noran Oz/Nikon TE 300) was used to visualise activation of neurones. All experiments were performed in the presence of nicardipine 10^{-6}M to reduce tissue movement. Images were analysed using Scion image and a specifically developed software routine to correct for residual movements.
Results : Application of a 75mM K^+ Krebs solution identified 432 neurones in 18 myenteric ganglia. Ghrelin 1 mM (n = 66), caused a transient increase in intracellular calcium in 27.3% of the neurones. Application of GHRP-6 induced calcium transients in a dose-dependent manner (14%, 15%, 20% and 36% for respectively 0.1(n = 51), 1(n = 52), 10 (n = 80) and 100mM (n = 42)). The number of responsive neurones did not differ significantly between Ghrelin and GHRP-6. Sequential application of increasing concentrations GHRP-6 (0.1 to 1, 10 and 100 mM, n = 51) suggested sensitisation at 1 mM and desensitisation at 10 and 100 mM. The number of neurones responding to 1 mM rose to 31% after sensitisation with 0.1 mM (p = 0.06 95% CI 0.23-1.04). At the highest concentrations respectively only 10% and 12% of the neurones were recruited, which differed from those responding to lower concentrations. After removal of extracellular calcium, application of 10 mM GHRP-6 activated 24.4% (n = 78) of the neurones. In the presence of the N-type calcium-blocker w-conotoxin $5x10^{-7}$M, 10 mM GHRP-6 elicited a response in 50% (n = 12) of the neurones. These observations suggest that GHRP-6-induced calcium transients do not require influx of external calcium and they do not depend on synaptic transmission.
Conclusion : Ghrelin and GHRP-6 activate a subset of myenteric neurones in the guinea-pig jejunum. These responses are due to direct activation of the neurones, which likely induced calcium release from intracellular stores. Ghrelin may regulate gastro-intestinal motility by acting on myenteric neurones.

- B05 -

EFFECT OF GHRELIN ON GASTRIC EMPTYING AND INTESTINAL TRANSIT IN CONTROL AND SEPTIC MICE. B.Y. De Winter, J.G. De Man, T.C. Seerden, A.G. Herman*, P.A. Pelckmans. Div. of Gastroenterology and *Pharmacology, University of Antwerp (UIA), 2610 Antwerp, Belgium.

The pathogenesis of septic ileus is still unclear. Ghrelin, an orexigenic peptide, has prokinetic effects on gastric emptying and intestinal transit in rats. We investigated the effect of ghrelin on gastric emptying and intestinal transit in control mice and in septic mice with ileus. Methods : Gastric emptying (GE) and intestinal transit were measured 15 min after intragastric injection of 0.1 ml Evans blue in 0.5% methylcellulose. Septic ileus was induced by an intraperitoneal (IP) injection of endotoxins (LPS, E. coli 20 mg/kg, 16 to 18 h before Evans blue). Ghrelin 20 or 100 ?g/kg or saline were injected IP 1 h before Evans blue. Results : In control mice, 20 ?g/kg ghrelin had no significant effect on GE, whereas 100 µg/kg ghrelin significantly increased GE. Intestinal transit was not significantly increased by either dose of ghrelin. LPS significantly delayed GE and intestinal transit in saline-treated mice. Ghrelin 20 ?g/kg ameliorated GE in septic mice since GE rates in control and LPS mice were no longer statistically different. Ghrelin 20 ?g/kg had no effect on the endotoxin-induced delay in intestinal transit. Ghrelin 100 ?g/kg had no significant effect on the endotoxin-induced delay in GE or intestinal transit. Conclusions : In control mice, ghrelin 100 µg/kg had prokinetic effects on gastric emptying but not on intestinal transit. In septic mice, gastric emptying and intestinal transit were significantly delayed. Only ghrelin 20 ?g/kg ameliorated gastric emptying significantly. Ghrelin could not reverse the endotoxin-induced delay in intestinal transit.

		saline	**ghrelin 20**	**ghrelin 100**
% GE	*Control*	57.7 ± 3.1%	58.4 ± 5.2%	72.7 ± 3.5% #
	LPS	35.5 ± 6.5% *	51.2 ± 4.4%	45.1 ± 8.2% *
Cm transit	*Control*	15.8 ± 2.3 cm	16.7 ± 1.8 cm	20.4 ± 1.7 cm
	LPS	8.9 ± 1.3 cm *	9.4 ± 0.8 cm *	9.9 ± 0.8 cm *

Table : *Effect of saline, ghrelin 20-100 µg/kg on% GE and cm transit in control and LPS mice. *, p£0.05, statistically different from control mice (two-way ANOVA and Student's t-test)* ; *#, p£0.05, statistically different from saline-treated mice (two-way ANOVA and one-way ANOVA plus Dunnett posthoc test)* ; *n = 5-7.*

- B06 -

GENE EXPRESSION PROFILING OF INTERSTITIAL CELLS OF CAJAL BY SUPPRESSION SUBTRACTIVE HYBRIDISATION. Mira Wouters (1,2), Karine Smans (1), Alban de Kerchove d'Exaerde (2) and Jean-Marie Vanderwinden (2). (1) Dept. Gastro-intestinal Pharmacology, Janssen Pharmaceutics, Division of Pharmacological Research and Development and (2) Labo. Neurophysiology, Université Libre de Bruxelles (Belgium).

Interstitial cells of Cajal (ICC) are important for the generation of slow waves in the intestine and thus for proper peristaltic movements along the GI tract. W/Wv and Sl/Sld mice, which are deficient in ICC and in slow wave activity, provide valuable models in the quest for ICC specific genes. The pool of genes expressed in the muscle coats of the mouse intestine in controls and ICC deficient littermates was compared by suppression subtractive hybridization (SSH, Clontech). Differential expression of candidate genes picked up by SSH was confirmed by real time quantitative PCR (RT-QPCR). Unknown transcripts were analyzed by Northern blotting and their full-length sequence was identified by SMART-RACE (Clontech). Tissular localization by in situ hybridization (ISH) is ongoing. SSH identified 52 out of 4000 candidate genes putatively upregulated in WT versus ICC deficient animals in both the W/Wv and Sl/Sld models. RT-QPCR was used to confirm the differential expression of these 52 genes and of 3 genes, COX VII, SORCIN and ACLP1, described to be upregulated in WT versus W/Wv by Takayama I. *et al.*, (2001 ; 2002). However, our mouse models did not corrobate Takayama's findings. From our own 52 candidates, 5 known genes, including c-kit and 4 unknown genes were confirmed to be upregulated. The unknown transcripts were analyzed by multi-tissue Northern blot. Their expression level was, as c-kit, almost undetectable in the GI-tract. In thyroid, salivary gland and prostate however, a low expression of all 4 unknown transcripts was visible, with sizes varying between 4.5 and 7.5 kb. This difference in expression level of small intestine versus thyroid and salivary gland was confirmed by RT-QPCR. So far, we succeeded in identifying the full length sequence by SMART-RACE for 3 out of 4 genes. Although none of these full-length cDNAs corresponded with a gene with known function, using bio-informatics we were able to predict open reading frames (ORF) in which domains with a putative function could be identified, such as an ion channel related protein, an ion cotransporter and some Kelch domains. Localization of the candidate genes by ISH to identify those genes that are truly ICC specific is ongoing. The involvement of genes expressed in ICC in the generation of slow waves will be further electrophysiological investigated on primary ICC cell cultures.

- B07 -

DIVERGENT ROLE OF THE PERIPHERAL CRF1 AND CRF2 RECEPTOR IN THE MODULATION OF VISCERAL PAIN IN THE FREELY MOVING RAT. N. Ongenae, A. Meulemans, B. Coulie, M. Nijsen. Janssen Pharmaceutica, dept. Gastrointestinal and Emerging Disease, Turnhoutseweg 30, 2340 Beerse, Belgium.

This study was aimed to elucidate the role of peripheral CRF and its receptors in the modulation of visceral pain in freely moving rats. Both nociceptive and antinociceptive effects of systemically administered CRF have been reported previously. In the present study this dual action of CRF was unraveled by selective activation of the peripheral CRF_1 and CRF_2 receptor. A telemetry transmitter, consisting of a bipolar electrode pair, was chronically implanted into the rat to register abdominal electromyography (EMG). A balloon catheter was chronically implanted in the duodenum to deliver volume-fixed staircase distensions (0.1 to 0.6 ml). Rats were studied 14 days after surgery. Behavioral responses and changes in area under the curve (AUC) of the EMG signal to duodenal distension were calculated to evaluate the degree of visceral nociception. Distension-induced discomfort (behavioral activation) occurred at a volume of 0.2-0.3 ml and pain (stretching) at a volume of 0.4 ml. In addition, duodenal distension significantly increased AUC of baseline EMG ($p < 0.05$). Intraperitoneal (ip) injection of CRF ($n = 6$; 50 μg/kg) decreased the perception thresholds for discomfort (0.1 ml ; $p < 0.01$) and pain (0.2 ml ; $p < 0.005$) as compared to vehicle treatment ($n = 6$). This response could be inhibited by ip CP-154,526 ($n = 6$; 10 mg/kg, $p < 0.05$), a selective CRF_1 receptor antagonist. Furthermore, ip CRF increased the abdominal EMG response to duodenal distension ($p < 0.05$) as compared to vehicle treatment, an effect, which was augmented by ip pre-treatment of the selective CRF_2 antagonist anti-sauvagine30 ($n = 6$; 100 μg/kg ; $p < 0.001$). In addition, ip injection of selective CRF_2 agonists, stresscopin ($n = 4$; 120 μg/kg) or stresscopin-related peptide ($n = 4$; 25 μg/kg), increased the perception thresholds for discomfort (0.4 ml ; $p < 0.005$) and pain behavior (0.5-0.6 ml ; $p < 0.005$) as compared to vehicle treatment ($n = 5$). Furthermore, both CRF_2 agonists decreased the abdominal EMG response to visceral pain ($p < 0.05$) in comparison to vehicle-treated rats. Our findings demonstrate that activation of the peripheral CRF_1 receptor leads to a facilitation of afferent transmission of visceral nociceptive stimuli, whereas activation of the CRF_2 receptor leads to antinociceptive action.

- B08 -

NITRERGIC-PURINERGIC INTERACTIONS IN RAT DISTAL COLON MOTILITY. K. Van Crombruggen, R.A. Lefebvre. Heymans Institute of Pharmacology, University of Ghent, 9000 Ghent, Belgium.

Objectives : Evaluating the interplay between NO and ATP as mediators of NANC relaxations in the circular muscle layer of rat distal colon.
Methods : In the presence of guanethidine (4×10^{-6} M), mucosa-free circular muscle strips, pre-contracted with methacholine (10^{-4} M), were subjected to electrical field stimulation (EFS) and exogenous NO/ATP in the absence or presence of various agents that interfere with NO synthesis or NO/ATP transduction mechanisms.
Results : EFS (40V, 0.05 ms, 0.5-4 Hz for 30 sec) yielded tetrodotoxin (TTX ; 3×10^{-6} M)-sensitive relaxations which were not altered by the NO-synthase inhibitor N(omega)-nitro-L-arginine methyl ester (L-NAME ; 3×10^{-4} M), the soluble guanylyl-cyclase inhibitor 1H[1,2,4,]oxadiazolo[4,3-a]quinoxalin-1-one (ODQ ; 10^{-5} M) or the purinergic receptor P2Y antagonist Reactive Blue 2 (RB2 ; 3×10^{-5}M). The small conductance Ca^{2+}-sensitive K^+ (SK) channel blocker apamin (APA ; 5×10^{-7} M) moderately shortened the electrically-induced relaxations. L-NAME + APA however, nearly abolished these relaxations. The combinations ODQ + APA and RB2 + L-NAME significantly reduced the duration of the EFS-induced relaxation but did not significantly influence the amplitude. Exogenous NO (10^{-6}-10^{-4} M) elicited concentration-dependent, TTX-insensitive relaxations. ODQ reduced the length and amplitude, while APA only shortened the relaxations. ODQ + APA showed a marked inhibitory effect on the length and amplitude of the NO-induced relaxations. TTX, L-NAME, APA and RB2 shortened the relaxations induced by exogenous ATP (10^{-3} M) but did not influence the amplitude. ODQ had no effect. Adding APA to L-NAME and L-NAME to RB2 resulted in a more pronounced reduction in the duration than with L-NAME alone, but still had no effect on the amplitude of the ATP-induced relaxations. The combination APA + ODQ was not able to shorten ATP-induced relaxation more than APA alone and TTX + L-NAME did not yield a more pronounced inhibitory effect than TTX alone.
Discussion : These results indicate that in rat distal colon, both the nitrergic and the purinergic pathway must be blocked to inhibit EFS-induced relaxations. NO increases the sensitivity of the SK-channels to the co-released ATP via cGMP. Exogenous ATP (10^{-3}M) elicits relaxations by activating P2Y receptors with subsequent activation of SK channels and induces additional release of NO that directly activates SK channels.

- B09 -

POSSIBLE ROLE OF SERCA IN THE NITRERGIC RELAXATION OF RAT GASTRIC FUNDUS. L.A. Van Geldre, R.A. Lefebvre. Heymans Institute of Pharmacology, Ghent University, De Pintelaan 185, B-9000 Gent, Belgium.

Objectives : The aim of this study was to investigate whether nitrergic relaxation in rat gastric fundus involves the activation of the sarcoplasmic/endoplasmic reticulum Ca^{2+} ATPase (SERCA). Activation of SERCA will lower intracellular Ca^{2+} concentration directly by removing Ca^{2+} from the cytosol into the sarcoplasmic reticulum (SR) and indirectly by repleting the SR and removing the trigger for extracellular Ca^{2+} entry via the store operated Ca^{2+} channels.
Methods : Rat gastric fundus longitudinal smooth muscle strips were suspended in organ baths and changes in tension were measured auxotonically. Relaxation induced by nitric oxide (NO) (10^{-7} M, 3×10^{-7} M, 10^{-6} M, 3×10^{-6} M) and electrical field stimulation (EFS) (40 V, 0.5 msec duration, 10 sec train at 1, 2, 4 or 8 Hz) was assessed on tone raised by prostaglandin F_{2a} ($PGF_{2?}$) , thapsigargin (TSG), a SERCA inhibitor, or $PGF_{2?}$ in the presence of nifedipine.
Results : 1. Strips contracted by 10^{-7} M $PGF_{2?}$ were completely relaxed by nifedipine (10^{-6} M) and SKF 96365 (10^{-5} M). Strips contracted by TSG (10^{-6} M) were only for 20 ± 6% (n = 6) relaxed by nifedipine, but completely relaxed by SKF 96365. Tissues contracted by $PGF_{2?}$ in the presence of nifedipine were greatly but not completely relaxed by SKF 96365. 2. NO and EFS concentration- respectively frequency-dependently induced relaxation of $PGF_{2?}$-induced tone. The relaxation induced by EFS (1 - 8 Hz) and NO (10^{-7} M - 3×10^{-6} M) on TSG-induced tone was significantly decreased versus the responses on PGF_{2a}-induced tone. 3. In the presence of nifedipine, higher concentrations of PGF_{2a} still induce contractions. When tested on tone induced by $PGF_{2?}$ in the presence of nifedipine, the NO-mediated relaxation was unaffected, whereas EFS (1, 2, 4 and 8 Hz)-induced relaxation was significantly reduced. 4. The N-type Ca^{2+} channel antagonist conotoxin GVIA (10^{-7} M) significantly but only partially antagonized EFS-induced relaxation when tested on PGF_{2a}-induced tone.
Conclusion : The NO-mediated relaxation possibly involves the activation of SERCA. The reduction of EFS-induced relaxation when contraction is induced by $PGF_{2?}$ in the presence of nifedipine, suggests that L-type Ca^{2+} channels are involved in the release of endogenous NO.

- B10 -

EFFECT OF SILDENAFIL ON ESOPHAGEAL FUNCTION IN MAN. Xin Zhang, Magnus Simren, Roberto Dantas, Daniel Sifrim. Center for Gastroenterological Research, K.U. Leuven, 3000 Leuven, Belgium

Sildenafil, a phosphodiasterase 5 inhibitor that increases cGMP, has been used as to investigate the role of the NO-cGMP pathway in the esophagus. In man, sildenafil reduces basal LES pressure in patients with achalasia and reduces amplitude of contractions in nutcracker esophagus. In healthy subjects, sildenafil produces abnormal peristalsis. After acid reflux, esophageal clearance consists of an initial volume clearance followed by neutralization of the acidified mucosa by swallowed saliva (chemical clearance). Abnormal peristalsis or ineffective esophageal motility (IEM) has been claimed to affect saliva transport and esophageal emptying. We aimed to evaluate the effect of sildenafil on saliva transport and acid clearance in normal subjects.
Methods : Esophageal peristalsis was assessed in 14 healthy volunteers before and after sildenafil (50 mg). In 7 subjects, motility was studied together with transit of 2 ml of artificial saliva measured scintigraphicaly. In 10 subjects, motility was studied together with acid clearance tests performed with simultaneous pH and impedance.
Results : Sildenafil neither affect saliva secretion nor peristalsis in the proximal esophagus, but significantly reduced the amplitude or even abolished contractions at 15 cm distal to UES. Sildenafil provoked a graded impairment in esophageal motility but did not impaired the arrival of saliva to the distal esophagus. Sildeanfil prolonged both volume clearance and chemical clearance in supine position but only with severe IEM. In upright position, volume clearance was affected with severe IEM, but chemical clearace was not.
Conclusions : Sildenafil has profound effects on esophageal motility in healthy volunteers, however, this effect did not affect saliva transport and only sildenafil-induced severe IEM impaired esophageal clearance in supine position.

- B11 -

CLONING AND EXPRESSION PROFILING OF CANINE NK1, NK2 AND NK3 RECEPTORS. P. Peeters, B. Moreaux, R. De Hoogt, J. Van Den Berg, P. Verhasselt , A. Meulemans, B. Coulie. Dept. of Gastrointestinal and Emerging Diseases, Johnson and Johnson Pharmaceutical Research and Development, 2340 Beerse, Belgium.

Background : Studies on the role of NK_1, NK_2 and NK_3 receptors (NK_1R, NK_2 and NK_3R) in visceral pain are limited to rodents. At a pharmacological and molecular level human NK_1R, NK_2R and NK_3R differ from their rodent counterparts. We hypothesized that canine neurokinin receptors might constitute closer homologues to the human neurokinin receptors. AIMS : 1) To identify the cDNA sequence of canine NK_1R, NK_2R and NK_3R and to do sequence comparison across species. 2) To assess expression levels of neurokinin receptors in canine peripheral nervous and colo-rectal tissues.
Methods : Dog genomic libraries were screened with cDNA probes derived from human NK_1R, NK_2R and NK_3R in order to isolate canine NK receptor related sequences. Based upon these sequences RACE was performed on RNA from ascending colon and dorsal root ganglia resulting in full length cDNA encoding the canine NK_1R, NK_2R and NK_3R. Real time quantitative RT-PCR was performed on RNA derived from dog peripheral nervous and colo-rectal tissues to quantify expression levels of neurokinin receptors.
Results : The amino acid sequences of dog NK_1R, NK_2R and NK_3R resemble more closely human NK_1R, NK_2R and NK_3R (98%, 88%, and 91% homology, respectively) than those of mouse (96%, 86% and 74% homologous to human, respectively) and rat (96%, 88% and 88% homologous to human, respectively). High expression levels of NK_1R were found in lumbar and sacral parts of the spinal cord and their respectively dorsal root ganglia. In addition lower expression levels were detected in colo-rectal tissues. In contrast to NK_1R, expression of NK_2R was confined to colo-rectal tissues and urinary bladder. Expression of NK_3R was complementary to that of NK_2R since it was only detected in central and peripheral nervous tissues. Centrally expression was detected in thalamus, amygdala and frontal cortex whereas in the periphery expression was detected in cervical, lumbar and sacral parts of the spinal cord and their respectively dorsal root ganglia, thalamus, amygdala and frontal cortex.
Conclusion : We have demonstrated that canine neurokinin receptors closely resemble the human receptors. The NK_1R is mainly expressed on peripheral nervous tissues and colo-rectal tissues whereas NK_2R is exclusively expressed in colo-rectal tissues. The canine NK_3R is only expressed in central and peripheral nervous tissues.

- B12 -

STUDY ON THE NON-ADRENERGIC NON-CHOLINERGIC EXCITATORY NEUROTRANSMITTER IN MOUSE ILEAL CIRCULAR MUSCLE. Heiko U. De Schepper, Joris G. De Man, Benedicte Y. De Winter, Tom C. Seerden, Arnold G. Herman*, Paul A. Pelckmans. University of Antwerp, Division of Gastroenterology and *Pharmacology, Universiteitsplein 1, B-2610 Wilrijk, Belgium.

We studied the excitatory neurotransmission of mouse ileal circular muscle. Muscle strips were mounted in organ baths for isometric tension recording. Responses are expressed as % of a 50mM KCl contraction. Electrical stimulation (ES, 1-8 Hz) induced frequency-dependent contractions that were transient at 1 and 2 Hz and sustained at 4 and 8 Hz. All contractions were significantly enhanced by 0.3mM L-NNA (NOS blocker, ES 2Hz : 12 ± 2% to 29 ± 2% ; ES 4Hz : 17 ± 2% to 39 ± 2%, controls vs LNNA, n = 6). In the presence of L-NNA, 1µM atropine significantly reduced the contractions to 1 and 2 Hz but had no effect on those to 4 and 8 Hz (ES 2Hz : 29 ± 2% to 19 ± 3% ; ES 4 Hz : 39 ± 2% to 34 ± 4%, LNNA vs LNNA + atropine, n = 6). The residual contractions to ES, obtained in the presence of LNNA + atropine, were not affected by 1µM propranolol and 3µM phentolamine but abolished by 2µM TTX (blocks nerve-conductance). NK receptor desensitisation, which was achieved by prolongued incubation of separate muscle strips with septide, beta-A-NKA or senktide (all 1µM) during 20min, significantly reduced the contractions to ES (contraction to 4Hz was reduced from 28 ± 2% to 14 ± 2% after septide incubation ; from 31 ± 3% to 16 ± 5% after beta-A-NKA incubation ; from 28 ± 3% to 15 ± 2% after senktide incubation (all n = 4-6). Strips incubated with septide still contracted to beta-A-NKA and vice versa indicating that there was no cross-desensitisation. Substance P (SP, 1-100nM) induced dose-dependent sustained contractions. These were mimicked by the specific NK1 and NK2 receptor agonists septide and beta-A-NKA respectively (both 1-100nM) while the NK3 receptor agonist senktide (1nM-1µM) had no contractile effect. The contractions to SP and beta-A-NKA were not significantly affected by L-NNA and atropine. The contractions to septide were slightly inhibited by atropine and significantly enhanced by L-NNA (10 nM septide : from 6 ± 1% in controls to 3 ± 1% by atropine and to 20 ± 2 by atropine+LNNA, n = 5). In the presence of LNNA+atropine, 2µM TTX had no further effect on the response to SP, septide and beta-A-NKA. Our results suggest that a tachykinergic neurotransmitter is released from enteric nerves innervating the circular muscle of the mouse ileum and that NK1, NK2 and NK3 receptors are functionally active in this tissue. Activation of NK1, NK2 and NK3 receptors exerts a neurogenic effect involving nitrergic, cholinergic and tachykinergic nerves. In addition, activation of NK1 and NK2 receptors also exerts a direct smooth muscle effect.

- B13 -

EFFICACY DISTRIBUTION OF 5-HT7 RECEPTORS THROUGHOUT THE CANINE GASTRIC CORPUS. *[a]P. Janssen, *N.H. Prins, *A. Meulemans, [a]R.A. Lefebvre. *Johnson & Johnson Pharmaceutical Research and Development, Beerse, Belgium, [a]Heymans Institute of Pharmacology, Ghent University, Gent, Belgium.

Background and aim : We previously demonstrated the presence of relaxatory smooth muscle 5-HT_7 receptors in longitudinal muscle of canine proximal stomach. The aim of this study was to investigate the efficacy distribution of 5-HT_7 receptors throughout the canine gastric corpus.
Methods : The gastric corpus was divided in 6 ventral regions. Mucosa- and submucosa-denuded longitudinal muscle strips (MS) were cut from these regions and mounted in a classical organ bath set-up for isotonic measurement. On $PGF_{2?}$-induced sub-maximal contraction the selective 5-HT_7 receptor antagonist SB-269970 (10 nM) or saline was left to incubate at least 15 min before the selective 5-$HT_{1/7}$ receptor agonist 5-carboxamidotryptamine (5-CT) was added in a cumulative manner (1 nM - 0.1 mM). All experiments were done in the presence of antagonists blocking 5-HT_{1A}, 5-$HT_{1B/1D}$, 5-HT_{2A}, 5-HT_{2B}, 5-HT_3 and 5-HT_4 receptors. The operational model of agonism (a theoretical model for agonist action) was used to estimate the affinity (K_A) and relative efficacy (? representing the ratio of receptor density over transductional mechanism efficiency) of 5-CT in the different regions.
Results : 5-CT relaxed all PGF_{2a}-contracted MS ; the distal region close to the minor curvature showed the highest potency to 5-CT (pEC_{50} = 7.58 ± 0.16) with the largest maximal effect (108 ± 2%), while the proximal region close to the greater curvature showed the lowest potency to 5-CT (pEC_{50} = 5.96 ± 0.10) with the smallest maximal effect (75 ± 9%). SB-269970 antagonised in all regions the 5-CT-induced effects without affecting slope and maximum effect. The associated pA_2 value ranged from 8.37 ± 0.13 to 8.72 ± 0.14, this indicated 5-HT_7 receptor involvement in all regions. The affinity as well as the E_{max} parameter for 5-CT was fixed (pK_A = 6.2, E_{max} = 110) to estimate ? in the different regions. In the distal region close to the minor curvature ? yielded 32 ± 11, whereas ? in the proximal region close to the greater curvature was 2.0 ± 0.39. Overall, 5-HT_7 receptors in distal regions were more efficacious compared to those in proximal regions and 5-HT_7 receptors in regions close to the minor curvature were more efficacious to 5-CT compared to those in the regions close to the greater curvature.
Conclusion : This study illustrates that 5-HT_7 receptors are present throughout the ventral wall of the canine gastric corpus ; these receptors show the highest efficacy in the distal part of the corpus, close to the minor curvature.

- B14 -

GLIAL CELLS, BUT NOT INTERSTITIAL CELLS, EXPRESS P2X7, A IONOTROPIC PURINERGIC RECEPTOR, IN THE RAT GASTROINTESTINAL MUSCULATURE. Jean-Marie Vanderwinden, Jean-Pierre Timmermans*, Serge N. Schiffmann. Laboratoire de Neurophysiologie, Université Libre de Bruxelles, Belgium ; * Laboratory of Cell Biology and Histology, University of Antwerpen, Belgium.

Purinergic (ATP) neurotransmission is a component of the inhibitory response of the musculature in various regions of the gastrointestinal (GI) tract. So far seven ionotropic purinergic receptors (P2X1-7) have been cloned. As specific antibodies become available, their respective distribution in the GI tract can be elucidated. Here we used high resolution tricolor confocal microscopy as previously described to study the distribution of P2X7 immunoreactivity (-ir) in the muscularis propria of the rat stomach, small intestine and colon. In all the regions studied, P2 × 7-ir was observed in the myenteric and submucosal ganglia. Nerve terminals appeared prominently labeled. In the muscle layers, cells expressing P2 × 7-ir were also observed. Smooth muscle cells, Kit-ir interstitial cells of Cajal and CD34/SK3-ir fibroblast–like cells were P2 × 7 negative, while P2 × 7-ir was observed in nerves and in S100-ir glial cells. In the rat GI tract, P2 × 7-ir is present in nerves and S100-ir glial cells but not in smooth muscle nor in interstitial cells. This suggests a role for glial cells in the purinergic neurotransmission in the GI tract.

- B15 -

EFFECTS OF INTESTINAL SCHISTOSOMIASIS ON SOMATOSTATIN AND SOMATOSTATIN RECEPTOR 2A EXPRESSION IN MURINE ILEUM. F. De Jonge (1), L. Van Nassauw (1), J.G. De Man (2), B.Y. De Winter (2), F. Van Meir (1), I. Depoortere (3), T.L. Peeters (3), P.A. Pelckmans (2), E. Van Marck (4) and J.-P. Timmermans (1). (1) Laboratory of Cell Biology and Histology ; (2) Laboratory of Gastroenterology ; (3) Centre for Gastroenterological Research, University of Leuven ; (4) Laboratory of Pathology, University of Antwerp.

Intestinal schistosomiasis is characterized by motility-related disorders. In this study, the presence and effects on intestinal contractility of somatostatin and its receptor, SSTR2A, were investigated in the ileum of normal and infected mice. The distribution of somatostatin and SSTR2A was visualized using immunocytochemistry. Radioimmunoassay combined with oogram studies was performed to determine somatostatin levels, and contractility measurements were done in organ bath experiments. Schistosomiasis resulted in a significant decrease in somatostatin-positive endocrine cells, whereas the number of somatostatin-immunoreactive neuronal cell bodies did not change. From 8 weeks postinfection onwards, an increase was noted in somatostatin-immunoreactive nerve fibers in both villi and granulomas. SSTR2A, expressed in somatostatin-negative myenteric cholinergic neurons, was upregulated during infection. In infected mice, somatostatin levels were negatively correlated with the number of eggs during the acute phase, and were elevated during the chronic phase. Pharmacological experiments revealed that schistosomiasis diminished the inhibitory effect of somatostatin on neurogenic contractions. Schistosomiasis influences the distribution and concentration of somatostatin and SSTR2A in the murine ileum, and disturbs the inhibitory action of somatostatin on neurogenic contraction.

- B16 -

THE NEUROPEPTIDE SOMATOSTATIN MAY DETERMINE FIBROSIS IN SCHISTOSOMIASIS. S. Chatterjee (1), A. Mbaye (2), J. Weyler (3), P. Van Damme (3), A. Deelder (4), E. A. E. Van Marck (1). (1) Pathology Unit, Dept. of Medicine, University of Antwerp, Belgium ; (2) Medical Region of Saint-Louis, BP394 Saint-Louis, Senegal ; (3) Epidemiology & Social Health, Univ. of Antwerp, Belgium ; (4) Leiden Univ. Medical Center, Leiden, The Netherlands.

Background : Variceal bleeding due to portal hypertension is frequently encountered in liver cirrhosis patients, and at present the neuropeptide somatostatin is the drug of choice for this indication. Similar pathology is also caused by Symmers pipe-stem fibrosis, generated by the blood fluke *Schistosoma mansoni*. During chronic infection, activated hepatic stellate cells (HSC) produce extracellular matrix proteins in the liver, thereby generating fibrosis. Recent studies demonstrate the presence of somatostatin receptors on the surface of the HSC, whereby somatostatin exerts a direct antifibrotic effect on the HSC in vitro, and reduces fibrosis and morbidity in *S. mansoni* infected animals.
Objective : In recent years, cases of severe morbidity (fibrosis, haematemesis, hepatosplenomegaly, ascites) due to *S. mansoni* infections are on the rise in Northern Senegal. Our objective was to study possible correlation between fibrosis and the inability to generate substantial levels of endogenous somatostatin, in *S. mansoni* infected subjects.
Design : Human volunteers from the district dispensary at Richard Toll, in the Medical Region of Saint-Louis, Senegal, were classified according to age, sex, occupation, height, weight, and parasite eggs per gram. They participated in a water contact and morbidity questionnaire, underwent a clinical examination and donated 5ml of peripheral blood for plasma levels of somatostatin, detected by an enzyme immunoassay (sensitivity 0.06-.08 ng/ml, range 0-25ng/ml). Ultrasonography following the WHO approved Niamey-Belo Horizonte method, was used to detect fibrosis grade in all subjects. Normal liver was termed Pattern A, echogenic, peripheral thickening was scored B-F.
Result : A t-test showed significantly lower somatostatin levels in severe morbidity patients ($p = 0.000002$), as compared to exposed but uninfected subjects residing in the same region. Multiple logistic regression analysis taking into account age, sex and prior treatment showed an adjusted odds ratio of 0.344 ($p = 0.003$). Non-fibrotics had more circulating somatostatin (N = 22, median = 4.214, Lower 95% CI = 3.401, Upper 95% CI = 4.980) than fibrotics (N = 30, median = 2.376, Lower 95% CI = 2.152, Upper 95% CI = 3.328) (Mann-Whitney U = 170, P = 0.0031).
Conclusion : In schistosomiasis patients, physiological levels of somatostatin may determine disposition of particular individuals towards fibrosis as opposed to others. Host pathology can thus be alleviated by somatostatin's therapeutic ability to treat bleeding oesophageal varices, reduce portal pressure and treat fibrosis in schistosomiasis patients.

DIFFERENCES IN THE ABILITY OF MOTILIDES TO INDUCE MOTILIN RECEPTOR INTERNALIZATION UNDERLY THEIR DESENSITIZING CAPACITY. L. Thielemans, J. Perret*, I. Depoortere, P. Robberecht*, T.L. Peeters. Gut Hormone Lab, University of Leuven and *Department of Biochemistry and Nutrition, Universite Libre de Bruxelles, Belgium.

Background : There are marked differences in the ability to desensitize the motiline receptor (MTLR) between the motilides ABT-229 and erythromycin-A (EM-A), which cannot be explained by differences in potency (*Gastroenterol*., 2002, 122(4) W1030). Aim. To explore whether this translates into differences in MTLR internalization.
Methods : A CHO-K1 cell line containing the Ca^{2+} indicator apoaequorin was stably transfected with a plasmid containing MTLR C-terminally tagged with EFGP (Enhanced Green Fluorescent Protein). Desensitization was studied by preincubation of the cells with 10^{-5} M of motilin, EM-A or ABT-229 prior to stimulation with motilin. The maximal response to the second stimulation was expressed as a percentage of control (no prestimulation). For visualization of endocytosis, images of stimulated cells were analyzed by the Scion Image Software. Internalization was also quantified by determining the residual binding of radio-iodinated motilin after prestimulation with agonists.
Results : The maximal response to motilin was reduced to 19 ± 2 and 3 ± 1% after prestimulation with motilin or ABT-229, but was barely affected after EM-A (99 ± 8%). Pictures of cells before and after stimulation for 1h at 37°C show that all agonists (10^{-5} M) induced significant (at least $p < 0.005$) changes in the distribution of the MTLR. Membrane fluorescence significantly decreased by 16 ± 2, 25 ± 2 and 8 ± 2% for motilin, ABT-229 and *EM-A resp ($p < 0.0001$; *$p = 0.04$ vs control), while cytosol fluorescence increased by 24 ± 2, 25 ± 2 and 19 ± 2% ($p < 0.0001$ vs control). Receptor binding studies confirmed that stimulation for 1h at 37°C with EM-A did not induce MTLR internalization, as residual binding remained at 96 ± 4% compared to 31 ± 3% and 21 ± 1% after stimulation with motilin and ABT-229.
Conclusion : The extent of receptor internalization for ABT-229, motilin and EM-A corresponds to their ability to desensitize the motilin receptor. The strong desensitizing capacity of ABT-229 may have contributed to the failure of ABT-229 in clinical trials.

ACHIS-DPHE2 - VIP/GRF-A VPAC1 RECEPTOR ANTAGONIST- IS AN INVRSE AGONIST ON TWO CONSTITUTIVELY ACTIVE TRUNCATED VPAC1 RECEPTOR. P. Vertongen, C. Langlet, I. Langer, N. Gaspard, J. Cnudde, P. Robberecht. Department of Biochemistry and Nutrition, Faculté de Médecine, Université Libre de Bruxelles.

The relative contribution to the coupling to the effectors of the different intracellular domains of the human VPAC1 receptor was not yet systematically studied. We evaluated the role of the carboxy terminal tail by progressive deletions. The study was conducted on CHO cells stably expressing the recombinant constructions. Binding studies and adenylate cyclase activity determination were performed. The truncated receptors (1-398), (1-421), (1-429), (1-433), (1-436), (1-441), (1-444) were compared to the (1-457) wild type receptor. All the truncated receptors except the (1-441) and (1-436) were comparable to the wild type receptor when considering the following parameters : receptor density, binding properties of agonists and antagonist, adenylate cyclase activation. Cells expressing the (1-441) and (1-436) VPAC1 receptors had the following properties :
a)They expressed the receptor of a lower density but the receptors had binding properties comparable to that of the wild type receptor.
b) the basal adenylate cyclase activity was increased 3 fold as compared to the wild type receptor, but the stimulability of VIP was maintained.
c) the VPAC1 antagonist (AcHis - DPhe2-VIP/GRF) inhibited by 40 to 60% the basal adenylate cyclase activity with a EC50 value identical to its IC50 value for binding inhibition.
Conclusion : 1. The carboxy terminal tail of the VPAC1 is involved in the equilibrium between the active and inactive forms of the receptor. 2. The VPAC1 antagonist behaves like an inverse agonist on the weak constitutively active receptors obtained by truncation.

- C01 -

ANTIMICROBIAL RESISTANCE RATES OF HELICOBACTER PYLORI IN BELGIUM : PRESENTATION OF THE A NATIONAL SURVEILLANCE PROGRAMME. A. Burette (1), Y. Glupczynski (2) and the Belgian H.pylori Study Group. (1) Gastroenterology Unit, CHIREC-Nouvelle Clinique de la Basilique ; (2) Microbiology Dept, Cliniques Universitaires St-Luc, Brussels, Belgium.

Aim of the study : Awareness of the local and national resistance rates for metronidazole and clarithromycin is thus essential for effective treatment and to select the first line eradication regimen accordingly. There is also an urgent need for annual national survey of antimicrobial resistance rates in Belgium because of the increasing incidence of *Hp* strains resistant to antibacterial drugs. The prevalence of multi-resistant strains is also increasing and may therefore render the first-line regimens less useful or even useless in the years to come.
Method : 13 centres (able to performed the sampling and to freeze and keep the samples at –70°C for later collecting) have accepted to participate to a national surveillance study of anti-microbial resistance of *Hp* strains to macrolides, imidazoles, amoxycillin, tetracycline, etc. The geographic distribution of the centres covers an area located in the centre-north and centre-south of Belgium (Antwerpen, Hasselt, Brussels, Charleroi, Namur, Liège). The definitive protocol will be conducted during pre-defined 8 weeks period each year (march + april) with collection of samples from 15-25 consecutive naïve patients, who never received anti-*Hp* therapy (and no history of recent antimicrobial, bismuth or PPI therapy within the last 2-3 weeks). At least 1 (or 2 if possible) biopsy sample(s) from each naïve patient will be placed in a special transport medium and kept, within 4-6 h from collection, at –70°C. One biopsy urease test will also be performed in the antrum after sampling for the culture in order to identify those samples, which are to be taken in account for positive culture. Urease test and portagerm for culture will be send to the different centres after definitive confirmation of their participation. Participant will also be asked to complete a sampling information list including : N° and date of sampling, patients initials and birth date, patient gender and ethnic origin (Caucasian, Maghrebian, African, Asian,…) and the patient's address post-code. Collection of the samples will be organized at the end of the sampling period for central proceeding of the cultures.
Results : The results of such an inquiry and of the yearly prevalence of resistance of *Hp* to antimicrobials could be presented each year at the Belgian Week meeting. The last 2002 data concerning antimicrobial resistance rates from 5 different centres in Belgium who perform regularly *Hp*-cultures and antimicrobial susceptibility testing (Brussels 4x, Mont-Godinne and Charleroi/Jumet) will be presented.

- C02 -

QUADRUPLE THERAPY WITH OMEPRAZOLE, RANITIDINE-BISMUTH CITRATE, TETRACYCLINE AND METRONIDAZOLE TO CURE CLARITHROMYCIN-RESISTANT H.PYLORI. A. Burette (1), P. Deprez (2), C. DePrez (3), Y. Glupczynski (4). (Belgian H.pylori Study Group). (1) Gastroenterology Unit, CHIREC-Nouvelle Clinique de la Basilique ; (2) Gastroenterology Dept ; (3) Pathology Dept, CHU Brugmann ; (4) Microbiology Dept, Cliniques Universitaires St-Luc, Brussels, Belgium.

Aim : Eradication of clarithromycin-resistant *H.pylori* (*Hp*) is not easy. A rescue quadruple therapy including PPI bid + CBS 120 mg bid + T 500 mg qid + M 500 mg tid for 7 days (OBTM7) is proposed by the 'Maastricht 2-2000' consensus to cure the infection in those patients. However the only bismuth salt still available in Belgium is the ranitidine-bismuth citrate (RBC) whose substitution in place of CBS in the recommended classical quadruple therapy has not been assessed. The aim of this prospective double-centre study is to assess the efficacy of a one week quadruple therapy with Omeprazole (0), RBC (B_R), Tetracycline (T) and metronidazole (M) to cure Clarithromycin(C)-resistant *H.pylori* (*Hp)* infection according to pre-study susceptibility testing.
Method : Patients with primary or post-treatment C-resistant *Hp*+ve gastro-duodenal ulcer, oesophagitis or gastritis were given O 20 mg bid + R 400 mg bid + T 500 mg qid + M 500 mg tid for 7 days (OB_RTM7). At inclusion, *Hp* status was assessed in antral and body biopsies by urease test, histology and culture. Post-T_R assessment (endoscopy as pre-study or ^{13}C-UBT) was performed D4-8 weeks after therapy : patients were considered positive if any of the post treatment tests was positive. Susceptibility testing to M and C was performed by disc diffusion method or by E-test. Eradication rates are reported on a per protocol analysis.
Results : 38 patients (27 consecutive from centre A and 11 from centre B ; M/F = 10/28, mean age 54 y) were enrolled and received the OB_RTM7 regimen and returned for post-treatment assessment. All were considered compliant. The treatment was well tolerated in most of the patients. 30/38 patients experienced a previous failed therapy (1 TRT : 21 pts ; 2 TRT : 7 pts ; 3 TRT : 2 pts). Overall, eradication of *Hp* was confirmed in 74% (28/38) of the patients : 89% (24/27) from centre A and 36% (4/11) from centre B. All the patients infected with M-sensitive *Hp* strains were cured although 85% and 22% of those infected with double C + M-resistant strains were cured in centre A and B respectively.
Conclusion : OB_RTM7 regimen is a safe and well tolerated in most of the patients. Eradication of clarithromycin-resistant *H.pylori* was achieved in 100% of the patients infected with M-sensitive Hp strains and 66% of the patients infected with double C + M-resistant strains, although important difference in eradication rates were observed among the 2 centres. Quadruple therapy eradication rates from centre A are similar using either with CBS or RBC as Bi salt (94 vs 89%).

- C03 -

H PYLORI AND REFLUX DISEASE. E. De Koster, Gastroenterology Department, Brugmann University Hospital (VUB-ULB), Brussels, Belgium.

In this review we will confront the Maastricht 2-2000 guidelines on HP and GERD with new litterature data.
The Maastricht 2-2000 Consensus Report states that :
(1) *H pylori eradication does not exacerbate pre-existing GERD*. This is confirmed by Schwizer et al (Lancet 2001 ; 357 : 1738-42), who find that HP eradication may postpone GERD symptom relapse, and Moayyedi *et al.* (GE 2001 ;121 : 1120-6), who show that HP status or HP eradication has no influence on GERD symptom relapse.
(2) *H pylori eradication is not associated with the development of GERD...* This is confirmed by Malfertheiner et al (APT 2002 ;16 : 1431-42), who find less heartburn after HP eradication in duodenal ulcer (DU) patients (pts), and less heartburn after gastric ulcer treatment, independent of HP status. Ulcer relapse is an important cause for heartburn relapse. Laine et al (Am J GE 2002 ; 97 : 2992-7) found that after HP eradication in DU patients, erosive esophagitis developed in 4% of HP eradicated pts vs 3% of not-HP eradicated pts (ns), de novo GERD symptoms develop in 14% of HP eradicated pts vs 20% of not-HP eradicated pts (ns), and GERD symptoms worsened in 7% of HP eradicated pts vs 15% of not-HP eradicated pts ($p = 0.02$). Laine et al (APT 2002 ; 16 : 1143-8) also showed that HP eradication in dyspepsia patients does not worsen quality of life due to reflux symptoms.
(3*)… although there is a suggestion that patients with predominant corpus gastritis could be at risk…* This is confirmed by Feldman et al (Am J Physiol 1999 G1159–G1164) who find an increase in basal gastric acidity and oesophageal acid exposure in HP-eradicated asymptomatic subjects, while these parameters did not change after HP eradication failure. Koike et al. (APT 2001 ; 15(6) : 813-20) found that increased gastric acid secretion after HPeradication is a risk factor for developing reflux oesophagitis.
(4*) … suggests that long-term profound acid suppression may accelerate the progression of H.pylori-induced corpus atrophic gastritis, although not all studies agree.* No new data on the role of acid inhibition on acceleration of corpus atrophic gastritis. However, it could be argued that the shift to corpus –predominant gastritis induced by acid suppression is in se reason enough to eradicate HP, because corpus-predominant gastritis is an important rik factor for gastric cancer development (RR 34.5) (Uemura et al NEJM 2001 ; 345 : 784-9).

- C04 -

WHAT'S NEW IN H. PYLORI AND NSAIDS ? A. Burette, Gastroenterology Unit, CHIREC-Nouvelle Clinique de la Basilique.

The role of *H.pylori* infection to ulcerogenesis and to upper gastro-intestinal bleeding in users of NSAIDs is complex as *Hp* interacts with NSAIDs in different ways. Whether an ulcer will occur is influenced by factors such as previous exposure to NSAIDs, past history of ulcer/ulcer complication, mucosal neutrophil infiltration, gastric acid output and the use of acid-suppressive therapy. The Maastricht 2-2000 consensus meeting concluded that *Hp* and NSAIDs/aspirin are independent risk factors for peptic ulcer and peptic ulcer bleeding, based on level 2 evidence, and, additionally, that NSAIDs should be considered separately from aspirin in this respect. Until recently, the relation between *Hp* infection and use of NSAIDs in the pathogenesis of PUD was controversial, because studies examining these 2 risk factors in this disorder have given conflicting results, which probably reflect the complex relationship between these 2 factors as well as methodological heterogeneity between studies. The more recent studies from the last 2-3 years -including observational and interventional studies- have brought some progress/confirmations in our understanding of the interactions between *Hp* and NSAIDs. It is now evident that both *Hp* and NSAID use independently and significantly increase the risk of peptic ulcer and ulcer bleeding but also that there is a synergism for the development of peptic ulcer (particularly DU) and ulcer bleeding between these 2 factors. Data also suggest that low-dose aspirin and NSAIDs may have different interactions with *Hp* in terms of the risk of peptic ulcer bleeding. Based on the existing evidence, several recommendations on *Hp* eradication are suggested for the prevention of NSAID-induced ulcers. For NSAID-naïve patients who also have high-risk factor(s) for developing NSAID-gastropathy (e.g. old age or past history of ulcer), or for those with a past history of peptic ulcer (particularly DU), the policy of test-and-treat for *Hp* before initiating NSAID therapy should be recommended. Testing for *Hp* infection would not be necessary for patients who had already been receiving NSAID for a long time without developing adverse events. However, *Hp* eradication cannot replace maintenance treatment with acid suppressive agents or misoprostol in regular NSAID takers at high risk of ulcer bleeding. Curing *Hp* infection alone may also be adequate for patients with ulcer complications associated with low dose aspirin.

- C05 -

HELICOBACTER PYLORI AND DYSPEPSIA. P. Lammens, St-Jean, UCL, Brussels.

The management of dyspepsia in the young patient (< 45-55 years) remains controversial, with 4 differents “first step” options described in the literature :
1. Empirical medical therapy (PPI, prokinetics…)
2. Endoscopy and biopsy (“gold standard”, mandatory > 45 - 55 years, and with “alarm” symptoms).
3. Test HP (UBT, serology…) and scope if positive.
4. Test and treat HP.
The role of HP in non-ulcer dyspepsia (NUD) remains unclear and also controversial.
New data give more precisions related to the topography of the lesions :
1. Cancer relative risk of 34 in corpus gastritis (1).
2. Good therapeutic response in antrum dominant gastritis (2).
All recent data (2,3) favour HP eradication in all symptomatic patients.
In Belgium, where the cost of the technique is low, endoscopy is probably the best way to manage and reassure the patient.

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3. Dyspepsia - Management Guidelines, April 2002, British Society of Gastro-enterology (www-bsg.org.uk/clinical-prac/guidelines/dyspepsia.htm).

- C06 -

DO WE NEED BIOPSIES FROM THE GASTRIC MUCOSA ? N. Ectors. Department of Pathology, University Hospitals Leuven, KULeuven, B-3000 Leuven, Belgium.

The gastric mucosa is a specialized organ and in the lifespan of most individuals is exposed to a variety of “injurious” agents. Consequently gastritis is an extremely common condition, while peptic ulcer disease used to be so. Furthermore, gastric cancer is still the fifth cause of death worldwide. The introduction of endoscopic examination has provided access to almost the entire gastro-intestinal tract. Except for the obvious direct visual diagnostic properties this approach allowed for therapeutic interventions. Moreover, mucosal samples could be obtained allowing for further diagnostic investigations such as histology. After the initial apprehension and challenge the sampling of the mucosa has become an integral – automatic - extension of the examination itself, resulting in publications entitled “Gastroscopy is incomplete without biopsies” (Carpenter e.a., 1995) on the one hand and specific reimbursement rates for endoscopy with and without biopsies on the other hand. More recently, clinical guidelines have been introduced to promote “best practices” in order to improve the outcomes of treatment. For example European and national guidelines have been issued for the eradication of Helicobacter pylori (Maastricht Concensus report, 1997). The (updated) Sydney classification aimed at stratifying endoscopy and histology (Dixon e.a., 1996). Reimbursement rates for powerful drugs such as proton pump inhibitors have been linked to the prelevation of gastric biopsies in order to exclude malignancy. However, guidelines place most weight on evidence generated in randomised controlled trials i.e. “evidence based medicine” but do also rest on a number of assumptions. The more recent awareness of the cost of health services and especially the resource constrains have announced a new era. Cost effectiveness of management strategies, including diagnosis, treatment and reimbursement, are under scrutiny. It appears the need to evaluate clinical effectiveness, cost and repercussions in real terms before the widespread dissemination has not always been acknowledged.

- D01 -

AB INITIO COMPLETELY STEROID-FREE IMMUNOSUPPRESSION DURING AND AFTER LIVER TRANSPLANTATION : LONG-TERM 3 YEAR FOLLOW-UP REPORT. J. Pirenne, F. Nevens, C. Verslype, T. Roskams, P. Yap, W. Van Steenbergen, R. Aerts, J. Fevery. U.Z. Gasthuisberg, Leuven, Belgium.

Steroids have traditionally been used in liver transplantation (LTx) as a part of induction and maintenance immunosuppression (IS) regimen. Steroids act non specifically and cause multiple side effects. Most LTx centers reduce the dosage of steroids and eventually withdraw them after various time intervals. A few completely steroid-free IS trials have been recently conducted after LTx but long-term data are not yet available. In addition, in these trials steroids were usually given during surgery. We report the longest-term (median = 40 months) follow-up data of a prospective pilot study designed to determine whether LTx can be performed with no steroids at all (neither during nor after surgery). Methods. 21 consecutive LTx in 20 adult patients between 08/1998 and 07/1999 were prospectively included in an *ab initio* steroid-free immunosuppressive protocol. Mean age was 54 years (40-67). Tacrolimus (through levels, 8-10 ng/ml) and azathioprine (1 to 2 mg/kg) were started after LTx. Patients were given no steroid neither during nor after LTx except in the event of rejection or in case of tacrolimus or azathioprine toxicity requiring significant dose reduction and/or withdrawal. Results. There has been no case of primary graft dysfunction or non function. 11 of 21 LTx (52%) received no steroids throughout the whole study. Early acute rejection developed in 5 of 21 LTx (23.5%). Those rejections responded to standard iv steroids (plus ATG in one patient), followed by an oral steroid taper stopped 3 months after rejection. There was no case of chronic rejection. Steroids were transiently given in 6 LTx for non-immune reasons : 2 with tacrolimus-induced neurotoxicity, 3 in whom azathioprine was discontinued, and 1 for an allergic reaction ; 4 of these 6 patients are off steroids at last follow-up. The 3 year graft and patient survival is 95% and 100%, respectively. Conclusions. Steroids are not necessary in more than 50% of LTx. Steroids were transiently needed to treat acute rejection in 23.5% LTx and for toxicity of calcineurin inhibitors or azathioprine or other reason in 28%. Of the patients who received steroids the majority (70%) was eventually taken off steroids. This prospective single-center pilot study shows that LTx without steroids (during and after surgery) is feasible and yields no penalty in terms of acute and chronic rejection, immune graft loss, graft function, patient and graft survival.

- D02 -

PREDICTIVE MODELS OF SHORT- AND LONG-TERM SURVIVAL IN PATIENTS WITH NON BILIARY CIRRHOSIS. G. Longheval (1), P. Vereerstraeten (2), P. Thiry (3), M. Delhaye (1), O. Le Moine (1), J. Devière (1), N. Bourgeois (1), M. Adler (1). (1) Dpt of Gastroenterology ; (2) Nephrology and (3) Clinical Chemistry, Erasme Hospital, 1070 Brussels, Belgium.

The limited number of donor organs has placed a burden on the medical community to improve patient selection and timing of liver transplantation. We aimed to evaluate short and long-term survival of 124 consecutive patients with the diagnosis of non biliary cirrhosis. Seventeen clinical, biochemical, functional and hemodynamic parameters were computed. Patient survival was evaluated in the short-term (3 months) by logistic regression and the predictive power of the model was evaluated using receiver operating characteristic (ROC) curves and the likelihood ratio test. For the long-term (up to 5 years) prognosis, the Cox proportional model was used. During the follow-up, 54 patients died and 20 were transplanted. In the short-term study, the MELD score (including bilirubin, INR and creatinine) was as predictive as to our score, which contain only 2 independent indicators (bilirubin and creatinine). In the long-term study, 3 independent variables (albumin, INR and creatinine) emerged from the Cox model and patients were classified into three survival risk groups according to a prognostic index : $-1.039 \times \text{albumin (g/dl)} + 1.909 \times \log_e \text{INR} + 1.207 \times \log_e$ serum creatinine (mg/dl). Survival probability at 1 and 5 years was 89% and 80%, 63% and 52%, 23% and 10% respectively with a low, medium and high prognostic index. The validation study using the split-sample technique and the data of independent patients confirmed that a high PI (> –2.5) identifies patients with a bad prognosis within 5 years. We have thus demonstrated and validated that the risk of death at short and long-term of patients with non-biliary cirrhosis can be predicted with a great accuracy using models containing few, simple and easily obtained objective variables and these survival models are useful tools in clinical decision making, especially in deciding listing patients for liver transplantation and prioritization on the liver waiting list.

- D03 -

PSYCHOLOGICAL ISSUES AFTER DONATION : A RETROSPECTIVE DONOR SURVEY FOLLOWING LIVING DONOR LIVER TRANSPLANTATION IN ADULT (ALDLT). R. Troisi*, H. Dick**, G. De Cuypere**, S. Ricciardi*, D. Vogelaers#, I. Colle***, H. Van Vlierberghe***, G. Militerno*, U.J. Hesse*, B. de Hemptinne*. Dept. of *General, Hepato-Biliary and Liver Tx Surgery, **Psychiatry, #Internal Medicine, ***Hepato-Gastroenterology, Ghent University Hospital Medical School, Gent-Belgium.

Introduction : ALDLT is an accepted alternative to cadaveric organ transplantation. Potential donor candidates are asked to decide within a short time whether to become a donor, especially when recipient's conditions are worsening. We review our experience focusing on the decision making process and on the occurrence of personal and familial problems. Quality of life (QOL) was assessed after donation.
Methods : Questionnaires were sent to 24 donors that underwent right or left hepatectomy from 9/99 and 6/2002. The questionnaire was used to inquire about the decision-making process, personal, familial problems or economic consequences. The QOL was done using a standard SF-36 Healthy Survey (Italian, Dutch and French versions). Impaired QOL was assumed in case of T scores £30.
Results : Of a total of 24 donors, 22 replied (92%). No questionnaires were answered by phone. Among 22 donors, there were 13 man and 9 women with a mean age of 33 ± 7 years. The shortest FU was of 5 months. The decision to donate was easy to take in most of the donors (17/22). Familial problems after donation did not worsen (21/22) : one donor changed the partner thereafter. No major medical complications were recorded and no one was reoperated. However, most of donors experienced severe postoperative pain (15/22). Surgical scar was not considered a problem in the majority (19/22). No one had any problem with his or her employer as a result of mean temporary interruption of 9 weeks (range 3 to 36). Financial problems were recorded in 5/22 donors. The majority of donors (21/22) had no doubts concerning the decision to donate (96% in favour). QOL resulted in average values of 50 for "Physical and Emotional Sum Score".
Conclusion : Donors viewed ALDLT positively, however, there is a prolonged period of physical rehabilitation and financial disadvantages are encountered.

- D04 -

FIRST CLINICAL EXPERIENCE WITH AN E-PTFE-COVERED NITINOL ENDOPROSTHESIS FOR TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT PROCEDURES. G. Maleux (1), F. Nevens (2), J. Vaninbroukx (1), M. Thijs (1), S. Yap (2), C. Verslype (2), J. Fevery (2). Dpt of Radiology (1) and Hepatology (2), University Hospitals, 3000 Leuven, Belgium.

To evaluate the feasibility, safety and efficacy of transjugular intrahepatic portosystemic shunts (TIPS) with expanded-polytetrafluoroethylene (e-PTFE)-covered stents and its influence on TIPS-induced hepatic encephalopathy. Between August 2000 and November 2002, an e-PTFE covered nitinol stent-graft was implanted to create TIPS in 48 patients. Indications for TIPS were recurrent variceal bleeding (n = 21), refractory ascites (n = 32), haemorrhagic gastropathy (n = 4), hepatic hydrothorax (n = 7) and other complications of cirrhosis (n = 4). Twelve patients were treated for TIPS-stent occlusion after placement of a classic bare stent (Wallstent), and 36 patients treated as de novo TIPS. Patients underwent Doppler sonography at discharge and at 1,6,12 and 24 months. Invasive venography with pressure measurements is performed if there was clinical or sonographic evidence of TIPS-dysfunction or when sonography was inconclusive. Stent-graft implantation was successful in all patients. Adverse events during follow-up (mean : 185 days ; range 1–720 days) included 1 portal vein tear, 1 temporary upper limb paresis, 1 instent restenosis and 1 shunt occlusion (4%). In 10 patients (20%) clinical signs of isolated TIPS-induced hepatic encephalopathy were detected. These symptoms were treated successfully by medical therapy in 6 patients. Placement of a reduction stent was necessary in 2 patients. Two other patients with hepatic encephalopathy died during the first month of follow-up. Three patients (6%) developed severe liver failure after TIPS ; in total 13 patients (27%) had a liver related death. Eight patients (17%) underwent orthotopic liver transplantation (OLT) (interval 4–479 days ; mean 80.8 days) during follow-up. The placement of a TIPS stent-graft is feasible and safe and short- and midterm follow-up data concerning shunt patency are very encouraging. However, post-TIPS hepatic encephalopathy is the major drawback of this new technique.

- D05 -

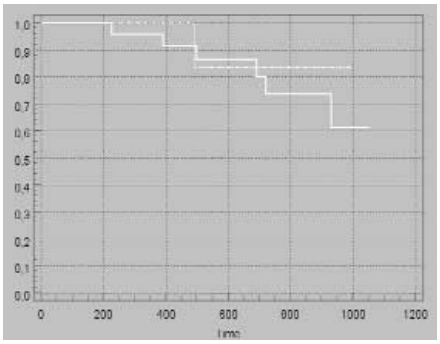
MECHANISMS FOR IMPAIRED LIVER REGENERATION IN OB/OB MICE AFTER TOXIC LIVER INJURY : ROLES OF LEPTIN, TNF AND STAT3. I. Leclercq, J. Field, G.C. Farrell. Storr Liver Unit, Westmead Millennium Institute, University of Sydney, NSW 2145, Australia.

Profound impairment of liver regeneration is found in rodents with leptin deficiency or dysfunctional leptin receptors, and has been attribute to fatty liver disorders.
Aim of the study is to establish whether defective liver regeneration in leptin-deficient *ob/ob* mice is a direct consequence of leptin-dependent, intracellular signaling mechansisms controlling cell cycle regulation in hepatocytes.
Methods : After exposure to a single hepatotoxic dose of CCl_4, hepatic injury and regenerative response were studied in leptin-deficient *ob/ob* and control mice. The effects of leptin supplementation (100 µg/kg/d) were examined. We assessed entry into and progression through the cell cycle and activation of key signaling intermediates and transcritpional regulators.
Results : CCl_4-induced liver injury was similarly severe in *ob/ob* and control mice. However, it was associated in leptin-deficient mice with exaggerated activation of NF-kB and STAT3 during the priming phase, abrogation of TNF and IL6 release at the time of G1/S transition, and failure of hepatocyte to induce cyclin D1 and enter the cell cylce. Leptin replacement corrected these defects in *ob/ob* mice : it restored TNF and IL-6 release, cyclin D1 induction. As a result, hepatocytes entered S phase and progressed, as in wild-type mice, to vigorous mitosis and normal hepatic regenerative response. In *ob/ob* mice, low doses of TNF prior to CCl_4 were also associated with restitution of TNF release and proliferative capabilities.
Conclusions : Impaired liver regeneration in *ob/ob* mice is due to leptin deficiency. Therefore, leptin is physiologically required for liver regeneration and hepatic fibrosis, both components of wound healing in the liver. We propose that defective cytokine production is part of the mechanisms responsible for impaired proliferation in *ob/ob* mice.

- D06 -

HEPATITIS C INFECTION (HCV) DOES NOT WORSEN GENERAL OUTCOME IN ADULT LIVING LIVER TRANSPLANTATION (ALLTX). H. Van Vlierberghe*, R. Troisi**, I. Colle , S. Ricciardi**, M. Praet#, U.J. Hesse**, B. de Hemptinne**. Department of *Gastroenterology and Hepatology, **Department of General, Hepato-Biliary and Liver Tx Surgery, #Department of Pathology, Ghent University Hospital, Belgium.

Introduction : ALLTx is an established treatment option for selected patients with end stage liver disease. Preliminary data demonstrate that the recurrence of hepatitis C is earlier and more severe in comparison to cadaveric liver transplantation (CLTx) (*Transplantation, 2002 ;4* : *Abstract 228 and 229*). We report on the one-year follow up of our cohort of HCV patients receiving ALLTx or CLTx.
Patients and methods : Between 10/1999 and 09/2002, 26 patients (6 female/20 male) (age : 60 ± 7 years) with end stage liver cirrhosis related to HCV received a CLTx and 17 patients (5 female/12 male) (age : 56 ± 4 years) received a ALLTx. The diagnosis of recurrent HCV was made on increased transaminases, detectable HCV RNA level and histological findings on liver biopsy. Liver biopsies were performed for clinical indications and not on a protocol basis. Bilirubin concentration, PTT and ALT activity was compared between the two groups at different time intervals : 4, 12, 24, 36 and 48 weeks after transplantation.
Results : The follow up time for patients receiving a CLTx was higher than for patients receiving an ALLTx (645 ± 297 days versus 432 ± 241 days, p = 0.02). HCV recurrence was seen in 10/26 CLTx patients versus in 6/17 ALLTx patients (p = 0.1). Time until recurrence was, although not significantly, longer in patients receiving a ALLTx (158 ± 114 days versus 227 ± 154 days, p = 0.4). Of the biochemical parameters, only bilirubin concentration at week 4 was significantly different between ALLTx and CLTx patients (3.1 ± 4.3 mg/dl versus 1.26 ± 0.83, p = 0.04), reflecting the presence of sub clinical small for size syndrome in the ALLTx group. Thirteen CLTx patients and 9 ALLTx patients received a liver biopsy (p = 0.9). Timing of the liver biopsy, grade of activity and fibrosis and overall survival (fig) were similar in both groups.



Conclusion : At a follow up period of one year, there is no difference in outcome between end stage HCV patients receiving an ALLTx or CLTx. Considering long term outcome does not differ, ALLTx is a good treatment option for patients with HCV end stage liver disease.

- D07 -

HEPATORENAL SYNDROME. P. Ginès. Liver Unit, Hospital Clínic, University of Barcelona, Catalaunya, Spain.

Hepatorenal syndrome is a common complication of advanced cirrhosis characterized by renal failure and marked alterations in circulatory function. Renal failure is due to an intense vasoconstriction of the renal circulation. Hepatorenal syndrome is probably the final consequence of an extreme underfilling of the arterial circulation secondary to an arterial vasodilation located in the splanchnic vascular bed. Besides the renal circulation most extrasplanchnic vascular beds are vasoconstricted. The diagnosis of hepatorenal syndrome is based on the exclusion of non-functional causes of renal failure, mainly volume depletion due to excessive diuretic therapy, acute tubular necrosis due to hypovolemic or septic shock, administration of nephrotoxic drugs, and parenchymal renal failure, particularly glomerlonephritis. Prognosis is very poor, especially when there is a rapidly progressive renal failure (type 1 hepatorenal syndrome). Liver transplantation is the best option in patients without contraindications to the procedure, but it is not always applicable due to the short survival expectancy. Therapies introduced during the last few years, such as vasoconstrictor drugs (vasopressin analogues, alpha-adrenergic agonists) or the transjugular intrahepatic portosystemic shunt are effective in improving renal function. Nevertheless, liver transplantation should still be performed in candidate patients even after improvement of renal function due to poor outcome. Finally, the development of hepatorenal syndrome in the setting of spontaneous bacterial peritonitis can be prevented by the administration of albumin together with the antibiotic therapy, while hepatorenal syndrome occurring in severe alcoholic hepatitis is effectively prevented by pentoxyfilline.

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- D08 -

CLINICAL, NUTRITIONAL, METABOLIC, AND FUNCTIONAL EFFECTS OF ANTI-OXYDANT SUPPLEMENTATION : A PROSPECTIVE RANDOMIZED STUDY IN PATIENTS WITH CHRONIC PANCREATITIS. P. Deprez, S. Delazzer, L. Galanti, A. Geubel, Y. Horsmans. Gastroenterology Dpt, Clin Universitaires St-Luc, Av Hippocrate 10, 1200 Brussels.

The **aim** of our study was to compare the nutritional, metabolic, functional and clinical effects of a diet adapted to chronic pancreatitis versus anti-oxidant supplementation.
Patients : Thirty patients with chronic pancreatitis were given an adapted diet plus or minus anti-oxidant supplementation (Quatral[Registered] tid) in a prospective, randomized study with a crossover after 3 months. The dietary counseling was aimed to correct all errors detected during a preliminary dietary evaluation. The latter showed an insufficient intake of vit A (33% of patients), vit D (93%), vit E (86.7%), vit C (76.7%), copper (83.3%), zinc (30%), selenium (56.7%). During the study, dietary assessment, clinical pain evaluation (VAS), nutritional and metabolic assessment (BMI, fat mass, basal metabolism), determination of vitamins and anti-oxidants blood levels and measurement of exocrine (fecal elastase and steatorrhea) and endocrine function (HOMA test) were performed at start point, after 3 and 6 months.
Results : In basal state, a significant percentage of patients was shown to have a hypermetabolic status (46.7%), an excessive BET (60%) with a correct nutrient repartition (lipid 35%, protein 16% and glucids 46%), a low BMI (33.3%), and low levels of albumin and pre-albumin (10.7%, 22.2%, respectively), vit D (60.7%), vit C (64.3%), and zinc (33.3%). The anti-oxidant system was impaired in half our patients (total anti-oxidant level) with decreased plasma glutathion peroxidase levels in 25% and superoxyde dismutase in 43.5% of patients. Exocrine function was impaired in 66.7% of our patients and diabetes was present in 26.7%. Mean pain score was 31.7%. No significant changes were seen with the adapted diet. The oral antioxidant supplements significantly increased levels of vit C, vit E, carotene, zinc, selenium, glutathion peroxydase and superoxyde dismutase ($P < 0.05$). No effect on exocrine or endocrine function was shown. Pain was only present in 1 patient at the end of the study.
Conclusion : A poor nutritional status was confirmed in most of our patients, mainly in smokers, diabetics or patients with advanced disease. Although their diet could be improved, especially for vitamins and anti-oxidants, no significant effect was observed after 3 months of adapted diet. Supplementation seems therefore necessary to achieve correction of the numerous deficiencies but its effect on pancreatic endocrine and exocrine function will need long-term studies.

- D09 -

THE ROLE OF MAGNETIC RESONANCE IMAGING IN THE ASSESSMENT OF ACUTE PANCREATITIS : CORRELATION WITH COMPUTED TOMOGRAPHY AND WITH CLINICAL SEVERITY AND OUTCOME.
M. Arvanitakis, M. Delhaye, Dpt of Gastroenterology, M. Bali, D. Van Gansbeke, Dpt of Radiology, J. Devière, Dpt of Gastroenterology, C. Matos, Dpt of Radiology, Erasme University Hospital, 1070 Brussels, Belgium.

Introduction : Magnetic Resonance Imaging (MRI) is increasingly used in bilio-pancreatic diseases. The aim of this study was to compare the value of MRI with that of computed tomography (CT) in acute pancreatitis (AP) and to correlate MRI with clinical outcome.
Patients and Methods : Patients with AP were investigated by contrast-enhanced CT and MRI on admission (within 48 hours from onset of symptoms), 7 and 30 days thereafter. MRI was performed with intravenous secretin and contrast medium administration. The Balthazar's scoring system was used for CT (Computed Tomography Severity Index, CTSI) and MRI (Magnetic Resonance Severity Index, MRSI). The nonparametric Spearman rank test was used to assess the correlation between the two imaging procedures and between clinical outcome and MRI severity score.
Results : Thirty-nine patients (23 males, 16 females), with a median age of 47 years (range : 15-86) were studied during a 21-month-period. AP was considered of biliary etiology in 19 patients (48.7%). The Ranson score was > or = to 3 for 18 patients (46%). A strong correlation was demonstrated between CTSI and MRSI on admission ($r = 0.863$, $p < 0.01$) and after 7 days ($r = 0.893$, $p < 0.01$), C-reactive protein levels 48 hours following admission ($r = 0.764$, $p < 0.01$), length of hospitalization ($r = 0.656$, $p < 0.01$) and clinical outcome regarding morbidity (local and systemic complications) ($r = 0.688$, $p < 0.01$). An abnormal duodenal filling and pancreatic duct irregularities detected at MR Cholangiopancreatography after IV secretin injection (S-MRCP) were associated with a Ranson score > or = to 3 (respectively $p = 0.058$ and $p = 0.002$) and a MRSI > or = to 3 (respectively $p = 0.003$ and $p = 0.001$). S-MRCP detected early pancreatic duct leakage in three patients (7.6%), who required further endoscopic drainage procedures.
Conclusions : MRI is a reliable method for staging AP severity and it has a prognostic value for clinical outcome. It can also reveal pancreatic duct rupture, which can occur early in the course of AP. Furthermore, S-MRCP can detect pancreatic duct irregularity and abnormal duodenal filling, which are associated with severe AP.

- D10 -

PANCREATIC PERFUSION MEASUREMENTS USING A 3D GRADIENT-ECHO MRI-SEQUENCE WITH BOLUS-INJECTION OF GD-DTPA : COMPARISON OF PERFUSION PARAMETERS IN NORMAL VOLUNTEERS AND PATIENTS WITH CHRONIC PANCREATITIS.
K. Coenegrachts (1), W. Van Steenbergen (2), D. Vanbeckevoort (1), D. Bielen (1), C. Feng (1), G. Marchal (1), H. Bosmans (1). Dpt of Radiology (1) and Hepatology (2), Catholic Universities of Leuven, 3000 Leuven, Belgium.

Introduction and objectives : In the early stage of chronic pancreatitis (CP), morphologic changes may be absent or discrete making the diagnosis difficult. In this study, we have explored a new approach using perfusion-weighted MRI. The purpose of this study was to compare perfusion-related data in volunteers (V) and in patients with proven CP.
Material and Methods : Thirty-one V (mean age 38 yrs) and 19 pts with moderate to severe CP (mean age 45 yrs) were imaged. Perfusion studies were performed with 1ml of Gd-DTPA/5kg b.wt. Signal enhancement curves at the level of the pancreatic head, body and tail were obtained. The following perfusion parameters (PP) were calculated : maximal enhancement (Enh_{max}) (defined in arbitrary units, a.u.), maximal relative enhancement ($RelEnh_{max}$), time of arrival of contrast inflow (T_0), time-to-peak (T-peak), wash-in (W_{in})and wash-out (W_{out}) rates, and brevity-of-enhancement (time between point of wash-in and wash-out rate) (BrevEnh).
Results : PP for the pancreatic head are shown in the table.
Discussion : MRI-PP most representative for CP were T-peak, W_{in}, and BrevEnh. This is compatible with the hypothesis of an increased resistance to the normal parenchymal perfusion due to tissue ischemia. A limitation is that all patients had moderate to severe CP. The significant difference of PP in CP vs. normal volunteers is not yet proven in patients with mild forms of CP. Additional studies in patients with upper abdominal pain suggestive of CP are being performed.

	p-values	**Volunteers** *Mean ± S.D.*	**CP patients** *Mean ± S.D.*
$RelEnh_{max}$ (%)	0,23	124,8 ± 47,7	140,6 ± 39,5
T-peak (sec)	1,35E-12	15,4 ± 6,1	46,6 ± 16,6
W_{in} (a.u./sec)	7,09E-05	99,6 ± 39,5	58,8 ± 13,3
W_{out} (a.u./sec)	0,50	48,4 ± 25,5	42,3 ± 34,4
BrevEnh (sec)	2,59E-10	21,5 ± 12,3	53,3 ± 15,8

- D11 -

FIBROGENESIS IN PANCREATIC ADENOCARCINOMA AND ITS RELATION TO GROWTH FACTOR EXPRESSION BY THE NEOPLASTIC EPITHELIUM. P. Demetter, M. Van Waes, J.A. Van Huysse, U.J. Hesse (1), C.A. Cuvelier. Departments of Pathology and (1) Surgery, Ghent University Hospital, 9000 Gent, Belgium.

Background and aims : In contrast to the liver, fibrogenesis in the pancreas has been studied poorly. It is well known that pancreatic fibroblasts produce extracellular matrix (ECM) proteins. Moreover, recent evidence demonstrates that pancreatic stellate cells significantly contribute to ECM production. In the present study we wanted to elucidate a possible role for pancreatic adenocarcinoma cells in the development of fibrotic changes, seen in pancreatic adenocarcinoma.
Methods : 21 pancreatic tissue samples from patients with pancreatic adenocarcinoma were stained immunohistochemically for transforming growth factor (TGF) beta, TGF beta receptor, fibroblast growth factor (FGF), FGF receptor, platelet derived growth factor (PDGF), PDGF receptor, connective tissue growth factor (CTGF), epidermal growth factor (EGF) and vascular endothelial growth factor (VEGF). Expression of these factors by pancreatic adenocarcinoma cells and degree of fibrosis were scored semiquantitatively. Correlations between degree of fibrosis and expression of growth factors were calculated using the Spearman's rho test. $p < 0.05$ was considered to be significant.
Results : All growth factors and receptors studied were expressed by neoplastic epithelial cells in at least part of the samples. Degree of fibrosis correlated with expression of EGF ($r = 0.662$ $p = 0.001$). There were inverse correlations between degree of fibrosis and expression of PDGF ($r = -0,454$ $p = 0,039$), TGF beta receptor ($r = -0,560$ $p = 0,008$) and VEGF ($r = -0,505$ $p = 0,020$). No correlations were found between degree of fibrosis and expression of TGF beta, FGF, FGF receptor, PDGF receptor and CTGF.
Conclusions : Our immunohistochemical findings show that pancreatic adenocarcinoma cells are able to produce several types of growth factors and their receptors. The ability of EGF to stimulate epithelial cell and fibroblast proliferation is well documented ; the correlation between degree of fibrosis and expression of EGF, detected in this study, suggests that pancreatic adenocarcinoma cells play an active role in the development of fibrotic changes, associated with adenocarcinoma.

- D12 -

RESULTS OF INTESTINAL TRANSPLANTATION USING LOW-DOSE IMMUNOSUPPRESSION. J. Pirenne, M. Hiele, M. Waer, K. Geboes, F. Nevens, M.P. Emonds, T. Koshiba, H. Kitade, P. Ferdinande. U.Z. Gasthuisberg, Leuven, Belgium.

Rejection remains a major obstacle to intestinal transplantation (Itx). For that reason, current protocols use heavy immunosuppresion (IS) but this causes infection/lymphoma. Wider application of Itx depends on the development of "immunomodulatory" strategies to promote engraftment while reducing IS. Based on previous animal work, we developed a novel protocol including portal delivery of donor antigens, no steroid bolus (shown to break tolerance) and low maintenance IS. Method. 2 females (55/57 yo) with short-gut syndrome + TPN-induced liver failure received liver + Itx. Blood was taken from donor at procurement and transfused in the recipient vena porta after graft reperfusion. For induction IS, no iv steroid bolus was given, but only 2 doses of anti-IL-2 receptor antibody. Patients received postTx maintenance IS with lower FK506 levels than average for this type of Tx (15ng/ml 1st mth ; 5-10ng/ml thereafter), low dose azathioprine (1mg/kg 1st–3rd mth ; .5mg/kg thereafter) and low dose steroids (medrol 8mgx2 daily tapered to 2mgx2 by 3rd mth). Standard anti-bacterial, -fungal, -viral prophylaxis was given. Patients were monitored for rejection, GVHD, infection, lymphoma. Biopsies were taken from the distal stomy. Result. Despite exposure to low IS, clinical, endoscopic, histologic signs of rejection did not develop. Chimerism (presence of donor cells in peripheral blood) was identified in patient 1 but disappeared spontaneously. GVHD was absent in both patients. Under this low IS, both patients remained free of systemic opportunistic infections, lymphoma and drug toxicity. Patient 1 needed reoperation for Tx pancreatitis and Patient 2, for intestinal graft obstruction. TPN was stopped at 7 weeks and at 3 weeks postTx, respectively. Both are nutritionally independent and well 24 and 4 months postTx. Stomies were closed. Last biopsies show normal intestinal mucosa.
In conclusion we describe a new immunomodulatory protocol that could eliminate rejection and restore nutritional independence in 2 consecutive Itx recipients. Maintenance IS used in these patients is less than commonly used in kidney Tx or in some patients with chronic inflammatory bowel disease. If these results are confirmed in the longer-term, Itx could be become an alternative to life-time TPN in patients suffering from irreversible short-gut syndrome (like kidney Tx for dialysis patients). Mechanisms of operational tolerance in these patients - in particular the development of regulatory cells - need to be investigated.

- D13 -

OF PREOPERATIVE CHEMORADIOTHERAPY ON POSTOPERATIVE MORBIDITY AND MORTALITY OF CT4 +/- CM + LYMPH OESOPHAGEAL CARCINOMA RESECTION. O. Hagry, W. Coosemans, P. De Leyn, G. Decker, J. Moons, P. Nafteux, D. Van Raemdonck, T. Lerut. Department of Thoracic Surgery, University Hospitals, UZ Gasthuisberg, Leuven, Belgium.

Objective : Effects assessment of induction chemoradiotherapy on postoperative courses after resection of locally advanced oesophageal carcinoma ($_{c}T4 + _{c}M+_{Lymph}$).
Methods : Induction chemoradiotherapy was completely performed in 109 patients. Surgery concerned 90 patients (operability : 90/109 = 83%) : resection in 85 patients (resecability : 85/109 = 78%), by-pass in 5 patients. Surgery was impossible in 19 patients. Induction therapy associated 5FU d1-5 and d21-25, CDDP d1 + d21 and concomitant radiotherapy 18 sessions.
Results : Resection was complete (R0) in 70 patients (70/90 = 78%). Mean duration of surgery was 427min ([240 ; 690]). Peroperative complications were haemorrhage in 3 patients (3.3%), splenectomy in 1 patient, tracheobronchial perforation in 3 patients (3.3%). Mean total hospital stay was 32 days ([8-355]). Mean duration of intubation was 6 days ([1 ;190]) ; 67 patients (74.4%) were intubated less than 2 days. Major morbidity concerned 26 patients (28.9%), hospital mortality 9 patients (10%). Medical morbidity was pulmonary in 43 patients (47.8%), atelectasis in 12 patients (13.3%), cardiac in 23 patients (25.6%), sepsis in 10 patients (11.1%) and ARDS in 9 patients (10%). Surgical morbidity was pleural effusion in 17 patients (18.9%), tracheal fistula in 4 patients (4.4%), chylothorax in 3 patients (3.3%) and acute pancreatitis in 1 patient. 11 patients (12.2%) had a radiologically confirmed anastomotic leak ; however only 5 out of them had clinical manifestation ; treatment of leak was conservative in all patients.
Conclusion : Chemoradiotherapy followed by resection of cT4 +/- $cM+_{lymph}$ oesophageal carcinoma is feasible with acceptable mortality, morbidity, but higher when compared to primary surgery.

- D14 -

CIRCUMFERENTIAL RESECTION MARGIN INVOLVEMENT – A POSTOPERATIVE PREDICTOR OF SURVIVAL IN DISTAL OESOPHAGEAL AND CARDIA CANCER. A. Driessen*, J. Moons, H. Alaerts, P. Nafteux, K. Haustermans, E. Van Cutsem, T. Lerut, N. Ectors. University Hospital Maastricht*, The Netherlands, University Hospitals Leuven, Belgium.

Oesophageal cancer, which is the fifth most common cause of cancer mortality, shows a significant rise. Similarly, the incidence of gastro-oesophageal adenocarcinomas, which also have a poor prognosis, is increasing. Surgery is the standard treatment for both cancers. The single most important prognostic factor is complete resection (R0). The presence of margin involvement determines local recurrence and prognosis. Hence the aim was to determine the prognosis in function of the distance between the invasion front and the circumferential margin by analogy to rectal cancer. Our retrospective study comprised 146 patients treated by primary surgery for an adenocarcinoma of the distal oesophageal and cardia, extending into the oesophagus (63 yr, range 32 – 88 yr, M/F = 7.3). The distance between the tumour and the circumferential margin (painted with ink) was measured on representative formal-fixed, paraffin embedded transversal sections from resection specimens by microscopical analysis of the oesophagus. Based on the distance (mm) the patients were subdivided into 3 categories : A. £ 1 mm (n = 60 ; 63 yr, 37 – 88 yr, M/F = 5), B. £ 2 mm (n = 32, 65 yr, 40 – 77 yr, M/F = 5.4) and C. > 2 mm (n = 54 ; 63 yr, range 32 – 84 yr, M/F = 9.8). Survival analysis was done using a Kaplan-Meier method and a log rank test. The overall survival in our population was 38 months (mo) (median 20 mo, range 1 – 141 mo). The median survival for category A was 14 mo (95% CI 9 – 17 mo) whereas the median survival for category B and C was 26 mo (95% CI 17 – 36 mo) and 31 mo (95% CI 24 – 39 mo) respectively. The prognosis worsened as the distance between tumour and circumferential margin decreased. Category A (< 1 mm) patients had a significantly less good prognosis than category B (p = 0.007) and category C patients (p = 0.0003). The finding of tumour within 1 mm of the circumferential margin following what would otherwise be regarded as a potentially curative resection (R0) greatly increases the risk of the patient dying from their cancer.

- D15 -

ENDOSCOPIC MUCOSAL RESECTION IN SUPERFICIAL TUMOURS OF THE OESOPHAGUS. H. Piessevaux ; S. Laurent, J. Grodos*, C. Sempoux*, Y. Horsmans, P. Deprez. Departments of Gastroenterology and Pathology (*), Cliniques Universitaires St-Luc (UCL), 1200 Brussels, Belgium.

Background : Endoscopic mucosal resection (EMR) is a valuable alternative to surgical resection of superficial tumours in the gastro-intestinal tract.
Aim : To prospectively evaluate EMR, if necessary combined with Argon Plasma Coagulation (APC) in T1 (m1-2, sm1-3) N0 malignant tumours of the oesophagus.
Patients and methods : Staining with Lugol for squamous lesions or Methylene blue for adenomatous lesions was applied during conventional or high magnification endoscopy (if available). Depth of tumoral invasion was evaluated using EUS (high frequency miniprobe, 20MHz Fujinon). Resection was performed using the Olympus EMR device, after submucosal saline or hypromellose solution injection. If necessary, APC (Valleylab) was used. Patients were classified according to Ell et al. (Gastroenterology 2000) in low risk or high risk groups. Complete remission was defined as the absence of high-grade dysplasia or invasive cancer at the last follow-up examination.
Results : Twenty-nine lesions in 28 patients were treated (mean age 70, range 48-83, 23 men). Adenocarcinoma was found in 5, high grade dysplasia in Barrett's oesophagus in 13 and spinocellular cancer in 11. Resection was feasible in all cases. Complications occurred in 3 patients : 1 bleeding treated by hemoclips and 2 oesophageal stenoses requiring 2 sessions of endoscopic dilatation. All patients with spinocellular cancer were in complete local remission after maximum two sessions ($p = 0.07$ vs other lesions). Complete local remission was significantly more frequent in T1m lesions (17/18 (94%)) as compared to T1sm lesions (5/9 (55%)).
Conclusions : The combination of EMR and APC is safe and efficient for malignant oesophageal lesions. EUS staging accurately predicted the likelihood of obtaining complete sustained local remission.

Number of patients	**Group A (low risk) 18 (62%)**	**Group B (high risk)** : **11(38%)**
N of EMR sessions	1.3	2.0 (t test ; $p = 0.04$)
Use of APC	6 (33%)	10 (91%) (?? ; $p < 0.01$)
Complete local remissions	14/15 (93%)	6/9 (67%) (?? ; $p = 0.09$)
Need for subsequent surgery	0	2/11 (18%)

- D16 -

THREE FIELD LYMPHADENECTOMY FOR CARCINOMA OF THE ESOPHAGUS AND GASTROESOPHAGEAL JUNCTION IN 174 R0 RESECTIONS. IMPACT ON TNM STAGING AND OUTCOME. T. Lerut, W. Coosemans, G. Decker, P. De Leyn, Ph. Nafteux, J. Moons, D. Van Raemdonck. KUL Leuven.

Background and objective : Three field lymphadenectomy (3 FL) for carcinoma of the esophagus and GEJ is rarely performed in Western centers. The aim of this study is to analyse the prevalence of cervical lymph node metastasis after three field lymphadenectomy and to determine its impact on staging and outcome.
Material and methods : Between 1991-1999 primary surgery with 3 FL was performed in 188 patients of which a cohort of 174 R0 (92%) resections was used for further analysis.
Results : Hospital mortality was 1,2%. Overall morbidity occurred in 58%. Pulmonary complications (57 or 32.7%) and cardiac disrythmias (18 or 10.3%) being the most common complications. Overall 3 and 5 year survival was 51% and 41.9% respectively (both 80.2% for node negatives versus 37.7% and 24.5% for node positives. Twenty three% of the patients with adenocarcinoma (25% distal third and 15% GEJ) and 25% of the patients with squamous (26% middle third) cell carcinoma had positive cervical nodes resulting in a change of staging in 15%. Three and 5-year survival for patients with positive cervical nodes were 36.3% and 27.2%, respectively, for middle third SCC, 35.7% and 12% for distal third adenocarcinomas. No GEJ adenocarcinoma with positive cervical nodes survived for 5 years.
Conclusion : Prevalence of involved cervical lymphnodes is high. The overall 41.9% 5 year survival rate and the 5 year survival rate of 27.2% in middle third squamous cell carcinoma and 12% in distal third adenocarcinoma with positive cervical nodes may suggest a beneficial effect of 3 FL. The value of the actual AJCC/UICC staging system is questioned**.**

- D17 -

EFFECT OF INTRAPYLORIC INJECTION OF BOTULINUM TOXIN ON GASTRIC EMPTYING AND MEAL-RELATED SYMPTOMS IN GASTROPARESIS. S. Van Gool, J. Arts, P. Caenepeel, J. Janssens, J. Tack Divisions of Gastroenterology and Endoscopy, University Hospitals Leuven, Belgium.

Current pharmacological treatment of gastroparesis focuses on the use of gastroprokinetic drugs. Recent observations in limited numbers of patients suggest a potential benefit of intrapyloric injection of botulinum toxin (Lacy 2002, Miller 2002). However, the effect of botulinum toxin on liquid emptying is unknown and the symptomatic benefit has not been fully characterized.
Aim : To study the effect of botulinum toxin injection on gastric emptying rate and on meal-related symptoms in patients with gastroparesis.
Methods : In 20 patients with gastroparesis (17 women and 3 men, mean age 37 ± 3 years, 3 diabetic and 17 idiopathic) gastric emptying was measured twice, before and one month after intrapyloric injection of botulinum toxin 4 × 25 U. Gastric emptying rates for solids and liquids were determined using the ^{14}C octanoic acid and ^{13}C glycin breath test. Breath samples were taken before the meal and at 15 minute intervals for a period of 240 minutes postprandially, and gastric half emptying time (t1/2) was calculated from the data. At each breath sampling, the patient was asked to grade the intensity (0-3 ; 0 = absent, 1 = mild, 2 = relevant and 3 = severe) of six different symptoms (epigastric pain, bloating, postprandial fullness, nausea, belching and epigastric burning). For each symptom, a meal-related severity score was obtained by adding all intensities over the whole study period. A cumulative symptom score was obtained by adding individual symptom severity scores. All data are given as mean ± SEM. They were compared using paired Student's t test.
Results : Treatment with botulinum toxin significantly enhanced the gastric emptying rate for solids (t1/2 131.8 ± 16.0 vs. 203.9 ± 35.3 min. baseline, $p < 0.05$) but not for liquids (92.3 ± 9.8 vs. 104.1 ± 10.6 min. baseline, NS). Treatment with botulinum toxin significantly decreased the cumulative meal-related symptom score (73.5 ± 16.3 vs. 103.9 ± 17.1 baseline, $p = 0.01$). Individual symptom severity scores for postprandial fullness (20.0 ± 4.6 vs. 28.4 ± 5.0 baseline, $p < 0.05$) and for belching (4.8 ± 1.4 vs. 18.9 ± 4.3 baseline, $p < 0.005$) were significantly improved by treatment with botulinum toxin.
Conclusion : Botulinum toxin improved solid but not liquid gastric emptying rate, and this was accompanied by signficant improvement of meal-related symptoms, mainly fullness and belching, in patients with gastroparesis. These findings require confirmation in a controlled study.

- D18 -

STUDY IN CHC PATIENTS COMPARING THREE DIFFERENT COMBINATION THERAPIES WITH INTERFERON ALPHA-2B (IFN) AND RIBAVIRIN (REBETOL) : WEEKLY PEG-IFN (PEG- INTRON) VERSUS DAILY IFN (INTRON A PEN) VERSUS STANDARD REGIMEN OF IFN (INTRON A PEN). Y. Horsmans(1), I. Colle & H. Van Vlierberghe (2) Ph. Langlet (3), M. Adler (4), R. Brenard (5), P. Michielsen (6), N. Bourgeois (4), V. Lefèbvre (7), J. Henrion (8), X. De Koninck (9), L. Bruckers (10), on behalf of the Belgian Association for the Study of the Liver. (1) Clin. Univ. St-Luc, Université Catholique de louvain, 1200 Bruxelles, Belgium ; (2) UZ Gent, 9000 Gent ; (3) CHU Brugmann, 1020 Bruxelles ; (4) Hôp. Erasme, 1070 Bruxelles ; (5) Hôp. St-Joseph 6060 Gilly ; (6) UIAntwerpen, 2000 Antwerpen ; (7) CHR Namur, 5000 Namur ; (8) Hôp. Jolimont, 7100 Haine St Paul ; (9) Clin. St-Pierre, 1340 Ottignies ; (10) Center for Statistics, Limburgs Universitair Centrum, 3590 Diepenbeek.

The combination of PEG-interferon a-2b and ribavirin is considered to be the standard treatment for naïve chronic HCV patients. A study was initiated to compare the sustained virological response and safety of daily IntronA® versus PegIntron®, both in combination with Rebetol®. Naïve chronic HCV patients were randomized in three groups with a ratio of 2:2:1. Group A : daily interferon a-2b (4 MIU s.c. for patients > 65 kg or 0.06 MIU/ kg for patients ≤ 65 kg) and ribavirin, group B : PEG-interferon a-2b (100 µg s.c. weekly for patients > 65 kg or 1.5 µg/kg weekly for patients ≤ 65 kg) and ribavirin and group C (reference arm) : interferon a-2b (3 MIU s.c. TWI) and ribavirin. The duration of the treatment was 48 weeks for all 3 groups, with a 6 month follow-up period. 317 patients were enrolled : 130 in group A, 119 in group B and 68 in group C. We are presenting the results of an interim analysis performed on the available patient data. Demographic data, PCR results and reasons for early withdrawal have been statistically analysed. At baseline, the 3 groups didn't show any statistical difference regarding age, gender, race, genotype and METAVIR score. At week 24 on treatment, HCV RNA (Amplicor) was undetectable in 86% in group A, in 80% in group B and in 67% in group C. At the end of treatment, 69% 70% and 55% respectively, had a negative PCR result. At week 24 of follow-up, these results were 60%, 52% and 29%, respectively. When comparing the efficacy of the daily interferon (+ ribavirin) and the PEG-interferon (+ ribavirin) regimen, no statistical difference was found ($p = 0.378$). 78 patients withdrew before termination of the treatment : 30 in group A, 22 in group B and 26 in group C. In group A, 43% of drop-outs were due to adverse events compared to 18% in group B and 19% in group C. Regarding safety, no statistical difference was found for the drop-out rate in the daily interferon (+ ribavirin) regimen versus the PEG-interferon (+ ribavirin) arm ($p = 0.420$). In contrast, a statistical higher rate of drop-out was observed in the old standard therapy (group C) versus group A ($p = 0.024$) and versus group B ($p = 0.004$). In conclusion, daily weight based IntronA dosing and PEG-Intron weighed based dosing once weekly both in combination with Ribavirin offer the same efficacy and safety rates.

- D19 -

NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) : WHICH PATIENT SHOULD BE PROPOSED FOR LIVER BIOPSY? Lambert A.S., Henrion J., Peny M.O., De Maeght S., Deltenre P., Maisin J.M., Ghilain J.M., Schapira M. and Heller F. Hôpital de Jolimont, Haine Saint Paul, Belgium.

The epidemiology of NAFLD differs among studies depending on recruitment through the liver or endocrinology clinics and according to ethnic or other local characteristics. Moreover, the role of liver biopsy remains hotly debated.
Aims : 1/ to evaluate the demographic characteristics of NAFLD at the outpatient liver clinics in our general hospital ; 2/ to validate predefineal criteria for liver biopsy.
Patients and methods : from September 2001, patients were included in a prospective registry of NAFLD if they fulfilled the following criteria : 1/ any risk factor for NAFLD ; 2/ elevation of serum ALAT ; 3/ hyperechogenoic liver at US and 4/ exclusion of other causes of liver disease. Liver biopsy was proposed when serum ALAT was ≥ 2 N and when 2 of the 4 following conditions were met : age ≥ 45 y, BMI ≥ 30 kg/m?, glycemia ≥ 110 mg/dl, triglyceridemia ≥ 150 mg/dl according to 2 recent studies (Angulo, Hepatology 99 ; Ratziu, Gastroenterology 2000).
Results : 52 cases were collected, gender 36 M/16 F, mean age 48 (R : 16-77). The refering reason for consultation was elevation of serum ALAT in 48 cases (92.3%) and suspicion of genetic hemochromatosis in 4 (7.7%). Mean BMI was 31.2 kg/m? (R : 24-44.1) and the median ALAT elevation was 1.8 x N (R : 1-5 x N). The prevalence of main clinical indicators of insulin resistance were : BMI ≥ 25 kg/m? in 48/52 (92%), hyperglycemia 21/52 (40.4%), hypertriglyceridemia in 45/52 (86%) and arterial hypertension in 18/52 (34.6%). Thirty patients fulfilled the criteria for liver biopsy that was performed in 24 of them. According to the staging of E. Brunt, fibrosis F0-F1 was observed in 9, and F2-F4 in 15. Fasting insulinemia and insulin resistance according to homeostasis model assessment (HOMA IR : fasting glucose mmol/L x fasting insulin µIU/ml/22.5) were the main predictive factors of significant fibrosis : mean insulin (µIU/ml) 16 (R : 9-24.5) versus 32.3 (R :12-85.6) and HOMA IR 4.4 (R : 1.9-8.1) versus 9.3 (R : 3-26.3) in F0-F1 versus F2-F4 fibrosis, respectively ($p < 0.01$).
Conclusions : 1/ the typical patient in our region is of male gender and exhibits overweight or moderate obesity with hypertriglyceridemia ; 2/ the criteria for liver biopsy currently used are appropriate for the discovery of significant liver fibrosis ; 3/ fasting insulin and HOMA IR are predictive factors of significant fibrosis in non alcoholic steatohepatitis.

- D20 -

INDICATIONS, PITFALLS AND GENERAL OUTCOME IN LIVING DONOR LIVER TRANSPLANTATION IN ADULTS (ALDLT). R. Troisi (1), S. Ricciardi (1), I. Colle (2), H. Van Vlierberghe (2), J. Decruyenaere (3), E. Hoste (3), P. Smeets (4), D. Vogelaers (5), M. Praet (6), G. Militerno (1), U.J. Hesse (1), B. de Hemptinne (1). Dept. of (1) General, Hepato-Biliary and Liver Tx Surgery ; (2) Dept. of Hepato-Gastroenterology ; (3) Intensive Care Unit ; (4) Dept. of Radiology ; (5) Internal Medicine ; (6) Dept. of Pathology, Ghent University Hospital Medical School, Gent-Belgium.

Introduction : ALDLT is an accepted treatment option for end-stage liver disease and is currently considered as a valid alternative in selected patients. We review the three-year experience focusing on the recipient's disease and indications, technical issues, postoperative complications and general outcome.
Methods : Between 9/1999 and 11/2002, 35 recipients underwent ALDLT with the right (RL) or the left lobe (LL) in our institution. There were 21 (60%) male and 14 (40%) female with a mean age of 53 ± 15 y (range 19-67). Disease etiology, presence of tumor, UNOS status, ACR, postoperative morbidity and mortality rates were evaluated.
Results : The mean FU was of 12 ± 8 m (1-39). Main indications were HCC and HCV cirrhosis (83%). Forty-nine % of all recipients were UNOS 2A (n = 5) or B (n = 12). Extended indications for HCC were accepted in 9 patients (65%). Two (6%) patients previously transplanted with a cadaveric liver underwent re-Tx with ALDLT procedure. Small grafts (GRBWR < 1%) were engrafted in 13 (37%) recipients, 5 (38%) of whom due to pitfalls in donor anatomy assessment. Accessory venous and portal reconstruction or additional surgical procedures (i.e. splenic artery ligature, portal vein banding, side-to-side portocaval shunts) were needed in 28 (80%) recipients to optimalize graft inflow and outflow. ACR occurred in 14 (40%) patients. HCC recurred in 1 (8%) patient and HCV relapse was seen in 6 (35%) without graft loss. Biliary complications (early and late) were seen in 9 (26%) patients. Small-for-size syndrome (SFSS) occurred in three (8,6%) patients but not when graft inflow was intraoperatively lowered. Five (14%) recipients died following sepsis, pulmonary embolism and MOF on chronic rejection. No one was lost in the group of extended indications for HCC. Overall survival is 86%.
Conclusions : ALDLT is a demanding procedure that requires additional surgical procedures to adjust graft inflow and outflow. HCV relapse does not influence general outcome and HCC outside standard criteria seems to have a less recurrence rate than usually thought. UNOS 2A and B patients could benefit from this procedure. Avoiding of SFSS and adequate postoperative graft regeneration remains the crucial point-influencing outcome in ALDLT.

- D21 -

ENDOSONOGRAPHIC (EUS) CYSTOGASTROSTOMY OR CYSTENTEROSTOMY IN ACUTE AND CHRONIC PANCREATITIS. C. Gillain, H. Piessevaux, Ch. Descamps, J.F. Gigot*, Y. Horsmans, P. Deprez. Dpts of Gastroenterology and *Digestive Surgery, Cliniques Univ. St-Luc, UCL, Av Hippocrate 10, 1200 Brussels, Belgium.

Background : With the progress of therapeutic EUS, most symptomatic collections complicating acute and chronic pancreatitis can now be drained endoscopically. EUS was claimed to decrease the risk of bleeding and perforation due to its direct visual guidance. The aim of our study was to compare endoscopic cystogastrostomy and cystenterostomy performed with or without EUS.
Patients and methods : Forty-nine endoscopic drainages were performed in 47 patients, mean age 48, range 4-80, 32 men, presenting with symptomatic fluid collection occurring during acute (n = 15) or chronic (n = 34) pancreatitis. Disease was related to alcohol consumption in 30 pts, biliary lithiasis in 7, pancreas divisum in 3 and was idiopathic in 6. Diagnostic EUS was performed in all cases to assess the cyst content, the distance between the collection and the digestive lumen (4.5 mm, range 2-12), the presence of abnormal vessels (interposition of varices in 5 pts) and to locate the best site for puncture. EUS drainage was performed in one single endoscopic session with a Pentax FG-UX36 or 38 scopes in all non-bulging collections (n = 25) whereas bulging cysts were conventionally drained with a TJF140 or 160R Olympus duodenoscope.
Results : The short-term and long-term outcomes (median 24 months, range 2-84) of the 35 cystogastrostomies and 14 cystoduodenostomies were characterized by a symptomatic remission in all but 2 pts (96%) and complete cyst resolution in 40 pts (85%). Three patients had small (< 2 cm) residual asymptomatic collections and 3 experienced a recurrence of a pancreatic cyst at 3 months, 1 year and 5 years, respectively. Local complications were observed in 7 pts (14.8%) and consisted of 1 mild hemorrhage, 5 cyst infections and 1 stent migration, all treated by endoscopy. Cyst infection occurred mainly in pts with large bulging collections (129 mm, 80-170 vs. 77 mm, 37-140, P = 0.04) and when a cystogastrostomy was performed (4/5). Only one infection was associated with EUS drainage. Median duration of hospitalisation was 3.5 days, range 2-36. No differences of outcome could be seen between EUS and non-EUS drained pancreatic collections.
Conclusions : EUS cystogastrostomy or cystenterostomy can be safely performed in non-bulging pancreatic collections. Long-term outcome is excellent and morbidity is mainly related to the initial size of the cyst.

- D22 -

COLORECTAL NEOPLASMS : PREVALENCE AND DITRIBUTION IN 1000 PATIENTS SUBMITTED TO COLONOSCOPY. M. Suball, N. Nagy, D. Franchimont, A. Demols, J.-L. Van Laethem, A. Van Gossum, M. Adler. Medico-Surgical Dpt of Gastroenterology and Hepato-Pancreatology, Erasme Hospital, 1070 Brussels, Belgium.

Background : Colonoscopy is increasingly used to detect colorectal neoplasms both as a screening or a diagnostic procedure. The aim of our study was to evaluate the prevalence and distribution of colorectal neoplasms (i.e. adenoma or cancer) as well as their risk factors in a consecutive series of 1000 patients, over 50 years old, submitted between June 1999 and March 2002 to their first diagnostic (presence of alarm signs) or screening (absence or non-specific digestive signs) colonoscopy. Size and location of all polyps were determined and all retrieved specimens were classified histologically on the basis of their most advanced lesion.
Results : Mean (± SEM) age was 62 (± 9.8) years. Four hundred eighty six were male, 514 were female and a family history of colorectal neoplasm was present in 81 patients. The procedure was completed to the caecum in 97.1% of the cases. Based on the 953 evaluable patients, diagnostic and screening colonoscopy included 423 and 530 patients respectively. Rates of adenoma, advanced neoplasm (AN, i.e., villous adenoma or adenoma > 1 cm in diameter or adenoma with high grade dysplasia) and invasive cancer (IC) were 29.6% (n = 283), 11.4% (n = 109) and 3.1% (n = 30). Localization of the polyps was distal in 60% (n = 240), proximal in 32% (n = 127), proximal and distal in 8% (n = 32). Among the 139 advanced neoplasms, 78 (56%) were distal, 50 (35%) were proximal and 11 (9%) were proximal and distal. Risk factors for the presence of AN and IC included diagnostic (21.1%) vs. screening (9.5%, p 0.04) colonoscopy and age above 65 (20.2%) vs. 50-65 (8.5%, p = 0.003). There was no difference according to gender (p = 0.12). In the screening colonoscopy (n = 530) series, prevalence of AN or IC was 9.4% (n = 50). Twenty percent (n = 10) of the patients had isolated proximal AN or IC, giving a prevalence of 1.9% (10/530) : 0.39% below 65 years (n = 2) and 1.5% above 65 years (n = 8).
Conclusions : This study underlines the significant yield of colonoscopy in the detection of colorectal neoplasms both in the diagnostic and the screening settings and the high proportion (20-35%) of proximal polyps or advanced neoplasms without any distal endoscopic findings. Strategies using colonoscopy instead of sigmoidoscopy are thus preferable, particularly in patients more than 65 years old submitted to endoscopic colorectal cancer screening.

- D23 -

COMPUTED TOMOGRAPHIC COLONOGRAPHY : A FOUR YEARS EXPERIENCE. S. Gryspeerdt (1), Ph. Lefere (1), M. Baekelandt (1), B. Van Holsbeeck (1), J. Dewyspelaere (1), R. Deman (2), L. Rutgeerts (2). Departments of Radiology and Gastroenterology, Stedelijk Ziekenhuis (1) and H. Hart Ziekenhuis (2), 8800 Roeselare, Belgium.

Purpose : To retrospectively evaluate a four years experience with computed tomographic colonography (CTC). Materials and Methods In a four years period , we performed 506 CTC's. In 118 patients, CTC was performed after incomplete conventional colonoscopy (cC). This group is not included in this retrospective analysis. In 120 patients, CTC was performed in the setting of a study comparing CTC and cC. This group is reported as study group (stG). Based on the experience from this stG, the CTC technique was optimised. In 268 patients, using the optimised CTC technique, CTC triggered 72 cC. This group of 72 patients is referred to as the screening group (scrG). In the stG, 20 patients had standard colonoscopic preparation (ScCl) , 50 patients had a reduced preparation (RcCl) , and 50 patients were prepared with dietary fecal tagging (FT). In the scrG the colon cleansing technique was FT for all patients. In 12 patients in the scrG, CO2 instead of room air was used. In both groups of patients, sensitivity and specificity were calculated for polyp detection using cC as the gold standard. In the stG we also evaluated patient acceptance.
Results : Results of the stG showed that : A/ ScCl results in a clean colon, but produces fluid levels which hamper a complete CTC, resulting in false negative diagnosis (3 of 20 patients). Sensitivity and specificity were respectively 77% and 57%. B/ RcCl reduces the problem of fluid levels, but is then faced with the problem of fecal residues, resulting in false positive diagnosis (7 of 50 patients). Sensitivity and specificity were respectively 85% and 77%. C/ FT offers the possibility to obtain a dry colon, with tagged fecal residues, reducing false negative (2 of 50 patients) as well as false positive diagnosis (4 of 50 patients). Sensitivity and specificity were 88%. Optimisation of the diet and replacement of PEG by magnesium citrate in FT reduces the preparation related discomfort and improves final opinion (FT significantly better than RcCl : $p = 0.03$). Results of the scrG showed that : A/ cC confirmed all polyps, and additionally showed 9 polyps smaller than 1 cm in 7 patients ; B/ using optimised CTC technique, a total of 8 false positive diagosis were found in 6 patients ; with 5 being caused by diverticular disease ; C/ CO2 reduces dyscomfort during CTC.
Conclusion : Optimised CTC technique encompasses FT as preparation technique, and use of CO2 to inflate the colon. CTC results in acceptable sensitivy and specificity for detecting the clinically significant polyps. Diverticular disease remains a challenge to CTC.

- D24 -

IMPACT OF INFLIXIMAB ON WEIGHT REGULATION AND LIPID METABOLISM : IMMUNO-NEUTRALIZATION OF TNFA INDUCES LEPTINEMIA IN CROHN'S DISEASE. S. Roland, A. Van Gossum, S. Vermeire, T. Gustot, C. Gervy, E. Quertinmont, J. Devière, D. Franchimont. Dpt of Gastroenterology, Erasme University Hospital, ULB, Brussels, Belgium. Background.

Introduction : Tumor necrosis ? (cachectin ?) is a critical mediator of inflammation-induced weight loss. In mice, body weight and fat mass are tightly regulated by adipocyte-derived leptin. In human inflammatory diseases, how endogenous TNF? influences in vivo leptin secretion remains unexplored. Pharmacological deletion of TNF? offers a great opportunity to understand TNF? –mediated leptin regulation and to delineate the in vivo metabolic actions of TNF? in Crohnís disease.
Methods : We prospectively examined CD patients treated with infliximab (n = 16). Body weight, body mass index, bioimpedance- fat mass, muscular strength and CDAI were assessed before and after treatment at 1 and 4 weeks. Lipid changes (cholesterol, triglycerides and apolipoproteins) and plasma leptin levels were analyzed with cytokines profile (TNF?, IL-6, TNFRIIs and sICAM-1) and with thyroid/adrenal functions.
Results : Infliximab treatment was associated with a significant decrease in CDAI ($p < 0.01$), gain of weight ($p = 0.005$) and improvement of muscular strength ($p < 0.05$) at 4 weeks. Percentage of fat or lean mass was however not modified by this therapy. Surprisingly, leptinemia was significantly increased by infliximab treatment at 1 (18.64(.825 –100) vs 12.37 (.6-59.5) ng/ml, $p < 0.05$) and 4 weeks (17.47 (.71 –72.5) vs 12.37 (.6-59.5) ng/ml, $p = 0.006$) after treatment. Whereas plasma leptin level appears only regulated by weight and fat mass in healthy subjects, hyperleptinemia in this study occurred early, at 1 week when no significant weight and fat mass changes could already be observed. Furthermore, leptin increase was not correlated with fat mass increase. This hyperleptinemia was further confirmed when looking at other TNF? –regulated mediators such as TNFRIIs (3277+/1892 vs. 3583+/-1736 pg/ml, $p < 0.05$) and sICAM-1 (394+/-156 vs. 322+/-162 ng/ml, $p < 0.005$) which were drastically decreased together with C-reactive protein. Simultaneously, cholesterol (183+/-10 vs. 149+/-10 mg/dl, $p < 0.02$) and HDL-cholesterol were dramatically increased with A apolipoprotein ($P < 0.05$). Adrenal and thyroid functions were not homogeneously changed.
Conclusion : Infliximab induces weight gain and influences lipid profiles in Crohn's disease. The early regulation of leptinemia changes suggests a direct action of infliximab and, hence, of TNF? on leptin secretion. Targeting cytokines with monoclonal antibodies will help understand their influence on lipid metabolism during inflammation.

- D25 -

TOLL-LIKE RECEPTOR (TLR)-4 (ASP299GLY) POLYMORPHISM IS ASSOCIATED WITH ULCERATIVE COLITIS (UC). M. Pierik, S. Vermeire (1), H. El-Housni (2), G. Claessens (1), E. Quertinmont (2), S. Joossens (1), A. Van Gossum (2), J. Devière, P. Rutgeerts, D. Franchimont. Dpts of Gastroenterology, (1) University Hospital Gasthuisberg, Leuven, (2) Erasme University Hospital, Brussels.

Background and aim : Studies on genetically engineered animals suggest the critical role of colonic bacterial micro flora in the pathogenesis of ulcerative colitis. Toll-like receptors are pattern-recognition receptors (PRRs) involved in the early phase of the innate immune response to bacterial products. Toll–like receptor (*TLR*)-4 specifically binds lipopolysaccharides (*LPS*) and transduces its signal trough the NF-kB pathway. The recently described *Asp299Gly* polymorphism in the TLR4 gene is associated with impaired bacterial recognition (e.g. decreased sensitivity to LPS) and increased susceptibility to gram negative infections. We therefore hypothesised that TLR4 could be a good candidate gene in UC. Patients and Methods : A cohort of 163 patients with a well established diagnosis of UC and 136 healthy hospital workers were genotyped after informed consent for the TLR4 variant *Asp299Gly* and for the three CARD15 variants (Arg702Trp, Gly908Arg and Leu1007InsC) using Taqman PCR and PCR-RFLP's, respectively. Clinical charts were reviewed for the following phenotypes : localisation (rectosigmoiditis, left colitis and pancolitis), surgery, extra-intestinal manifestations, familial disease, pANCA and smoking at diagnosis. Groups were compared using Chi-square test.
Results : There were 31/163 (19.02%) UC patients carrying the TLR4 variant compared to only 13/136 (9.5%) healthy controls ($p = 0.021$). The mutated allele frequency was significantly higher in UC than in the control population (10.1% *vs*. 5.2%, $p = 0.015$). There were 2 UC patients homozygous for the mutant allele, compared to 1 control. Univariate analysis failed to show any significant association between TLR4 variant *Asp299Gly* and UC phenotypes. 4.9% of the patients were CARD15+/TLR4+, 12.3% were CARD15+/TLR4-, 14.1% CARD15-/TLR4+ and 68.7% CARD15-/TLR4-. Among the different combinations, CARD15-/TLR4+ was the only one significantly more frequent in UC than in controls ($p = 0.037$).
Conclusion : A positive association is observed between the TLR4 *Asp299Gly* polymorphism and UC. The frequency of this mutant allele was twice as high in UC patients compared to healthy controls. This association may further help to understand the role of the bacterial flora in the development of ulcerative colitis.

- D26 -

CROHN'S DISEASE IS ASSOCIATED WITH THE TOLL-LIKE RECEPTOR (TLR)–4 POLYMORPHISM ASP299GLY : FURTHER EVIDENCE FOR A DEFICIENT BACTERIAL RECOGNITION IN THE TRIGGERING OF THE DISEASE. Denis Franchimont, Séverine Vermeire, Hakim El Housni, Marieke Pierik, Thierry Gustot, Olivier Lemoine, Gilbert Vassart, Jacques Devière, André Van Gossum and Paul Rutgeerts. Department of Gastroenterology, Erasme University Hospital, Brussels and Department of Gatroenterology, Gasthuisberg, Leuven, Belgium.

Background and Aim : Elicitation of an innate immune response to bacterial products is mediated through families of pattern-recognition receptors (PRRs) including cell surface receptors, the toll-like receptors, and cytosolic receptors, the Nods. Mutations in the cytosolic receptor Nod2 (CARD15) have been associated with Crohn's disease (CD). The recently characterized TLR4 Asp299Gly polymorphism impairs LPS signaling and is associated with increased susceptibility to gram-negative bacteria in humans. We sought to determine if this TLR4 polymorphism was associated with CD and impact, alone or in interaction with Nod2, on a particular CD phenotype.
Patients and methods : Two independent cohorts of CD patients (cohort 1 n = 334 and cohort 2 n = 88) and 136 healthy controls were genotyped after informed consent for the TLR4 variant Asp299Gly using Taqman PCR and for the three disease-associated Nod2/CARD15 variants (Arg702Trp, Gly908Arg and Leu1007fsinsC) using PCR-RFLP. Results. In cohort 1, 68/334 (20.4%) CD patients carried TLR4-Asp299Gly compared to only 13/136 (9.5%) controls ($p = 0.0049$). Allele frequencies for the wild type and mutated allele respectively were 10.8% vs. 5.2% ($p < 0.001$). Of this cohort, 150/334 (44.9%) CD patients carried at least one Nod2 variant compared to 30/136 (22.0%) controls ($p < 0.0001$). These results were confirmed in cohort 2 with 18/88 (20.4%) CD patients carrying the TLR4-Asp299Gly variant ($p = 0.021$). The allele frequency for the mutated allele in this cohort was 10.8%. NOD2 prevalence was 42% ($p = 0.0014$). Univariate analysis performed on the total cohort of 422 patients failed to show any significant association between TLR4- Asp299Gly and a particular CD phenotype. In the combined cohort, 56.6% of patients carried CARD15 or NOD2 variants with 12.1% of patients Nod2-/TLR4+, 36.5% Nod2+/TLR4-, 43.1% Nod2-/TLR4- and 8.3% Nod2+/TLR4+ without phenotype association.
Conclusion : We report on a novel association between the TLR4 Asp299Gly polymorphism and CD which further underscores the important genetic influence of *PRR*s in Crohn's disease.

- D27 -

NEW FORMS OF IMMUNOSUPPRESSION IN IBD. Walter Reinisch. Univ.-Klinik für Innere Medizin IV, Abt. Gastroenterologie & Hepatologie, General Hospital Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria.

The consensus to implement “classical” immunosuppressive drugs, such as azathioprine/6-mercaptopurine (Aza/6-MP), methotrexate (MTX) and cyclosporine A (CyA) to the therapeutic armament against IBD has dramatically changed longterm outcome, especially in patients with refractory, chronic active, steroid-dependent or steroid-resistant disease. The disclosure of distinct immunological pathways relevant for the pathogenesis of IBD further revolutionizes current therapeutic approaches. Compounds derived from biological engineering, such as monoclonal antibodies to tumor necrosis factor alpha (infliximab) or alpha 4 integrin (natalizumab), specifically target molecules involved in the perpetuation of chronic inflammation and are of high efficacy. Despite their beneficial application in IBD the mode how “classical” and new immuno-suppressive/-modulatory drugs exert their action in vivo is only slowly elucitaded. This raises the question what is immunosuppression and which mechanisms are responsible to induce such as state ? e.g. Data emerges speculating that the long-time notion of anti-proliferative and anti-metabolic effects of Aza/6-MP oversimplifies the plethora of effects executed by this drug. Novel mechanisms, including the release of inhibitory cytokine networks, the activation of regulatory T cells, or the induction of apoptosis in cells of innate and/or adaptive immunity, might be involved in the action of “classical” and new immuno-suppressive/-modulatory drugs. These mechanisms could result in the actively induced state of peripheral T and B cell tolerance, which might explain why in some patients longterm clincal response to these drugs is maintained even after drug withdrawal. Clinical use of multiple immunosuppressants is primarily responsible for the success observed following organ transplantation, and might be also relevant for IBD, as shown for the combination of Aza/6-MP and infliximab. Therefore, the revelation of the exact mechanisms of these drugs is of paramount importance to develop strategies employing potentially synergistic effects. Furthermore, insights into the exact mechanisms of immunosuppressive drugs might also help to understand unfavourable outcomes and to avoid adverse effects on an individual basis. Based on these new knowlegdes “classical” immunosuppressives turn from old heros to new partners for the currently emerging “high tech” treatments.

- D28 -

TYPE 1-INSULIN-GROWTH-FACTOR-1-RECEPTOR EXPRESSION AND ITS CORRELATION TO FIBROSIS AND APOPTOSIS IN INTESTINAL LESIONS OF CROHN DISEASE. F. El Yafi, R. Winkler, P. Delvenne, N. Boussif, J. Belaiche, E. Louis. Dept of Gastroenterology, Molecular Oncology and Pathology, CHU of Liège, Belgium.

Aim of the study : Through their pro-fibrotic and anti-apoptotic effects, IGFs could play a role in the development of intestinal strictures and could take part in the perpetuation of chronic intestinal inflammatory reaction in Crohn’s disease (CD). In this study we first described Type 1-IGF-1 receptor (IGFR1) expression, which mediates all IGFs effects, within inflammatory and fibro-inflammatory intestinal lesions of CD. Then, we searched for a possible correlation with fibrosis and apoptosis.
Method : We performed our analyses on surgical specimens :12 fibrostenotic CD, 5 inflammatory CD and 9 controls. By immunohistochemistry, we localised cells expressing IGFR1 and cells expressing activated caspase 3, which is a membre of the apoptosis cascade, in the intestinal mucosa and submucosa. We counted IGFR1-positive cells, caspase-positive cells and also total inflammatory cells by field in purpose to express our results as absolute and relative values. Fibrosis was assessed by Trichrome staining, enabling us to classify the slides according to a fibrosis score (1-3).
Results : From a qualitative point of view, IGFR1 was mainly expressed by inflammatory cells (IC) in a transmural pattern. IGFR1 expression in IC and smooth muscle cells was found in CD as well as in controls. IGFR1 was also expressed by fibroblast-like cells in the submucosa, and rarely by serous adipous cells and intestinal neural cells in CD. From a quantitative point of view, we noticed a significant increase in the absolute number of IGFR1-positive IC in the mucosa and submucosa, in CD compared to controls ($p < 0,007$), and in involved areas of CD compared to uninvolved areas ($p < 0,03$). There was also a trend toward an increase in the relative number of IGFR1-positive cells. In the mucosa, this increase in IGFR1-positive IC did not correlate with the score of fibrosis nor with the number of apoptotic cells. In the sub-mucosa this increase tended to correlate positively with fibrosis in involved areas ($p = 0,09$) and correlated negatively with apoptosis in uninvolved areas ($p < 0,05$).
Conclusion : CD is characterized by an increased expression of IFGR1 by different cell types, including inflammatory cells and fibroblast-like cells. In the submucosa, IGFR1 expression correlates positively with the level of fibrosis and negatively with apoptosis.

- D29 -

PRE-OPERATIVE TREATMENT WITH INFLIXIMAB DOES NOT REDUCE THE LENGTH OF RESECTED BOWEL IN CROHN'S DISEASE. L. Marchal, G. D'Haens, G. Van Assche, P. Rutgeerts, F. Penninckx, A. D'Hoore, Dpt. of Gastroenterology, Catholic University Leuven, 3000 Leuven, Belgium.

Background : Infliximab, a chimeric monoclonal antibody to human tumor necrosis factor, is an effective treatment of inflammatory and fistulizing Crohn's disease. It also induces significant endoscopic healing and disappearance of inflammatory cells in the mucosa. Therefore, it may reduce the length of inflammation and, as a consequence, the length of bowel to be resected when it is administered in the pre-operative period.
Aim : To determine if the use of infliximab prior to surgery reduces the extent of intestinal resections.
Methods : 14 Crohn's disease patients who received infliximab at a dose of 5 mg/kg within two months prior to surgery were compared with a control group who underwent identical surgery but without pre-treatment with infliximab. Both groups were similar in age and gender. The length of inflammation was assessed on pre-operative small bowel follow-through. The surgical procedures consisted of small bowel resections, during which grossly inflamed bowel was resected with 5 cm healthy intestine at both ends. The length of resection was measured by the pathologist, after formaline fixation of the specimen.
Results : A significant although weak correlation was found between extent assessed on pre-operative small bowel follow-through and extent assessed by the pathologist on the surgical specimen ($r = 0.48$; $p < 0.02$). We did not observe a significant reduction in length of resection by administering infliximab in a pre-operative setting. Mean length of inflammatory small bowel in the infliximab-treated group was 19.4 cm (2-40 cm) prior to surgery and 24.9 cm (10-40 cm) at surgery. Mean length of inflammation in the non-infliximab-treated group was 21.5 cm (5-50 cm) prior to surgery and 29.2 cm (8-61 cm) at surgery.
Conclusion : If infliximab heals mucosal lesions it does not seem to cure transmural lesions in Crohn's disease and it does not seem to allow more limited resections when administered in the pre-operative period.

- D30 -

INFLIXIMAB DOES NOT INCREASE POSTOPERATIVE COMPLICATION RATES IN PATIENTS WITH CROHN'S DISEASE. L. Marchal, G. D'Haens, G. Van Assche, P. Rutgeerts, M. Hiele, F. Penninckx, A. D'Hoore, Dpt. of Gastroenterology, Catholic University Leuven, 3000 Leuven, Belgium.

Backgrounds : By neutralizing tumor necrosis factor with infliximab and thus suppressing the immune response in the pre-operative setting, the risk of post-operative complications may increase. Aim : To assess whether infliximab in the pre-operative period increases post-operative complications in patients operated on for Crohn's disease. Methods : Out of a cohort of 313 patients who received infliximab for Crohn's disease, 40 patients were identified who received one or more infusions prior to intestinal surgery (in 31 patients within 12 weeks). The post-operative events of these patients were compared with those of a control group of 39 patients who did not receive infliximab prior to surgery in the same period. The control group was adjusted for age, gender and surgical procedure. All patients underwent either small bowel resection, ileocolonic resection, left hemicolectomy or abdomino-perineal rectal amputation. We divided complications into major or minor complications, occurring either within ten days (early) or three months (late). Major complications included sepsis, anastomotic leak, peritonitis, local fistula or abscess recurrence, wound-infection, wound-failure, severe anemia and bulbar ulcer bleeding. Minor complications included haematoma, fever, delayed transit, infection and intestinal sub-obstruction. Results : The incidence of early minor (15.0% vs. 12.8%) and major (12.5% vs. 7.7%) complications and of late minor (2.5% vs. 5.1%) and major (17.5% vs. 12.8%) complications was not significantly different in both groups. Mean hospital-stay after surgery was comparable in both groups (10.3 ± 4.0 vs. 9.9 ± 5.5 days). When we compared infection rates during the first ten days after surgery in both groups, there was a trend towards an increased infection rate in infliximab-treated patients (6 vs. 2 patients ; $p = 0.14$). However, the number of patients receiving corticosteroids and/or immunosuppresives at surgery was significantly higher in the infliximab-treated group (29 vs. 16 patients ; $p < 0.05$). Infections in these patients included sepsis ($n = 2$), wound-infection ($n = 1$), upper airway infection ($n = 1$), infectious diarrhoea ($n = 2$) and yeast infection ($n = 1$). Infections in non-infliximab-treated patients included sepsis ($n = 1$) and peritonitis ($n = 1$). Conclusions : The use of infliximab before intestinal resection does not prolong hospital-stay and does not increase the rate of post-operative complications. Patients recently treated with infliximab can undergo surgery safely.

- D31 -

A POLYMORPHISM IN IGG FC RECEPTOR GENE FCGR3A IS ASSOCIATED WITH BIOLOGICAL RESPONSE TO INFLIXIMAB IN CROHN'S DISEASE. E. Louis, Z. El Ghoul, S. Vermeire, S. Dall'Ozzo, P. Rutgeerts, G. Paintaud, J. Belaiche, M. De Vos, A. Van Gossum, J.F. Colombel, H. Watier. Belgian Expanded Access Program of Infliximab study group ; laboratory of pharmacogenetics of monoclonal antibodies, Tours, France ; CHU of Lilles, France.

Background : The mechanism of action of infliximab in Crohn's disease (CD) is incompletely understood but a lysis of mononuclear cells expressing membrane TNF ? through apoptosis, complement activation or ADCC is suspected. A functionally significant polymorphism in *FCGR3A*, the gene coding for Fc?RIIIa expressed on macrophages and NK cells, has recently been found to be associated with a positive response to another recombinant IgG1 antibody, rituximab, in non HK lymphomas. The Fc?RIIIa-158V allotype has a higher affinity for IgG1 than the Fc?RIIIa-158F (phenylalanine) allotype and NK cells from V/V subjects are more potent in ADCC. We therefore tested the hypothesis of an association between *FCGR3A* gene polymorphism and response to infliximab.
Patients and methods : *FCGR3A*-158 polymorphism was determined in 206 CD patients having received infliximab for either refractory luminal (n = 147) or fistulizing (n = 59) CD. Clinical response was defined as complete, partial or absent according to the same definition as in controlled trials. Biological response was assessed in 83 patients who had elevated C-reactive protein (CRP) (> 2 x upper limit) before treatment and for whom CRP values were also available after treatment (4 weeks (luminal) or 10 weeks (fistulizing) after infliximab). A positive biological response was defined as a decrease in CRP of at least 50%. *FCGR3A*-158V/F polymorphism was determined using an allele-specific PCR assay.
Results : Complete, partial and no clinical response was observed in 108 (52.4%), 46 (22.3%) and 52 (25.2%) patients, respectively. Frequencies of *FCGR3A* V/V, V/F and F/F genotypes were 17%, 50.9% and 32%, respectively. There were 60% complete responders among V/V patients vs 50.9% among V/F and F/F (NS). A positive biological response was observed in 52/83 (62.7%) patients. There were 87.5% biological responders among V/V patients vs 56.7% among V/F and F/F (P = 0.02). Furthermore, 100% of V/V patients had a decrease of at least 25% of CRP after treatment compared to only 64.2% of V/F or F/F patients (P = 0.004). In this subgroup of 83 patients with high CRP before treatment, there was also a trend towards a better clinical response in V/V patients (66.7% complete responders vs 39.7% in V/F and F/F ; P = 0.08).
Conclusion : CD patients with *FCGR3A*-158V/V genotype have a better biological, and possibly clinical, response to infliximab. This may be due to a more effective ADCC-mediated lysis of mucosal cells expressing membrane TNF- ?.

- D32 -

HOW TO EVALUATE ATYPICAL PERINUCLEAR ANTINEUTROPHIL CYTOPLASMIC ANTIBODIES (PANCA) IN PATIENTS WITH ULCERATIVE COLITIS (UC)? RESULTS OF AN INTER-OBSERVER AND INTER-ASSAY STUDY. S. Joossens (1), M. Daperno (2), J. Goeken (3), Z. Shums (4), C. Trapani (2), G. Norman (4), G. Godefridis, G. Claessens, M. Pierik, S. Vermeire, X. Bossuyt, P. Rutgeerts (1). (1) University Hospital Gasthuisberg, Leuven, Belgium ; (2) Ospedale Mauriziano Umberto I, Torino, Italy ; (3), Immunology Laboratory, University of Iowa, USA ; (4) Inova Diagnostics Inc, San Diego, USA.

Introduction & aim : Atypical pANCA are associated with UC. Unlike ANCA present in vasculitis (pANCA) and in Wegener's granulomatosis (cANCA), the exact target of these UC antibodies has not been identified yet. Immunofluorescence microscopy is the only widely available technique for the detection of atypical pANCA in UC. It has been suggested that commercially available assays are not standardized and part of discrepancy on results could be due to differences among the products used, as recently shown (1). Since a solid phase assay is not available yet and specific microscopic criteria to distinguish atypical pANCA from pANCA vary according to each laboratory, discrepancy on results could also be due to the investigator's interpretation of the results. An inter-observer variability study, within the same assay and an inter-assay variability study have therefore been performed.
Methods : In a cohort of 50 well-defined UC patients ANCA was tested by an indirect immunofluorescence on ethanol and formalin fixed neutrophils. To study inter-observer variability, ANCA was determined with the INOVA assay in the same cohort by 4 independent laboratories (INOVA US, Leuven Belgium, Torino Italy and Iowa US). The inter-assay variability was evaluated in the same patient cohort at the laboratory in Leuven with 3 different assays (INOVA, IMMUNOCONCEPTS, US and BINDING SITE, UK). Prevalence was calculated as well as concordance (Kappa) to compare the results (pair-wise comparisons).
Results : For the inter-assay study, the prevalence of pANCA varied from 16% to 60% resulting in Kappa values ranging from 0.04 to 0.2. The results of the inter-observer study showed prevalence ranging from 40% to 64%. Kappa values in this group ranged from 0.23 to 0.54.
Conclusion : Differences in results on pANCA in UC are not only due to a lack of standardization of different assays but are also the consequence of different readings of the same assay. These problems can only be solved if a standardized ELISA for atypical pANCA could be developed. Therefore, however, the target antigen should be identified.
1. Sandborn W.J. Inflamm. Bowel Dis., 2001, 7 : 192-201.

- D33 -

OBSTRUCTION OF THE COLON TREATED BY EXPANDABLE STENTS. J. Vandervoort, V. Bouderez, J. Vandervoort, K. Hendrickx, J. Vanstiphout, L. Duville, M. De Man, P. Van der Spek, L. Lepoutre. Dpt. of Gastroenterology ; Onze-Lieve-Vrouw Ziekenhuis, 9300 Aalst, Belgium.

Aim : Gastrointestinal obstruction due to colorectal cancer (CRC) is usually treated by surgery. Use of Self-Expandable Metal Stents (SEMS) to relieve obstruction is effective and less invasive. We report on our experience.
Methods : We included 49 consecutive CR-stents inserted from 5/'98 until 11/'02 in 42 patients with obstructive CRC. Follow-up is complete on all patients.
Results : Our series consists of 49 SEMS placements in 42 patients (26 male, 16 female). Mean age was 68yrs (range 35-95). Stents were placed for adenocarcinoma in 46, extrinsic compression due to ovarian cancer in 1, and ischemic anastomotic stenosis in 2 patients. The majority of lesions was in the sigmoid (#28). Nine were located in the rectum, 6 in the descending colon, 4 transverse colon and 2 ascending colon. Enteral Wallstent" was used in 46, Ultraflex Precision" in 3. Seven SEMS were placed for pre-operative decompression, 40 for palliation and 2 in benign disease. Technical success was achieved in 98%(48/49), clinical success in 94%(46/49). In the palliative group (33pts) 24 patients died with a mean survival rate of 19 weeks (range 2-80 weeks) with stent patency until death. The other 9 patients are alive with a functioning stent (range 1w-37w). Six of seven pre-operative patients got a single-stage resection of the primary tumor. One patient got a decompressive colostomy. Mean time-interval to surgery was 3 weeks (range 2d-4w). An uneventful furhter disease course was seen in 74%(36/49) of patients. Thrithteen (26%) patients had some adverse event during their furhter course : i.e. re-obstruction in 5(10%), migration in 5(10%) and perforation in 3(6%). The majority of these (8/13) was treated again by endoscopic therapy with re-stenting or insertion of a second stent. Thus a total of 44/49 (90%) was successfully treated endoscopically. Four (8%) patients needed surgery. Two of them had an emergency colostomy and 2 had a side-to-side enterostomy due to persistent small bowel obstruction. One (2%) patient in poor general condition died of an E.Coli sepsis the following day.
Conclusion : Colorectal stenting is a feasible and highly effective treatment for acute colonic obstruction. It is safe with low morbidity and obviates more invasive treatment. The majority of stent related problems can again be treated by minimal invasive endoscopic therapy.

- D34 -

ACID ADAPTIVE GENES OF H. PYLORI AS NOVEL TARGETS FOR ERADICATION. George Sachs, Yi Wen, David Weeks, Lis Marcus and David Scott. UCLA and GWLHS Los Angeles, California, USA.

H. pylori is a unique neutralophile that has adapted to living on the generally acidic environment of the gastric surface. Earlier studies had shown that this was due to the expression of a neutral pH optimum urease and it was thought that tightly bound surface urease released due to "altruistic lysis" of neighbouring organisms generated a protective cloud of ammonia to neutralize the acid in the microenvironment of the bacteria. More recent work has shown that acid survival in vitro and infection of mouse and gerbil also depends on expression of UreI, a proton-gated urea channel that permits rapid access of urea to intra-bacterial urease and that survival to acid depends on cytoplasmic and periplasmic buffering by internal generation of ammonia since UreI plays no role in surface urease activity. However, since other genes have been shown to affect acid survival, the urease system is necessary but not sufficient for optimal habitation of the gastric environment.
Using a complete genomic microarray and cy3 and cy5 labelling of the cDNA, approximately 200 genes were upregulated > twofold as buffered medium pH fell from 7.4 to 6.2 to 5.5 and to 4.5 in the absence of urea and about 100 remained upregulated in the presence of 5mM urea. About 100 genes were downregulated in the absence and 50 in the presence of urea. The upregulated genes represented several functional groups, such as regulatory, pH homeostasis, motility, pathogenicity, metabolic, general stress response, protein and DNA biosynthesis, transport and outer membrane biosynthesis. Some genes were upregulated already at a medium pH of 6.2, even in the presence of urea, suggesting that periplasmic pH was able to signal gene expression. Of these, the sensor histidine kinase gene, HP0164/5, phosphorylates its response partner, ompR, that regulates expression of ~ 100 genes in *E. coli*, may be of particular interest since its single periplasmic domain contains several histidines that would respond at a pH of 6.2 by protonation. Periplasmic carbonic anhydrase was also a pH upregulated gene and deletion of this gene has been shown to impair acid survival in the presence of urea (Lee Y-C et al *Gastroenterology* 122 : A423, 2002), implying, perhaps, that both NH_3 and CO_2 as products of urease activity are used as buffers for the periplasm of *H. pylori*.

- D35 -

INVESTIGATIONS FOLLOWING THE USE OF AN INACTIVE BATCH OF CIDEX® SOLUTION IN BELGIAN HOSPITALS. H. Carsauw (1), M. Adler (2), P. Goubau (3), W. Peetermans (4). (1) Scientific Institute of Public Health, Unit of Epidemiology, Brussels ; (2) Dept of Gastroenterology, Erasme Hospital, Brussels ; (3) Dept of Virology, Cliniques Univers. St-Luc, UCL, Brussels ; (4) Dept of Internal Medicine, Gasthuisberg, KUL, Leuven ; Belgium.

Objectives : 1) To identify infections, in particular hepatitis B (HBV) and hepatitis C (HCV), in patients undergoing mainly endoscopic procedures with instruments treated with an inactive batch of Cidex disinfection solution. 2) To determine whether infections detected after a procedure with instruments treated with inactive Cidex may possibly be Cidex-related**.**
Methods : Hospitals concerned were asked to complete a questionnaire on the use of the inactive batch, patients at risk and infections possibly related to the incident. It was recommended that exposed patients be recalled and screened for HBV and HCV infection. Patients in whom an infection (HBV, HCV or other) was detected were offered evaluation by a committee of independent experts for a possible relation of the infection to the Cidex-problem. The manufacturer Johnson&Johnson agreed to compensate all infection cases for which the expert committee concluded that a relation to the Cidex-problem could not be excluded.
Results : Overall 34.870 patients were recalled and 25.589 (73.4%) had blood drawn for HBV and HCV screening. No acute infections nor clusters of infection with HBV or HCV were identified. For 18.026 patients, anonymised data were centralised at the IPH for further analysis. Age-adjusted prevalences for HBV and HCV were comparable with prevalences in a sample of the Flemish population (data 1993-94) : respectively HBsAg 0.5% (95% CI 0.4-0.6) vs 0.7% (0.5-1.0), anti-HBc 5.6% (5.3-6.0) vs 6.4% (5.7-7.3), anti-HCV 0.6% (0.5-0.8) vs 0.9% (0.5-1.1). Prevalence for HCV increased significantly with increasing age (p for trend < 0.0001). The expert committee received 46 patient records for evaluation, of which 15 were refused mainly because of absence of risk exposure. For 17 patients with HCV infection, 2 HBV carriers and 2 bacterial complications post-surgery, the experts concluded that a relation to the Cidex-problem could not be excluded.
Conclusions : No evidence for an increased number of infections with HBV or HCV after the Cidex-incident was found. For at least 21 patients (17 HCV, 2 HBV, 2 bacterial infections) an agreement for compensation of damages was made after evaluation of their case by an expert committee.

- D36 -

THE ASSOCIATION BETWEEN INTRAGASTRIC DISTRIBUTION AND DYSPEPTIC SYMPTOMS IS RESTRICTED TO FUNCTIONAL DYSPEPSIA. H. Piessevaux, S. Walrand*, S. Pauwels*, Y. Horsmans. Departments of Gastroenterology and Nuclear medicine*, Cliniques Universitaires St-Luc (UCL), 1200 Brussels, Belgium.

Abnormal intragastric distribution of food during gastric emptying is frequently found in functional dyspepsia (Troncon, 1994). In previous studies in functional dyspepsia, we have shown associations between early distal redistribution of a meal and the presence of early satiety and between late proximal retention and the presence of postprandial fullness (Piessevaux, 1999). We therefore wanted to study whether this finding was present in dyspeptic syndromes associated with other disorders.
Aim : To study the relationship between symptoms and regional distribution of liquids and solids using a conventional gastric emptying radionuclide study in non-functional dyspepsia patients.
Methods : In 75 patients with dyspepsia associated with various underlying conditions (31 men, mean age 49 +/- 2.6 years), the severity score (0-3, 0 = absent, 1 = mild, 2 = relevant, 3 = severe) for each of eight dyspeptic symptoms (epigastric pain, postprandial fullness, bloating, early satiety, nausea, vomiting, belching, heartburn) was obtained. All patients underwent a mixed radiolabeled (Tc99m /In) solid/liquid gastric emptying study. Acquisitions were performed immediately after the meal and every 20 minutes for 2 hours and the patients were asked to score each symptoms at each step. The stomach was divided in a proximal and distal compartment by an automated software. The ratio of proximal over distal counts was computed at all time intervals for both phases.
Results : The underlying disease was diabetes mellitus in 47 patients, end stage renal disease in 18, both in 7 and other various conditions in 3. Early satiety was present in 31 patients (41%). The proximal/distal ratio at time 0 5.2+/-0.5 in patients with and 5.1+/-0.4 in patients without early satiety. Similarly, there was no association between the presence of postprandial fullness and the presence of proximal retention. The severity of the different symptoms during the test was not correlated to the intragastric distribution.
Conclusion : Using a radionuclide gastric emptying study in non-functional dyspeptic patients, we could not reproduce the association between intragastric distribution patterns and specific symptoms. This result may indicate activation of different pathways in the genesis of dyspeptic symptoms in functional or non-functional dyspepsia.

- D37 -

UPPER GASTROINTESTINAL TRACT SYMPTOMS MANAGEMENT BY GENERAL PRACTITIONERS IN BELGIUM : EVOLUTION OVER TIME, DEPENDING ON REIMBURSEMENT OF ANTI-SECRETORY DRUGS. E. Louis, P. Eisenradth, G. Cooremans, A. Elewaut, C. Doyen, E. Billiet, M. Melange. Interuniversity group for the study of upper GI tract symptoms management in Belgium and Glaxo-SmithKline Belgium.

The **aim** of our work was to assess the evolution of upper gastrointestinal tract symptoms (UGIS) management by general practitioners (GP) in Belgium over a period of time of 18 months, characterized by access to reimbursement of unlimited H2-antagonist (category b) and short term PPI treatment free of endoscopy.
Methods : In January 2001 and in June 2002, 120 and 99 (unselected subgroup of the 120) GP respectively accepted to fill in a standardized questionnaire for 10 consecutive patients consulting for UGIS, without endoscopic diagnosis of oesophagitis or gastro-duodenal ulcer within the last 12 months.
Results : 1045 and 943 questionnaires were filled in 2001 and 2002, respectively.
Patients characteristics were : mean age 49 and 52 ; male gender : 49% and 50% ; smokers : 36% and 42% (P = 0.0105) ; alcohol drinkers : 12% and 14% ; NSAID : 34% and 39% (P = 0.0214) ; Bad food habit according to the GP : 34% and 40% (P = 0.0085) in 2001 and 2002, respectively.
Type of main symptom : typical reflux in 53% and 69% (P = 0.000) ; atypical reflux in 6% and 8% ; alarm symptom in 2% and 3% ; epigastric pain in 19% and 25% (P = 0.0013) ; dyspepsia-bloating in 19% and 16%, in 2001 and 2002, respectively. Symptoms were considered as mild in 23% and 29% (P = 0.0017) and were present since less than 1 month in 66% and 85% (P = 0.0000), in 2001 and 2002 respectively.
Upper GI endoscopy was directly prescribed in 25% and 18% (P = 0.0003), while another exploration was prescribed in 8% and 3% (P = 0.0000) in 2001 and 2002 respectively. Of note, in 2002, 31% of the patients had an endoscopy performed in the past (more than 12 months earlier) and GP would have prescribed an endoscopy in 75% in case of no response to empirical treatment.
Treatment was prescribed in 98% and 99% (H2-antagonists : 51% and 55% ; PPI : 21% and 31% (P = 0.0001) ; antacids : 10% and 8% ; prokinetics : 13% and 5% (P = 0.0000)), in 2001 and 2002 respectively.
Conclusions : there was a significant evolution between 2001 and 2002 in both characteristics of patients consulting for UGIS and their management. Patients had more frequently typical reflux symptoms, milder intensity and a more recent history in 2002 than in 2001. An endoscopy was less frequently prescribed as first approach, while almost all the patients got a treatment with an increased proportion of both H2-antagonist and PPI.

- D38 -

EFFICACY AND COSTS OF ON DEMAND TREATMENT WITH ESOMEPRAZOLE 20 MG IN PATIENTS WITH ENDOSCOPY NEGATIVE REFLUX DISEASE (ENRD). J. Tack (1), P. Deprez (2), G. Vandenhoven (3), K. Daems (3). (1) UZ Gasthuisberg, KUL, Leuven ; (2) Clin Univ St. Luc, UCL, Brussels ; (3) AstraZeneca, Brussels, Belgium.

Objective : The primary objective of this multicentre, open, phase IV study was to document the efficacy of on-demand treatment with esomeprazole 20 mg in maintaining heartburn control in patients with ENRD in Belgium. Secondary objectives were to assess medical costs (study and OTC medication, health care visits, GERD related tests), non-medical costs (transportation) and non-direct costs (absence from work) during the maintenance phase treatment.
Methods : In total, 379 patients with ENRD confirmed by upper GI endoscopy, who have been experiencing heartburn for ≥ 3 days during the week before inclusion, entered the acute phase of the study to receive esomeprazole 20 mg once daily for 4 weeks. Patients who were asymptomatic (complete resolution of heartburn or not more than 1 day with mild heartburn during the last 7 days prior to the visit) at the end of the acute treatment phase, were allowed to continue the 6-month maintenance phase, receiving esomeprazole 20 mg on demand. Analyses were performed on an intention to treat basis.
Results : The mean age and BMI (± SD) at entry were 48 ± 15 y and 25.4 ± 4.7, respectively. Sex ratio : 66.5% women and 33.5% men. Before inclusion, all patients had heartburn (14% mild, 65% moderate, 20% severe), 63% had epigastric pain, 72% had regurgitation and 13% had dysphagia complaints. After the acute phase, 311 (82%) patients were asymptomatic and 87% was satisfied with their treatment. 312 patients started the maintenance period, 259 completed the study. 274 (88%) patients, who completed the 6 months period or early teminated the study at 3 month, were satisfied with their therapy, only 16 (5.1%) patients were not satisfied and 22 (7%) patients dropped out between the start of the maintenance phase and month 3. 216 (69%) patients were asymptomatic, 73% free of epigastric pain, 76% free of acid regurgitation and 80% had no dysphagia complaints after 6 months (drop-outs were considered as treatment failures). Only 8 (2.6%) patients experienced a relapse. The direct medical daily cost was ± 0.8 (± 0.4)/day, whereas non-medical and non-direct costs were low compared to direct costs. Patients took on average 1 tablet every 2 days. 5 patients experienced a serious adverse event, which were not drug related. There were no ENRD-related hospitalisations.
Conclusions : This study demonstrates an effective symptom control in the long term on demand use of esomeprazole 20 mg, which also has a very low medical cost, in patients with ENRD.

- D39 -

ENDOLUMINAL GASTROPLICATION (ENDOCINCH®) IN GERD PATIENTS REFRACTORY TO PPI THERAPY AS AN ALTERNATIVE TREATMENT FOR NISSEN FUNDOPLICATION. J. Arts, P. Caenepeel, D. Sifrim, T. Lerut, P. Rutgeerts, J. Janssens, J. Tack. Divisions of Gastroenterology, Endoscopy and Esophageal Surgery, University Hospitals Leuven, Belgium.

In a subset of patients with gastroesophageal reflux disease (GERD), symptoms persist in spite of proton pump inhibitor (PPI) therapy. Nissen fundoplication is an alternative but complications and reduced effect on the long-term are important limitations of this treatment. Endoscopic gastro-plication (EG) was reported to provide a novel therapeutic option in GERD.
Aim : To evaluate EG as an alternative treatment for Nissen fundoplication in patients with persistent symptoms under PPI treatment.
Methods : Consecutive patients with established GERD and persisting reflux symptoms under PPI were recruited for EG using the Endocinch® Endoscopic Suturing kit. All patients were potential candidates for surgery. Exclusion criteria were age < 18, high grade esophagitis including Barrett's and hiatal hernia > 3cm. Symptoms were evaluated before and 12 months after the first EG ; 24 hour pH monitoring off PPI was performed before and after 12 months. All data are given as mean ± SD and were analyzed by Student's t test.
Results : 20 patients (10 females, mean age 44.7 ± 10.9 years) were recruited. Under conscious sedation with midazolam (6 ± 2mg) and pethidine (53 ± 5mg), a mean of 2.0 ± 0.2 sutures were applied during a mean procedure time of 33 ± 6 min during the first EG of each patient. In case of inadequate symptom relief during follow up a second (10 patients) or even third (one patient) EG for additional stitches was performed. Throat ache and mild epigastric pain up to 3 days after the procedure were the only adverse events. At 12 months, EG significantly improved symptoms (11.6 ± 6 vs. 7.1 ± 4.5, $p < 0.05$) and pH monitoring (% time pH < 4 : 17.0 ± 11.1 vs. 9.8 ± 4.1%, $p < 0.05$) ; DeMeester score : 62.5 ± 42 vs. 40.6 ± 19.6, $p < 0.05$). After 12 months 6 patients (30%) remained asymptomatic without PPI treatment and 5 patients (25%) under PPI treatment. Six patients had persistent, but acceptable symptoms. Three patients with insufficient response were referred for Nissen fundoplication.
Conclusion : EG is able to provide an alternative for surgery in half of the patients with reflux refractory to PPI treatment. A randomized study comparing EG and Nissen fundoplication seems warranted based on this observation.

- D40 -

ENDOSCOPIC ANTI-REFLUX GASTROPLASTY FOR REFRACTORY GERD : PRELIMINARY RESULTS. J.P. Martinet, T. De Ronde, D. Lejeune, M. Melange. Dpt of HepatoGastroenterology, UCL CLinics of Mont-Godinne, 5530 Yvoir, Belgium.

Endoscopic anti-reflux gastroplasty -EARG- (EndoCinch", Bard) has been advocated for the treatment of gastroesophageal reflux disease (GERD) refractory to potent acid secretion inhibitors, as Nissen surgical fundoplication has proved to allow insufficient long-term symptomatic relief and PPI-free remission rate?. We report on a preliminary cohort of 17 GERD patients presenting from October 2001 to October 2002 with refractory digestive (n = 17), ENT (n = 10) or respiratory (n = 4) symptoms who underwent EARG. Pre-EARG data included erosive œsophagitis (Los Angeles class A to C in 14 ; gastric metaplasia of lower œesophagus in 3), LES insufficiency at manometric study, and pathological 24-hour pHmetry in 15 (PPI could not been stopped in 2 because of severe reflux-related asthma). EARG procedure included one to three sutures aiming at the closing of the hiatal gap, lasted 41 min on average (18 – 55 min), and immediate endoscopic result was rated as good (5) to excellent (10) in most of them. There was no significant complication of the sedation or the suturing technique. The improvement of heartburn (76.5%), acid regurgitation (88%), ENT (75%) and respiratory (75%) symptoms relief and decrease in anti-reflux medications (88%) were assessed after one month, with a global satisfaction rate (visual analogical scale) of 75.2%. These results deteriorated at three months, except for ENT symptoms, with respective scores of 60, 80, 82, 75, 58 and 62%. Symptomatic relapses (4/15 at 3-mo) occurred abruptly and were correlated to the leakage of at least one suture in all cases (4/4). A second session succeeded in only one of them, probably because of the particularly wide gape of diaphragmatic hiatus in these patients, responsible for a too strong traction on the suturing threads. 3-months pHmetry studies showed an improvement in most patients with symptomatic improvement, but also in two who relapsed, with œsophageal pH < 4 during 5.93% of time (range : 0.4-25) as compared to pre-EARG values (9.3% ; range : 0.8-23). In **conclusion,** despite an unavoidable learning curve, encouraging short-term symptomatic, endoscopic and pHmetry results of EARG confirm a good control of GERD symptoms in refractory situations. Assessing long-term efficacy of the EndoCinch® device, especially in wider hiatal hernia, needs larger prospective trials.

1. Spechler *et al., JAMA*, 2001.

- D41 -

RADIOFREQUENCY DELIVERY AT THE GASTROESOPHAGEAL JUNCTION IN GERD IMPROVES ACID EXPOSURE AND SYMPTOMS AND DECREASES ESOPHAGEAL SENSITIVITY TO ACID INFUSION. J. Arts*, A. Van Olmen**, G. D'Haens **, D. Sifrim*, A. Lerut***, P. Rutgeerts*, J. Janssens*, J. Tack*. *Dpt of Gastroenterology and Endoscopy, University Hospital Gasthuisberg Leuven, **Dpt of Gastroenterology Imaldaziekenhuis Bonheiden, ***Department of Thoracic Surgery, University Hospital Gasthuisberg Leuven.

Introduction : Several studies, including a randomised double blind sham study have demonstrated that the radiofrequency delivery at the gastroesophageal junction (Stretta procedure) induces symptom relief in GERD. However, improvement of pH monitoring was less throughout the studies. There is probably a mechanical and neurological influence.
Objective : To evaluate the influence of Stretta procedure on symptoms, acid exposure and acid sensitivity of the distal esophagus in heartburn patients with proven GERD (> 4% of time pH < 4).
Methods : Thirteen patients with proven GERD (3 males, mean age 51 +/- 10 years) participated in the study. Before and 6 months after the Stretta procedure symptom score, pH-monitoring and Bernstein acid perfusion test were performed. The latter was done by infusing HCL (pH 0.1) at a rate of 6 ml/min 15 cm proximal to the gastroesophageal junction during max 30 min or until the patients experienced heartburn. Symptom severity, acid exposure and time to report symptoms (TRS) during Bernstein test were compared by Student's t test. The proportions of patients with negative Bernstein test were compared using Chi-square test.
Results : Stretta procedure time was 52 +/- 8 min. There were no complications. Six months after the procedure, symptom score was significantly improved (12 +/- 5 to 9 +/- 6, $p < 0.05$) and 7 patients no longer needed acid suppressive drugs. Acid exposure during pH monitoring was significantly decreased (13 +/- 4 to 9 +/- 5% of time, $p < 0.05$). Before treatment, all patients had a positive Bernstein test ; 6 months later 4 were insensitive to 30 min acid infusion ($p = 0.02$). The mean TRS was significantly prolonged from 9 +/- 6 to17 +/- 11 min ($p < 0.05$).
Conclusion : The Stretta procedure induces subjective improvement of GERD symptoms and decreases esophageal acid exposure. In addition esophageal acid sensitivity is decreased 6 months after Stretta procedure. The mechanism underlying this finding and its relevance to symptom control require further studies.

- D42 -

LOWER ESOPHAGEAL SPHINCTER FUNCTION AFTER ENDOSCOPIC EVOH POLYMER INJECTION FOR GERD TREATMENT : 1 YEAR RESULTS. H. Louis (1), W.A. Voderholzer (2), O. Le Moine (1), D.E. Silverman (3), J. Devière (1). (1) Department of Gastroenterology, Erasme Hospital, Free University of Brussels, 1070 Brussels, Belgium ; (2) Department of Gastroenterology, Medical Faculty Charite, Humboldt University, Berlin, Germany and (3) Enteric Medical Technologies, Palo Alto, California.

Introduction : Implantation of ethylene-vinyl-alcohol polymer (EVOH) in the lower esophageal sphincter (LES) improves symptoms in patients with gastroesophageal reflux disease (GERD).
Aims & methods : To analyze the effect of EVOH injection on the LES function, 13 patients (4 male, 9 female) with GERD (GERD symptoms controlled with PPI,% pH < 4 > 5) underwent esophageal manometry 30 min before and 90 min after a semiliquid meal, before and 1 month after EVOH implantation. Follow-up was obtained at 6 and 12 months for 7 patients. Twenty-four hour ambulatory pH-metry was performed before and 6 months after implantation.
Results : [median (range)] *$p < 0.05$, non parametric paired test] : One month after EVOH injection, basal and residual (swallow-induced relaxation) LES pressures were significantly increased. At 6 and 12 month follow-up, only residual LES pressure was significantly increased. Frequency of postprandial transient LES relaxations (TLESRs) decreased after treatment, although the difference did not reach significance. Relaxation pressure measured during TLESRs was increased in a similar value as after swallow-induced relaxations. LES length was not modified by EVOH implantation. A trend to a decrease in reflux episodes as well as a reduction in esophageal acid exposure at pH-metry was also observed. GERD symptoms were significantly improved as assessed by the GERD HRQL score.
Conclusion : EVOH polymer implantation in the LES increases residual relaxation pressure. Reduction in the frequency of TLESRs could be another mechanism of action, which awaits confirmation in larger studies.

	Pre-treatment	1 month	6 months	12 months
LES basal P (mm Hg)	10.4 (7.2-22.2)	16.8 (6.5-32.3) *	11.1 (8-23.4)	14.4 (6.1-29.4)
residual P (mm Hg)	.0 (0-1.3)	2.8 (0-18) *	1.7 (0-7.3) *	3.15 (0.3-6.7) *
TLESRs (n/h)	3 (0-7)	.0 (0-9)	1 (0-3)	1 (0-4)
GERD HRQL score	21 (5-27)	8.5 (0-28) *	11.5 (0-28) *	3 (0-22) *
N patients	13	13	7	7

- D43 -

HALOFUGINONE TREATMENT MIGHT AGGRAVATE FIBROSIS IN A RAT MODEL OF BILIARY CIRRHOSIS.
M. Van de Casteele, I. Vander Elst, J.F. van Pelt, T. Roskams*, J. Fevery, F. Nevens. Depts of Hepatology and *Pathology, UZ Gasthuisberg KU Leuven, Herestraat 49, Leuven, Belgium.

Background : Halofuginone (HF) reduced the fibrotic content in 2 toxic models of cirrhosis in rats. This was explained by reduction of collagen alpha-1(I) levels.
Aims : We wanted to know whether this beneficial antifibrotic effect could also be observed in biliary cirrhosis and if it led to less portal hypertension.
Methods : Four groups of rats (n = 12 each) with biliary cirrhosis due to bile duct excision and formol injection were used. Two groups received HF (Stenorol“) 5 ppm in the food ; the 2 other groups received food without additive. Aminopyrine breath test (ABT) and haemodynamic measurements (arterial pressure, portal pressure (PP), portosystemic shunting) under general anaesthesia were carried out at 3 wks or at 6 wks. Afterwards, liver biopsies were taken for Sirius red staining.
Results : Survival in the 3 wks groups was n = 7 with HF and n = 3 untreated ($p < 0.05$) but was similar at 6 wks (n = 5 HF and n = 6 untreated) ; no wound healing problems were seen in the HF treated groups. The ABTk parameter was significantly worse with HF (6 ± 3 and 4 ± 2) vs untreated groups (12 ± 3 and 8 ± 3 -10^{-3}/min ; $p < 0.05$). No differences in haemodynamic data, e.g. PP (8 ± 2 and 10 ± 3 with HF vs 10 ± 2 and 8 ± 2 mm Hg untreated ; NS), or liver weights were seen. Hepatic Sirius red stain was similar or paradoxically worse at 6 wks with HF vs untreated rats. More Sirius red stain coincided with prominent bile duct proliferation in several HF treated rats.
Conclusion : HF did not reduce fibrosis in biliary cirrhotic rats. This can be due to 1° insufficient drug uptake secondary to cholestasis or 2 completely different cellular mechanisms in biliary fibrosis as compared to toxic fibrosis in rats.

- D44 -

ULTRASOUND IN SCHISTOSOMIASIS : AN IMPORTANT TOOL TO STUDY LIVER PATHOLOGY AND A BASIS FOR EXAMINING OTHER INDICATORS OF MORBIDITY.
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In October 1996, in Niamey, Niger, a practical guide to the standardized use of ultrasonography, for the assessment of schistosomiasis-related morbidity was approved by the WHO. This guide states that in schistosomiasis control programmes aimed to reduce morbidity, the success of interventions using parameter like parasite egg count alone is not sufficient, as it measures the level of infection but does not provide any direct evidence about host pathological changes. Chronic S. mansoni infection affects the liver with hepatic fibrosis and portal hypertension. Sudden life-threatening haemorrhage may occur due to the rupture of gastro-oesophageal varices, the most common complication of periportal fibrosis. Ultrasonography can be used to detect periportal fibrosis and portal hypertension, and has proved to be more reliable than clinical methods for the diagnosis of hepatosplenic pathology. The Niamey-Belo-Horizonte approach of ultrasonographic examination provides opportunity to study association between schistosomiasis caused pathology as revealed by ultrasound and other indicators of morbidity. The neuropeptide somatostatin exerts an antifibrotic effect on the hepatic stellate cells in vitro, and reduce fibrosis and morbidity in S. mansoni infected animals. It is the drug of choice to control variceal bleeding and reduce portal pressure. In recent years, cases of fibrosis due to *S. mansoni* infections are on the rise in Northern Senegal. We studied possible association between fibrosis and circulating levels of somatostatin, in *S. mansoni* infected subjects. Following the Niamey-Belo Horizonte method to detect fibrosis grade in the subjects, 52 volunteers were examined using a standardized protocol. Normal liver was denoted Pattern A, echogenic, peripheral & portal thickening was graded and given a score ranging from B-F. Non-fibrotics had more circulating somatostatin (N = 22, median = 4.214, Lower 95% CI = 3.401, Upper 95% CI = 4.980) than fibrotics (N = 30, median = 2.376, Lower 95% CI = 2.152, Upper 95% CI = 3.328) (Mann-Whitney U = 170, P = 0.0031). Our study concluded that in schistosomiasis patients, physiological levels of somatostatin could determine disposition of particular individuals towards fibrosis as opposed to others. Ultrasonography and serological markers like somatostatin can be useful tools in the planning of interventions aimed at reducing liver damage.Host pathology could be alleviated by somatostatin’s therapeutic ability to treat bleeding oesophageal varices, reduce portal pressure and possibly revert fibrosis.

- D45 -

HEPATIC GRANULOMA FORMATION IS INDUCED BY GLYCOCONJUGATES OF SCHISTOSOMA MANSONI EGGS AND KEYHOLE LIMPET HAEMOCYANIN. K. Van de Vijver*°, C.H. Hokke°, A. Van Remoortere°, M. Robijn°, G. Vrolix*, W. Jacobs*, A.M. Deelder°, E.A. Van Marck*. (*) Dept. Pathology, Antwerp University, Antwerp, Belgium ; (°) Dept. Parasitology, LUMC, Leiden, The Netherlands.

Background : The major pathological manifestations of schistosomiasis are caused by the entrapment of eggs in the liver of an infected host. Periovular granuloma formation induced by soluble egg antigens (SEA) often leads to severe hepatic fibrosis. Several reports have highlighted the granulomogenic capacities of carbohydrate determinants prominent in both glycoproteins and glycolipids of SEA. These glycoconjugates contain among others the immunogenic Gal?1-4(Fuc?1-3)GlcNAc (Lewis X) and GalNAc?1-4(Fuc?1-2Fuc?1-3)GlcNAc (LDN-DF). Due to its cross-reactivity to schistosomal antigens, keyhole limpet haemocyanin (KLH) has been used for immunodiagnosis and is therefore suitable as a model antigen in experimental settings. Fucose-containing epitopes are known to be part of these cross-reactive antigens.
Our aim is to characterise defined glycoconjugate antigens of SEA and KLH, which induce granulomogenesis *in vivo*.
Methods : The immunological functionality of the carbohydrates of SEA and KLH was destroyed by periodate treatment, without damaging their protein backbone. Trypsin digestion of KLH enabled us to obtain glycopeptide fractions, with destruction of the protein fraction but leaving the glycans intact, by immunoaffinity chromatography and HPLC. The ability of intact, periodate-treated and trypsinised SEA and KLH to elicit granuloma formation was explored by hepatic implantation of conjugated Sepharose beads into naive BALb/c mice. RNAse A- (pure protein) and RNAse B- (glycoprotein with only oligomannoses) coated beads served as additional controls. The granulomatous response was evaluated on liver sections with H&E and immunofluorescent staining.
Results : SEA- and KLH-coated beads induce granulomas with macrophages, T-lymphocytes and numerous eosinophils. Beads conjugated with periodate-treated glycoproteins yielded only a monolayer of macrophages, similar to uncoated beads. Total trypsinised KLH and one HPLC-fraction of the trypsinised KLH, containing the fucose epitopes, were also shown to be active inducers of granulomas. RNAse A- and RNAse B-coated beads did not induce a granulomatous reaction, showing the possible importance of fucose-containing sugars.
Conclusions : These results indicate a major immunomodulatory role of carbohydrate determinants of SEA and KLH *in vivo*. Further characterisation of these carbohydrate components by mass spectrometry should lead to the identification of the molecular stimuli in the granulomogenesis in schistosomiasis.

- D46 -

SYSTEMIC AND SPLANCHNIC HEMODYNAMIC EFFECTS OF SILDENAFIL IN RATS WITH CIRRHOSIS AND PORTAL HYPERTENSION. Isabelle Colle, An De Vriese*, Hans Van Vlierberghe, Norbert Lameire*, Martine DeVos. Departments of Hepato-Gastroenterology and Nephrology*, University Hospital of Ghent, Belgium.

Objectives : Sildenafil (Viagra^{R})is a selective inhibitor of the cGMP-specific phosphodiesterase type V (PDE-V) in the corpus cavernosum. PDE-V is also present in the mesenteric artery. Cirrhosis is complicated by a splanchnic vasodilation attributed to a local overproduction of nitric oxide (NO). As sildenafil potentiates the effects of NO, it may further decrease mesenteric vascular tone and increase portal venous blood flow. The aim is to evaluate the effects of sildenafil on the systemic and splanchnic haemodynamics in an experimental model of cirrhosis.
Methods : Secondary biliary cirrhosis was induced in male Wistar rats by common bile duct ligation (CBDL, n = 8) ; control rats were sham-operated (sham, n = 7). Mean arterial pressure (MAP), portal venous pressure (PVP) and arterial mesenteric blood flow (MBF) were measured after intramesenteric (i.m.) (0.01 to 10 mg/kg) and after intravenous (i.v.) (0.01 to 10 mg/kg) administration of sildenafil.
Results : Baseline PVP was significantly higher in CBDL than in sham rats, whereas baseline MAP tended to be lower and MBF tended to be higher in CBDL compared with sham rats. Both intramesenteric and i.v. injection of sildenafil significantly decreased MAP and increased MBF and PVP in a dose-dependent way. The decrease in MAP was significantly lower in CBDL than in sham rats. The increase in MBF was significantly lower in CBDL than in sham rats. PVP tended to increase more importantly in sham rats than in CBDL.
Conclusion : Sildenafil increases MBF and PVP and induces systemic hypotension. The effects are less pronounced in cirrhosis, suggesting vascular hyporesponsiveness to sildenafil. Although the rise in PVP in cirrhotic animals is smaller than in controls, it may present a risk for hemorrhagic complications. Further studies are necessary before prescribing sildenafil to patients with cirrhosis.

BACLOFEN AS TREATMENT FOR INTRACTABLE HICCUP. T. Rondou, M. Hiele, J. Tack. Dpt. Gastroenterology, University Hospital Gasthuisberg, 3000 Leuven, Belgium.

Background : Hiccup is a spasmodic involuntary contraction of the inspiratory muscles, associated with an abrupt glottic closure. Short hiccup spells are frequent, innocent, and mostly self-limiting, and are not requiring medical treatment. In contrast, chronic hiccup, defined as spells lasting for more than 48 hrs or as recurring spells, is a rare phenomenon, may be associated with a wide variety of medical disorders and often requires medical treatment, as it can cause sleep deprivation, exhaustion and depression. Diagnostic investigations to rule out gastroenterological, neurological or other medical disorders are mandatory, though an etiologic condition is often not found. In these cases, symptomatic treatment is indicated. Classically, chlorpromazine is widely used for intractable hiccup, but it has important side-effects. The last ten years, baclofen, a GABA-analogue, has been described as a safe and often effective treatment. The aim of this report is to bring this elegant therapy under the attention of the gastroenterologic community.
Patients and results : Three male patients with intractable chronic hiccup are reported. The first patient presented with hiccup-spells for 5 months ; investigations for underlying conditions (chest CT-scan, gastroscopy, abdominal ultrasonography) were negative. The second patient underwent in 1998 a Nissen-fundoplication for GERD and intractable hiccup, with a persistent postoperative hiccup. Cerebral MRI, abdominal CT-scan, oesophageal manometry and gastroscopy were normal. Oesophageal X-ray showed a delayed evacuation and pH-metry a pathological reflux, but treatment with PPI was unsuccessful. The third patient presented with hiccup for 7 days following gastroenteritis. Chest and abdominal X-ray were normal as was an abdominal ultrasonography. Gastroscopy showed a discrete oesophagitis, but treatment with PPI was unsuccessful. All 3 patients had been treated with chlorpromazine and several other agents, all of which were unsuccessful or had important side-effects. We started treatment with baclofen 3×5 mg daily, and the hiccups disappeared within 24 hrs. The first 2 patients had to continue treatment because of recurrence when stopped, the third patient could stop baclofen.
Conclusions : Baclofen is a safe and very efficient treatment for intractable chronic hiccup. Due to the low number of side-effects, it should be considered as a first line therapy.

INCIDENCE OF INFLAMMATORY BOWEL DISEASE IN THE AGGLOMERATION OF ANTWERP. K. Van Herck, N. Büsher, J. Callens, L. Colemont, O. Peters, P. Pelckmans, D. Sprengers, D. Staessen, L. Terriere, V. Verdonck, L. Verbist, J. Holvoet for the Antwerpse Gastro-enterologen Club and Vakgroep ESOC, UIA.

Data have been published on the incidence of IBD in the regions of Liège and Brussels, but up to now none were available for the North of Belgium. In 1998, all gastroenterologists from a well-defined region around Antwerp completed a registration form for each newly diagnosed IBD case. In the course of one year 104 cases were collected in a population of 1.062.790 inhabitants. The estimated annual incidence per 100.000 inhabitants was 4.99 for Crohn's disease (CD), 3.01 for ulcerative colitis (UC) and 0.56 for indeterminate colitis (IND). 13 cases of microscopic colitis were registered. CD was diagnosed at a significantly younger age than UC ; mean age at presentation was 36.8 for CD and 46.1 for UC (t-test with separate variance estimates = 2.19 ;p = 0.03). The sex ratio was not significantly different for both groups ; M/F was 0.89 for CD 1.28 for UC.(C? = 0.66 ; p = 0.42). The proportion of patients who had never smoked was similar in both diseases (CD 49%, UC 50%). However, CD-patients more often actively smoked (37.5% versus 18.8% in UC) while the UC group contained more ex-smokers (31.2% versus 13.7% in CD) A trend for different smoking behaviour in the 2 groups could be shown (C? = 5.19 ; p = 0.075). CD was of the inflammatory type in 70.6%, stenosing in 23.5% and fistulising in 5.9%. Location was the terminal ileum in 49.1% ileocolon in 30.2%, colon in 24.5%, anal region in 13.2% and other in 7.5% (locations not mutually excusive. UC was pancolitic in 31.2%, left-sided in 40.6% and rectal in 28.1%. Conclusion : these data are similar to results from Liège and Brussels and confirm that in Belgium, as in northern France, CD is more frequent than UC.

- D49 -

FLEXIBLE ENDOSCOPIC MYOTOMY IS THE TREATMENT OF CHOICE OF ZENKER'S DIVERTICULUM. Paul Christiaens, August Van Olmen, Geert D'Haens. Bonheiden, Belgium.

Background : Zenker's diverticulum is a common cause of dysphagia in the elderly. Surgical treatment has been preferred in most countries by an external approach including transcervical diverticulectomy, myotomy and diverticulopexy or endoscopic myotomy by the ENT surgeons with a rigid endoscope. Recently endoscopic therapy by gastroenterologist has been proposed. We report a series of 5 patients with Zenker's diverticulum treated with a flexible endoscope.
Patients and methods : We present the results of 5 patients (3 male ; mean age 76.8 years) treated with a flexible endoscope using a monopolar coagulation forceps.All patients received topical sedation to the throat and intravenous conscious sedation. An oblique-end hood was attached to the tip of the endoscope for optimal visualisation of the septum between the Zenker's diverticulum and the oesophagus. The oesophageal inlet was intubated and a guide-wire was left behind in the stomach, over which a 10 french nasogastric tube was inserted. The scope was again positioned in front of the septum, after which a cricopharyngeal myotomy was carried out using a coagulation forceps with alligator jaws and rat teeth, applying blended cutting & coagulation current. The duration of the myotomy varied between 5 to 7 minutes after the nasogastric tube had been inserted.
Results : The pharyngoesophageal passage was successfully restored in a single session in all 5 patients. Bleeding or perforation did not occur. Oral feeding was resumed the following day. The mean duration of hospital stay was 2.5 days. Complete relief of dysphagia was reported by all patients during follow-up.
Conclusion : The flexible endoscopic approach for Zenker's diverticulum is safe and effective, no general anaesthesia is needed, oral feeding can be restarted the next day : the treatment of a Zenker' s diverticulum with a flexible endoscope has all the potentials to become the treatment of choice.

- D50 -

THE BURIED BUMPER SYNDROME : A NOVEL SIMPLE AND SINGLE STEP MANAGEMENT APPROACH OF REMOVAL AND REPLACEMENT. Paul Christiaens, August Van Olmen, Geert D'Haens. Bonheiden, Belgium.

Background : One of the complications of PEG (percutaneous endoscopic gastrostomy) insertion is the buried gastrostomy bumper syndrome in which there is a migration of the internal bumper into the gastric wall, causing pain, swelling, leakage or obstruction of the feeding tube with the inability to infuse feeding solution .
Methods : We report a case in which the internal bumper and distal end eroded completely into the stomach wall and was completely covered by hypertrofic gastric mucosa. Due to the inability to infuse feeding solution through the PEG tube an EGD was performed. A buried bumper syndrome was diagnosed : the internal bumper of the PEG-tube was completely eroded into the gastric wall and even the internal opening was overgrown by hypertrofic gastric mucosa. This resulted in a complete closure of the orifice : passage of a thread or guide-wire was not possible. Although overgrown, we could see clearly the impression of the bumper and the distal end in the gastric wall. With a needle-knife incision we exposed first the opening of the internal end, afterwards the internal bumper. Then we cut the PEG tube 3 cm above skin level. The double looped thread (provided with the PEG kit) was easily advanced trough the residual PEG tube into gastric lumen. The thread was grasped with a snare and was brought out through the biopsy channel of the endoscope, leaving the endoscope in place. Outside the residual PEG tube the looped thread was cut and became double in length : one end was firmly held outside the residual PEG tube, the other end at the biopsy channel of the endoscope. Now a foreign body forceps was introduced through the same biopsy channel. The PEG stump was removed, using the thread as a guide-wire. A new PEG tube was looped on the thread and was pulled into correct position using the same site. Feeding was resumed the next day and the patient was sent home.
Conclusion : Endoscopic removal of a PEG tube with a buried bumper and replacement by a new PEG- tube in this single step management approach is simple and uncomplicated.

- D51 -

RESECTABLE GASTRIC CANCER : A REPORT OF 66 CASES. A. Sermeus, M. De Ridder, G. Storme, D. Urbain. Dpts of Gastroenterology & Radiation Oncology, Academic Hospital A.Z.-V.U.B., 1090 Brussels, Belgium.

Surgical resection of adenocarcinoma of the stomach is curative in less than 40 percent of cases (Hundahl *et al.*, Cancer 2000). Intergroup-0116, a prospective phase III trial, investigated the effect of postoperative chemoradiation (5-FU, leucovorin with 45 Gy of radiation) versus surgery alone in patients with completely resected stage IB to stage IV M0 gastric cancer (MacDonald *et al.*, N Engl J Med, 2001). Median disease free survival (DFS) was 30 months for the chemoradiation group as compared to 19 months for the surgery alone group. Three-year DFS was 48% with adjuvant chemoradiation versus 31% for surgery alone. Grade 3, 4 and 5 toxicities occurred in respectively 41%, 31% and 1% of the patients receiving chemoradiation. The authors recommended a D2 resection, but only 10% of the patients underwent such an extensive dissection. One wanders therefore whether it is really worth giving chemoradiotherapy to stage IB to stage IV M0 gastric cancer after a D2 resection, which is the standard of care in our institution. The aim of this study was to retrospectively review all patients that were diagnosed and treated for respectable gastric cancer in our hospital between January 1991 and August 1999, to analyse which subgroups might benefit from adjuvant chemoradiation. Records, chosen by computer search, were reviewed and follow-up information was obtained until September 2002. Stage, histological grade, DFS using Kaplan-Meier analysis and site of relapse were used as endpoints for discussion. Sixty-six patients underwent a resection with curative intent. Five patients were excluded because of lost of follow-up, 4 because of positive section margins and 5 because of adjuvant treatment. Of the remaining 52 patients, 9 had stage IA disease, 7 stage IB, 5 stage II, 26 stage III and 5 stage IV M0. Eleven patients had a grade 1 tumour, 15 a grade 2 and 26 a grade 3.The overall median DFS was 53 months. None of the patients with stage I disease relapsed. The median DFS for stage II and III patients was 12 months with a three-year DFS of 32%. Eleven patients relapsed locoregionally, 10 distantly. The site of relapse and the DFS curves according to histological grade were not significantly different. In conclusion, patients with completely resected stage I disease have a favourable prognosis and do not need any adjuvant therapy. Patients with stage II and III gastric cancer have a poor prognosis with both locoregional and distant relapses. They should be considered candidates for clinical trials with less toxic (neo)adjuvant regimens.

- D52 -

ABSENCE OF ASSOCIATION BETWEEN PRESENCE OF GRANULOMAS AND NOD2/CARD15 VARIANTS IN CROHN'S DISEASE. V. Putzeys, E. Louis, J. Belaiche. Dept of Gastroenterology, CHU of Liège, Belgium.

Background : Granulomas, sign of a particular immunologic reaction specific for Crohn's disease (CD) are detected in 25% to 60% of the patients. NOD2/CARD15 variants are present in 25% to 50% of CD patients. Variants in this gene, which encodes for an intracellular receptor for bacterial components, are also found in Blau syndrome, another granulomatous disease. Therefore, we compared NOD2/CARD15 genotype frequencies in CD patients with or without granulomas.
Patients and methods : In our CD database, we listed 90 patients with granulomas. NOD2/CARD15 genotype was available for 32 of them. Among them, granulomas were found on surgical resection specimens in 22 and on intestinal biopsies in 10, using routine histological procedure that includes careful examination on semi-seried slides. This group of patients (granuloma +) was matched on the one hand for disease duration and number of surgeries (factors that can influence detection of granuloma) and on the other hand for disease location and age at diagnosis (factors associated in our population with NOD2/CARD15 variants) with 32 patients without granuloma (granuloma -). These two populations were compared for NOD2/CARD15 genotype, smoking, extra-intestinal manifestations, behavior of the disease and familial history of IBD.
Results : NOD2/CARD15 variants were found in 14/32 (43.8%) patients in both groups, including 9 heterozygous, 3 compound heterozygous and 2 homozygous vs 9 heterozygous, 2 compound heterozygous and 3 homozygous in granuloma + and granuloma -, respectively. No significant difference either was found for the other parameters : 33% and 40 of smokers, 43% and 25% of extra-intestinal manifestations, stricturing, penetrating and nonstricturing nonpenetrating disease at the time of last histologic examination in 37.5%, 34% and 28% vs 37%, 33% and 30%, familial history of IBD in 25% and 25%, in granuloma + and granuloma -, respectively.
Conclusion : We found no association between NOD2/CARD15 variants and presence of granuloma in CD patients. This could be explained by a dominant or necessary role of other genes or environmental factors in granuloma formation in CD.

CERULETIDE AS AN AGENT FOR THE RECOVERY OF GALLBLADDER BILE. W. Van Steenbergen, C. Verslype, L. Van Aken, A.M. Bergmans, M. Depré, A. Van Hecken, I. De Lepeleire, T. Laethem, J. Paolini, A. Campanile, V. Navarro, J. de Hoon. Dept. of Hepatology and Center for Clinical Pharmacology, UZ Gasthuisberg, 3000 Leuven.

Introduction and aim : Ceruletide (C, Takus^{R}) is a cholecystokinin decapeptide used in Europe to facilitate gallbladder contraction for the purpose of bile collection and gallbladder imaging. The threshold dose in man to contract the gallbladder is i.v. 0,5-1,0 ng/kg. C may potentially serve as a substitute for cholecystokinin octapeptide (sincalide, Kinevac^{R}) which has been used in the U.S. for the same purposes but which is currently unavailable. Our aim was to access the recovery rate of endoscopically collected gallbladder bile following C.
Methods : An open labelled, fixed sequence, two-period rising dose study was conducted in eigth healthy male volunteers (aged 18-45 yrs ; weights 64-92 kg), to determine the total lipid concentration (TLC) in endoscopically collected duodenal bile. After i.v. sedation with midazolam (6-11 mg), a duodenoscope was placed in the region of the ampulla. C 0,05 µg/kg (treatment A) or 0,1 µg/kg (treatment B) was infused over three minutes. Bile was aspirated continuously for 4 five-minute intervals, for a total of 20 minutes, beginning immediately after C infusion. TLC was determined from the darkest bile. A TLC of > 4 g/dl indicated bile that was of gallbladder origin. Treatment A and B were separated by at least two weeks.
Results : C-infusions and endoscopic bile collections were well tolerated. All subjects produced bile suitable for lipid analysis. Mean bile volumina were 6.5, 3.3, 5.1, and 4.6 ml, respectively, for the 4 consecutive samples after the 0,05 µg/kg dose, and 10.5, 7.0, 7.2, and 7.0 ml for the bile samples obtained after C 0,1 µg/kg. Gallbladder bile (TLC > 4 g/dl) was successfully recovered in 3 subjects after the 0,05 µg/kg dose, and in 4 subjects after the 0,1 µg/kg dose. Only 1 subject consistently produced gallbladder bile at both doses.
Conclusions : Based on the criterion of a TLC > 4 g/dl, Ceruletide seems to be of limited value for the recovery of gallbladder bile. Although bile volume increased dose-dependent, only 1 subject consistently produced the TLC-defined gallbladder bile at both doses. The reason for not meeting the TLC criterion could be related to a dilutional effect of the dose-dependent increase in bile volume. It remains undetermined whether the apparent lack of gallbladder bile recovery is due to the methodology used or to the proposed criterion of TLC for gallbladder bile.

ZENKER'S DIVERTICULUM : A NEW ENDOSCOPIC TREATMENT WITH A SOFT DIVERTICULOSCOPE. S. Evrard (*), O. Le Moine (*), S. Hassid (**), J. Devière (*). Department of Gastroenterology (*) and Otorhinolaryngology (**), Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium.

Background and aims : Recent treatments of Zenker's diverticulum (ZD) include the use of a flexible endoscope, which is minimally invasive. We report a new endoscopic approach using a soft diverticuloscope allowing perfect exposure of the operative site, and endoscope stability.
Patients and methods : Thirty patients (15 males, median age : 78 years) were treated with this diverticuloscope. All patients had significant symptoms such as dysphagia (n = 24, 80%) and/or regurgitation (n = 17, 56%). Eighteen (60%) had a large diverticulum (> 4cm).
Results : All patients were successfully treated in one session. In one patient, dysphagia persisted but was milder than before the treatment. Four patients (13%)experienced complications, in one (3%)case severe. During follow-up (median : 12.5 months), one patient experienced recurrent dysphagia a year after the initial procedure, but was successfully retreated by CO2 laser with rigid diverticuloscope. Four patients (13%) died of causes unrelated to the treatment.
Conclusions : Diverticulotomy using a flexible endoscope and soft diverticuloscope is very effective for treating ZD.

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CARD15 MUTATIONS AND ASCA ANTIBODIES IN PSORIASIS AND CROHN'S DISEASE (CD). M. Pierik (1), S. Vermeire (1), S. Joossens (1), G.Claessens (1), K. Van Steen (2), R.Vlietinck (3), H. Degreef (4) and P. Rutgeerts (1). Department of Gastroenterology (1), University Hospital Gasthuisberg, Leuven, Center for Statistics, Limburgs Universitair Centrum, Diepenbeek, Department of Epidemiology (2) and Human Genetics (3), Catholic University Leuven?, Department of Dermatology (4), University Hospital Gasthuisberg, Leuven, Belgium.

Background and aims : Psoriasis, a chronic inflammatory skin disease, and CD, a chronic inflammatory bowel disease (IBD) show many pathogenic resemblances. There is also an important clinical association between the disease. Both diseases have a polygenetic multifactorial origin and are characterized by a T helper 1 cell mediated immune response. Antibodies to *Saccharomyces cerevisiae* (ASCA) are associated with CD in about 60% of the patients. CARD15 the first gene for CD is an intracellular receptor for bacterial lipopolysaccharide and works through NF-kB. In the same region on 16 q that harbours CARD15, linkage for psoriasis has been described, therefore CARD15 would be a good candidate gene for psoriasis. We also wanted to investigate ASCA in patients with psoriasis.
Methods : We studied 313 CD patients, 43 patients with concomitant CD and psoriasis, 28 psoriasis patients and 141 healthy controls. The clinical charts of the psoriasis patients were reviewed for age at onset, smoking behaviour, subtype of psoriasis and joint involvement. All patients were genotyped for Arg702Trp, Leu3020InsC and Gly908Arg in CARD15 using PCR-RFLP. Statistical analyses was done using Chi-squared test or Fisher's exact test when appropriate.
Results :

	CARD15+	ASCA+
CD n = 313	44.4%	52.7%
CD + Psoriasis n = 43	53.5%	66.6%
Psoriasis n = 28	14.3%	9.1%
Controls n = 141	21.3%	4.9%

There was no significant difference in CARD15 prevalence or ASCA prevalence between psoriasis patients and controls or between patients with concomitant CD and psoriasis and CD patients.
Conclusions : Despite the observed linkage on the IBD1 locus in psoriasis, we did not observe an association between psoriasis and CARD15 variants in this small group. Other genes within this region are presently being studied.

ORAL BICARBONATE SUBSTITUTION IN ENTERICALLY DRAINED PANCREATIC ALLOGRAFTS. D. Meester, B. Van Vlem, N. Lameire, U. Hesse. Dpt of Surgery and Nephrology, Ghent University Hospital, 9000 Ghent, Belgium.

Enteric drainage for exocrine secretion has been proposed as a physiologic procedure in pancreatic transplantation and conversion from bladder to enteric drainage has been advocated for excessive Bicarbonate loss, dehydration and the requirement of oral Bicarbonate substitution. In the following study, the requirement for oral Bicarbonate substitution has been studied in enterically drained pancreatic grafts and compared to bladder drained grafts.
Patients and methods : A total of 33 pancreas transplant recipients were investigated (32 SPK, 1 PAK). Enteric drainage (ED) was performed in 22 and bladder drainage (BD) in 11 patients. Mean ± SD creatinine was 1.3 ± 0,3 mg/dl in ED and 1,5 ± 0,7 mg/dl in BD, all grafts were functioning for at least 3 months (3-72). Base excess and the amount of oral Bicarbonate substitute was analysed on day 1-20 posttransplant and weekly thereafter.
Results : Base excess measured between -12,5 and +5,4 meq/l in ED requiring Bicarbonate substitution in 5/22 (22,7%) patients in the immediate postoperative period and between -9,3 to +9meq/l in BD requiring substitutions in 8/11 (72,8%) of the patients (p = 0,008). The quantity of Bicarbonate required was between 1-3 g/day in ED and 2-15 g/day in BD patients.
Conclusions : The enteric drainage technique for pancreatic transplants does not prevent Bicarbonate loss and the need for oral substitution. However drainage of the exocrine secretions into the bladder is associated with a significantly higher degree of alkalosis due to Bicarbonate loss and requires more bicarbonate substitution.

TRANSANAL ENDOSCOPIC MICROSURGICAL (TEM) RESECTION OF SESSILE TUBULO-VENOUS ADENOMAS IN PATIENTS FOLLOWING LOCAL ABLATION OF POLYPS IN THE RECTUM. B. Van Ooteghem, D. De Looze, U. Hesse. Dpt of Surgery and Gastroenterology, Ghent University Hospital, 9000 Ghent, Belgium.

TEM is an established procedure for the primary treatment of rectal sessile adenom polyps. Its role in the treatment of recurrences and previous resections by electro-cautery however is unknown. A total of 40 TEM (Wolf Belgium) procedures were carried out in 35 patients (20 male, 15 female, with a mean age of 62.5 years (36-83 years)). The lesions were located at a mean of 9.2 cm ab ano (0-20 cm). 19 were clinical staging I, 21 were clinical staging II. The size of the lesions varied between 3-26 cm^2. In 23 (57%) cases the TEM followed local incomplete laser or electroresection or rectal resection. In 12 (30%) cases submucous resection was feasible and in 28 (70%) cases full or partial bowel resection was required. Suture of the mucosal defect was performed in 3 (75%) cases. On histology 26 were tubulovillous adenomas, 4 PT_1, 5 were PT_2 cancers and 5 others. In 2 patients, TEM was followed by a low anteriorresection, 1 for carcinoma, 1 for technical reasons. In 12 (30%) patients, 15 recurrences were diagnosed and treated. Only 4 (30%) had to be treated by TEM and 11 (70%) could be treated by local electroresection in a mean of 19 months (2-60) post TEM. The follow-up was 49.6 months (2-104 months). Recurrence occurred in 9 of 21 patients (43%) with previous electroresection and in 6 of 19 (31%) without ($p > 0,1$). Recurrences of rectal sessile polyps following TEM resection are occurring late post primary resection. The majority of cases (75%) can be performed by local electroresection.

FOLLICULAR DENDRITIC CELL SARCOMA OF THE STOMACH : CASE REPORT AND REVIEW OF THE LITERATURE. P. Demetter, A. Geerts (1), E. Lagae (2), K. Dhaene, M. Peeters (1), A. Waeytens, L. Defreyne (3), M. De Vos (1), P. Pattyn (2), C.A. Cuvelier. Departments of Pathology, (1) Gastroenterology, (2) Surgery and (3) Radiology, Ghent University Hospital, 9000 Gent, Belgium.

Follicular dendritic cell (FDC) sarcoma was first described in 1986 on the basis of a series of four cases, all of which occurred in lymph nodes. Recently, there has been a surge of interest in this tumour because of the ability to confirm FDC lineage by more sensitive markers. Today, approximately 65 cases of FDC sarcoma have been reported, mainly affecting the lymph nodes. However, in about one third of cases extranodal sites are involved, mostly intra-abdominal organs, oral cavity and tonsils. The gastrointestinal tract location is rare, and only three cases are described : one case involving the small intestine, one the colon and one presenting as a submucosal tumour of the stomach. As a result FDC sarcoma is an entity rarely listed in the differential diagnosis of spindle cell neoplasms of the gastrointestinal tract. The only identified predisposing factor is hyaline-vascular Castleman's disease, found in a minority of cases. Epstein-Barr virus has been demonstrated in a few FDC sarcomas, but does not appear to play a significant role. We report a case of a 40-year-old woman presenting with severe asthenia, nausea, back pain and loss of weight. Upper gastrointestinal tract endoscopy revealed a proliferating tumour in the stomach, of which biopsies were taken. A CT-scan of the abdomen showed a lobulated multinodular mass situated between the left liver lobe and the stomach, with compression of stomach and pancreas. A solitary nodule in the lobus quadratus of the left liver lobe was noted. Light microscopical examination showed a poorly differentiated tumour. A tentative diagnosis of gastrointestinal stromal tumour (GIST) was made. The tumour was resected en bloc. Histopathological examination of the resection specimen showed tumour cells with indistinct cytoplasmic outlines and ovoid vesicular nuclei with one or more eosinophylic nucleoli. These cells were positive for CD21, CD35, KI-M4p and vimentin, but negative for CD31, CD34, F VIII, CEA, CKs, EMA, SMA, MSA, myoglobin, desmin, c-kit, S-100, CD68, CD1a, myeloperoxidase, LCA and HMB-45. In situ hybridisation could not detect Epstein-Barr viral DNA. Based on histological and immunohistochemical findings, the diagnosis of FDC sarcoma was made – the second known case of FDC sarcoma presenting in the stomach.

A RETROSPECTIVE ANALYSIS OF THE EFFICACY AND TOXICITY OF IRINOTECAN AND 5FU/FA IN PATIENTS WITH ADVANCED CARCINOMA OF THE STOMACH OR OESOPHAGOGASTRIC JUNCTION.
Els Monsaert, Marc Peeters, Martine De Vos. Department of Gastroenterology, Ghent University Hospital, Belgium.

Objectives : To assess the safety profile and the therapeutic value of a fortnightly regimen containing irinotecan combined with 5-fluorouracil (5FU) and folinic acid (FA) in relapsed or refractory carcinoma of the stomach or oesophagogastric junction. Methods : We reviewed 15 patients with locally advanced or metastatic disease (10 adenocarcinoma, 5 linitis plastica) treated with irinotecan/5FU/FA in our centre between May 2001 and October 2002. They all had showed documented progression on or within 12 months following conventional chemotherapy. Irinotecan (180 mg/m?) was given with FA (200 mg/m?)and 5FU (400 mg/m?), followed by 5FU (2400 mg/m? CI over 46 hours), biweekly. CT response was assessed each two months. Treatment was continued until progression.
Results : Median age was 58.2 years. 12 patients (80%) had previously ondergone surgery and all patients had previously received platinum based chemotherapy. All patients had locally advanced or metastatic disease. 13 of the 15 patients were evaluable for response. The 2 remaining patients had to be switched to “best supportive care” within the first cycle (due to deterioration of the general condition) and were therefore not evaluable for response. A total of 36.5 cycles was admitted. Median follow-up was 7 months. Partial nor complete remission was observed. In 10 patients (76.9%) a stable disease was established which lasted on average 6.8 months. An improvement of the quality of life was documented in 11 patients, correlating with a clinical benefit rate of 84.6%. Therapy was well tolerated ; there was no grade 4 toxicity registered and there wasn’t any hospitalisation required due to toxicity. 1 patient (7.7%) suffered from grade 3 neutropenia, 4 patients (30.8%) from grade 2 neutropenia and 2 patients (15.4%) from grade 2 anemia. In 6 patients (46%) grade 2 diarrhoea occurred and 1 patient (7.7%) was confronted with grade 2 mucositis. Median PFS was 6.8 months and OS was 7.5 months.
Conclusion : The combination of irinotecan and 5FU/FA is a well-tolerated regimen and seems to be a valuable second line treatment for 5FU/platinum resistant cancer of the stomach and oesophagogastric junction, resulting in a significant improvement of the quality of life. Therefore this regimen should be further investigated by means of a randomized controlled trial.

COSTS OF ON DEMAND AND CONTINUOUS TREATMENT WITH ESOMEPRAZOLE 20 MG IN PATIENTS WITH GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD). P. Deprez (1), J. Tack (2), G. Vandenhoven (3), K. Daems.
(1) Clin Univ St. Luc, UCL, Brussels ; (2) UZ Gasthuisberg, KUL, Leuven ; (3) AstraZeneca, Brussels, Belgium.

Objective : The efficacy and cost of esomeprazole 20 mg in maintaining heartburn control in patients with GORD were documented in two Belgian, multicentre, open, phase IV studies.
Methods : 379 patients with endoscopy negative reflux disease (ENRD) were included in the DUO1 study and received a 4-week treatment course with esomeprazole 20 mg od. When symptom-free after 4 weeks, patients were offered an additional 6-month treatment with esomeprazole 20 mg on demand (max 1 tab/day). 428 patients with reflux oesophagitis (LA grades A-D) were included in the DUO2 study and received a 4-week continuous treatment with esomeprazole 40 mg od. When asymptomatic after 4 weeks, patients were proposed an additional 6 months with esomeprazole 20 mg od. Direct medical costs included study and OTC medication, unscheduled visits and GORD-related tests and procedures. Transport costs were considered as non-medical costs and costs of off-work days as indirect costs.
Results : mean (± SD) age at entry was 48 y (± 15) for the on demand study and 47 y (± 15) for the continuous treatment study. 312 patients started the 6-month on demand treatment period in the DUO1 study and 374 patients in the DUO2 study.

	DUO1 On demand	DUO2 Continuous esomeprazole
Patients asymptomatic at 6m §	69%	78%
Patients satisfied *	88%	89%
Unscheduled visits	6	10
GORD related tests	5	9
Patients that took OTC	9.6%	7.5%
Mean daily direct cost (±)	0.8 (± 0.4)	1.4 (± 0.3)

§ : drop-outs considered as treatment failures, * : percentage of patients satisfied at month 6 or month 3 in case of early termination. Patients that dropped out just after start of 6-month maintenance period were considered as failures. Patients from the DUO1 study took on average 1 tablet every other day. Non-medical and indirect costs were low in relation to direct costs.
Conclusions : The results suggest that the daily direct medical costs of esomeprazole in on demand treatment in ENRD is lower than that of continuous esomeprazole 20 mg in reflux oesphagitis.

- D61 -

PENETRATING CROHN'S DISEASE ACCORDING TO VIENNA CLASSIFICATION : A HETEROGENEOUS ENTITY. V. Michel, J. Belaiche, E. Louis. Dept of Gastroenterology, CHU of Liège, Belgium.

Vienna classification of Crohn's disease (CD) defines three disease behaviors : non stricturing non penetrating (B1), stricturing (B2), perforating (B3). This last subgroup includes both intrabdominal and perianal CD, but also simple perianal Crohn's fissures or ulcers. Our aim was to determine the proportion of these three subgroups and to compare their demographic, clinical and biological characteristics.
Methods : From our database and medical notes, we identified CD patients having developed a penetrating disease within 10 years after diagnosis. We classified them into intraabdominal (B3a) or perianal (B3b) penetrating disease, simple ulcers or fissures (B3c) and mixed intraabdominal and perianal forms (B3ab). When perianal fissures or ulcers coexisted with intrabdominal or perianal penetrating lesions, patients were classified as B3a or B3b, respectively. We compared these patients on the basis of age at diagnosis, location at diagnosis (ileal = L1, colonic = L2, ileocolonic = L3, upper GI tract = L4), gender, familial form of the disease, smoking, ASCA status and NOD2/CARD15 genotype.
Results : 99/297 (33.3%) patients had developed a perforating CD within 10 years after diagnosis, including 39 (39.4%) B3a, 49 (49.5%) B3b, 7 (7.1%) B3c and only 4 (4%) B3ab. Location of the disease at diagnosis was significantly different between subgroups B3a and B3b : 63.9%, 8.3%, 27.8%, 0% vs 15.8%, 50%, 31.6%, 2.6% for L1, L2, L3, L4, respectively ($P < 0.0001$). Proportion of women was significantly higher in B3b than B3a : 83.8% vs 59.5% ($P = 0.03$). There was no significant difference between groups according to age at diagnosis, familial forms, smoking, ASCA, or NOD2/CARD15 genotype.
Conclusions : perforating CD according to Vienna classification is a heterogeneous entity. The 2 main subgroups are intraabdominal perforating CD associated with ileal location and perianal perforating disease, associated with female gender and colonic location. Mixed perforating CD (both perianal and intraabdominal) as well as isolated perianal ulcers or fissures are rare.

- D62 -

INFLUENCES OF CHEMOTHERAPY ON HEALTHY AND METASTATIC LIVER PARENCHYMA IS LIMITED. P. Demetter, Dpt of Pathology, W. De Bock, N. Van Damme, M. De Vos, Dpt of Gastroenterology, B. de Hemptinne, Dpt of Surgery, L. Defreyne, Dpt of Radiology, M. Rottiers, M. Praet, Dpt of Pathology, M. Peeters, Dpt of Gastroenterology, Ghent University Hospital, 9000 Ghent, Belgium.

Background : Liver metastases are frequent in patients with colorectal cancer. Our attitude is more aggressive and an important fraction undergoes a resection. Today, no data are available on the effect of chemotherapy on liver parenchyma.
Patients and methods : Thirty-four patients (17 females and 17 men, with a mean age of 57 years) who underwent liver resections for hepatic metastasis from colorectal cancer were included in the study. Tissue samples taken from the tumour and surrounding liver parenchyma were light microscopically evaluated. The patients were divided in two groups : those (n = 14) who had no chemotherapy for at least 6 months before the liver resection and those (n = 20) who were treated with chemotherapy before the liver resection. Histological changes were statistically evaluated with the Mann-Whitney U test.
Results : Evaluation of samples taken from metastases showed no significant differences for% necrosis, the localisation, cell loss, apoptosis, peritumoural pseudocapsule, intratumoural pseudocapsule or fibrosis between patients receiving chemotherapy or no chemotherapy. Furthermore, no differences could be observed in the number of satellites. In the surrounding non-involved liver parenchyma also no differences could be observed for the same parameters. There were also no differences in cholestasis, fatdrops and lipofuscin in the hepatocytes in samples from patients receiving or not receiving chemotherapy.
Conclusion : No histological changes are observed in liver metastases from colorectal cancer patients and non-involved liver tissue under chemotherapy. Other markers such as p53 and E-cadherin will be investigated in the future.

- D63 -

THE USE OF MACRO-ARRAY TO STUDY THE EFFECT OF INTESTINAL TREFOIL FACTOR ON GENE EXPRESSION IN CACO-2 DERIVED ENTEROCYTES. J.A. Van Huysse (1), D. Laukens (2), P. Demetter (1), K. Vandenbroucke (2), M. De Vos (4), E.M. Veys (3), L. Steidler (2) and C.A. Cuvelier (1). Dpt of (1) Pathology ; (2) Molecular Biomedical Research, (3) Rheumatology and (4) Gastroenterology, Ghent University, Ghent, Belgium.

Intestinal trefoil factor (ITF) is a member of the trefoil family of peptides. It increases resistance to apoptosis, enhances mucosal healing and restitution in vivo and promotes migration of intestinal epithelial cells in vitro. The aim of this study was to investigate the influence of ITF on gene expression in intestinal epithelial cells.
The human colon carcinoma cell line Caco-2 develops structural and functional characteristics of normal enterocytes when kept in culture. Enterocyte-like Caco-2 cells were treated with murine recombinant ITF during 2 hours. Total RNA was isolated and labelled cDNA was synthesised using [33P] dCTP's. The cDNA probe was hybridised to the *Human Unigene Set 2* colony filters (RZPD), containing ~75.000 known and unknown EST's spotted in duplo. These filters cover more then 90% of the human genome. After several washing steps, the amount of signal was measured using a phospo-imager at time points 16, 24 and 96 hours, to cover a broad range of signal intensities. Spot intensities were measured and signal quality was evaluated. For each filter background correction and intra- and inter-filter normalisation was performed. Using a 2-fold increase or decrease as a cut off, comparison of the gene expression between un-stimulated Caco-2 cells and cells stimulated with ITF using the macro-array technique revealed a few thousand genes that were potentially differentially expressed. For example, in this experiment we see a more then 2-fold increase in the expression of ITF, auto-induction of expression has been reported in literature. The mRNA encoding for caspase 4, 8 and 10 shows a more then 2-fold decrease in expression, the anti-apoptotic properties of trefoil factor have been reported. Our data show that the macro-array is a powerful technique to screen for differential gene expression as a result of trefoil administration. However, it is necessary that the huge amount of data obtained is filtered through repeated hybridisations, only to retain the relevant changes and these data must be confirmed using other methods like quantitative Real-Time PCR and eventually studies at protein level.

- D64 -

EVALUATION OF RECTO-SIGMOÏDOSCOPY AS A SCREENING PROCEDURE FOR COLO-RECTAL CANCER : RETROSPECTIVE STUDY OF A PRIVATE COMPANY PREVENTIVE MEDICINE PROGRAM. S. Gielen, J. Belaiche, J. Demonty, E. Louis. Depts of gastroenterology and internal medicine, CHU of Liège, Belgium.

Background : Flexible recto-sigmoïdoscopy is currently an accepted procedure to screen for colo-rectal cancer in the general population. This retrospective study aimed at evaluating the acceptance of this procedure as a part of an open and free preventive medicine program offered by a private company to its employees as well as to calculate the percentage of polyps finding and the proportion of secondary colonoscopies performed in case of positive recto-sigmoïdoscopy.
Subjects and methods : between October 1996 and june 2001, 482 asymptomatic average-risk persons (aged > 45 years) were offered this screening recto-sigmoïdoscopy as part of preventive medicine screening program organised on one day at the same place. Patients were prepared with two enemas (the day before and a few hours before exploration). Recto-sigmoïdoscopies were performed using a flexible colonoscope. When a polyp was found, the patients were informed about the result and were advised to have contact with their GP to organize a total colonoscopy. A report was also sent to the GP. All the recto-sigmoïdoscopy protocols were retrospectively reviewed. When a polyp was found, a postal questionnaire followed by phone call to the general practitioner (GP) in charge of the patient were organized to collect information about the realisation of a secondary colonoscopy and its result.
Results : 310/482 subjects (mean age : 56.5 years) underwent the recto-sigmoïdoscopy (64.3%). The mean distance from the anal verge was 18.5 cm. A lesion was discovered in 21 subjects (6.8%, including 9.3% of men and 3.6% of women). Out of these, 17 (80.9%) underwent secondary total colonoscopy. The distal lesion was found and resected or biopsied in all the patients : 14 hyperplastic polyps (82.6%), 2 adenomas (11.8%) and 1 adenocarcinoma (5.9%). A synchronous proximal lesion was also found in 4 patients : all were hyperplastic polyps. There was no complication due the flexible recto-sigmoïdoscopy or secondary colonoscopy.
Conclusion : acceptance of the procedure was quite low (64.3%), despite it was free and proposed within a global preventive medicine program on the same day. Further, 19% of subjects with a positive recto-sigmoïdoscopy did not undergo total colonoscopy. A clinically significant lesion was found and treated in 0.97% of screened subjects.

ABDOMINAL TUBERCULOSIS : A RETROSPECTIVE STUDY OF 10 PATIENTS. D. Deeren, A.I. De Backer, P. Bomans, S. Bourgeois. Dpt of Internal Medicine, Algemeen Centrumziekenhuis Antwerpen Campus Stuivenberg, 2060 Antwerp, Belgium.

Objective : To study the clinical, laboratory, microbiological and imaging findings in patients with tuberculosis with abdominal involvement. Methods : We reviewed the medical charts of 10 patients with a diagnosis of abdominal tuberculosis. The criteria for inclusion were : microbiological (culture and/or polymerase chain reaction) diagnosis of tuberculosis from an abdominal or extra-abdominal specimen, and radiographic findings consistent with abdominal tuberculosis.
Results : Ten patients (9 immigrants from low-income countries ; 6 women, 4 men ; mean age 33.3 years) were studied. In 9 of them, extra-abdominal organ involvement was present : peripheral lymph nodes (n = 7), pulmonary (n = 6), mediastinal or hilar lymph nodes (n = 5), vertebral (n = 1). Three patients were diagnosed with human immunodeficiency virus (HIV) infection. In one of them tuberculosis was the first manifestation of HIV infection. The predominant symptoms (mean duration 117.5 days) were abdominal in 3 patients, constitutional in 4 and related to extra-abdominal organ involvement in 3. The erythrocyte sedimentation rate was increased in all patients, C-reactive protein was increased in nine. Other laboratory findings included anaemia, decreased mean corpuscular hemoglobin, decreased serum iron, increased lactate dehydrogenase, decreased albumin and polyclonal hypergammaglobulinaemia. A Mantoux test was performed in 4 patients and positive in 3. Ultrasonography, computerized tomography and/or magnetic resonance imaging findings consistent with abdominal involvement included enlarged lymph nodes, ascites, hepatomegaly or splenomegaly, and multiple splenic lesions. Chest radiograph showed pulmonary involvement in 5 patients. Mycobacterium tuberculosis was isolated in 9 patients, Mycobacterium bovis in 1.
Conclusions : Because of the lack of specific symptoms, abdominal involvement in disseminated tuberculosis may be underreported in the literature. Patients should be tested for HIV infection.

EFFICACY AND COSTS OF CONTINUOUS TREATMENT WITH ESOMEPRAZOLE 20 MG IN PATIENTS WITH REFLUX-OESOPHAGITIS (GRADE A-D). P. Deprez (1), J. Tack (2), G. Vandenhoven (3), K. Daems. (1) Clin Univ St. Luc, UCL, Brussels ; (2) UZ Gasthuisberg, KUL, Leuven ; (3) AstraZeneca, Brussels, Belgium.

Objective : The primary objective of this multicentre, open, phase IV study was to document the efficacy of a continuous treatment with esomeprazole 20 mg in maintaining heartburn control in patients with reflux oesophagitis in Belgium. Secondary objectives were to assess medical costs (study and OTC medication, health care visits, GERD related tests), non-medical costs (transportation) and non-direct costs (absence from work) during the maintenance phase treatment.
Methods : In total, 428 patients who have been experiencing heartburn for ≥ 3 days during the week before inclusion, entered the acute phase of the study to receive esomeprazole 40 mg once daily for 4 weeks. Patients who were asymptomatic (complete resolution of heartburn or not more than 1 day with mild heartburn during the last 7 days prior to the visit) at the end of the acute treatment phase, were allowed to continue the 6-month maintenance phase, receiving esomeprazole 20 mg continuous once daily. Analyses were performed on an intention to treat basis.
Results : The mean age and BMI (± SD) at entry was 47 y (± 15) and 27.3 (± 6.2), respectively. Sex ratio : 42.5% women and 57.5% men. Classification of oesophagitis was as follows : grade A (50%), B (33%), C (11%), D (3%). Before inclusion, all patients had heartburn (10% mild, 59% moderate, 30% severe), 62% had epigastric pain, 74% had regurgitation and 17% had dysphagia complaints. After the acute phase, 383 (89.5%) of the patients were asymptomatic and 93% was satisfied with their treatment. 374 patients started the maintenance period, 322 completed the study. 332 (89%) patients, who completed the 6 months period or early terminated the study at 3 months, were satisfied with their therapy, only 12 (3.2%) patients were not satisfied and 30 (8%) patients dropped out between the start of the maintenance phase and month 3. 290 (78%) were asymptomatic, 78% free of epigastric pain, 80% free of acid regurgitation and 84% had no dysphagia complaints after 6 months (drop-outs were considered as treatment failures). Only 9.6% of the patients experienced a relapse. The direct medical daily cost was 1.4 (± 0.3)/day, whereas non-medical and non-direct costs were low compared to direct costs. 8 patients experienced a serious adverse event, none was drug related. There were no GERD-related hospitalisations.
Conclusions : This study demonstrates effective symptom control in the long term continuous use of esomeprazole 20 mg od, which also has a very low medical cost, in patients with reflux oesophagitis.

- D67 -

IS PUSH ENTEROSCOPY USEFUL IN GASTROINTESTINAL BLEEDING? AB. Marks-Brunel. Dpt of Gastroenterology. Hospital, 59300 Valenciennes.V. Maunoury. Dpt of Gastroenterology. CHRU, 59000 Lille. M. Sperandio. Dpt of Anesthesiology. CHRU, 59000 Lille. JC. Paris. Dpt of Gastroenterology. CHRU, 59000 Lille. France.

The prevalence of unexplained anaemia after gastrointestinal explorations is not well known : it's value to 38% in case of occult bleeding. (1) The aim of this study was to assess retrospectively the impact of push enteroscopy on diagnosis and outcome of patients with unexplained anaemia.
Patients and methods : From june 1998 to april 20001, 57 patients (35 women) mean age 52, with supposed iron deficiency anaemia were explored by Push Enteroscopy. Patients had previously undergone standard endoscopies. Outcome in 2002 was collected by phone.
Results : PE identified a presumed bleeding source in 24 patients (42%) but only 12 had lesions located between second duodenum and ileum. Small bowel lesions were : angiodysplasia (8), portal hypertensive varices (2), adenocarcinoma (1), Crohn's disease (1). Angiodysplasia were diffuse in 4 cases. Six patients had risk factors (anticoagulant treatment, primary haemostasis abbnormalities, chronic renal failure). Endoscopic treatment can be performed six times. After mean follow-up of 28 months, five of 12 patients (42%) with intestinal lesions recidived (4 angiodysplasia which 3 prior treatment and 1 varice). On 33 patients with negative push enteroscopy, others investigations identified : fibroma (2), beta-thalassemia (1), myeloma (1), Crohn's disease (1), colorectal cancer (1). Anaemia was due to iron malabsorption : autoimmune chronic gastritis (2), gastrectomy (2), vegetarian (2). Five died or lost of view. After optimal iron supplementation, seven patients had no recidive but nine had yet an unexplained anaemia, so 56% of patients with no diagnostic.
Conclusion : Diagnostic yield of Push Enteroscopy can be optimized by prior confirmation deficiency iron anaemia, exclusion of extra-digestive or extra-intestinal causes (upper or lower gastrointestinal bleeding, iron malabsorption by gastric or duodenal atophy, diet) or Meckel's diverticulum. However, despite identifying origin of bleeding, 42% recidived. On the other hand, long term follow-up after negative Push Enteroscopy conclude to persistant or recidivant anaemia in fourth of cases.

Rockey D.C., Cello J.P. Evaluation of the gastrointestinal tract in patients with iron deficiency anemeia. *N. Engl. J. Med.*, 1993, 329 : 1691-5.

- D68 -

A SPONTANEOUS RUPTURE OF THE MAIN PANCREATIC DUCT DURING AN ACUTE PANCREATITIS EPISODE : IRM IMAGING AND TREATMENT. M. Delforge, A. Colard, D. Brisbois, B. Bastens, B. Dallemagne, J. Weerts. Service de Gastro-entérologie , Les Cliniques Saint Joseph, 75 rue de Hesbaye, 4000 Liège.

A 25 years old man, without noticeable previous medical history, was admitted for a first episode of severe acute pancreatitis. Etiology was most probably alcohol abuse. The recovery was uneventful and the patient was discharged after one month of treatment. Two months later, on a control IRM, the only finding was a little necrotic area of less than 2 cm in the isthmic part of the pancreas. At this stage, the patient was almost asymptomatic. Four weeks later, the patient presents recurrent persistant epigastric pain and a new IRM was performed : it showed a very large heterogenous retroperitoneal collection. There was a 3 cm loss of the main pancreatic duct in the body portion of the pancreas. A first drainage was performed by laparoscopy as a cystogastrostomy. The collection became infected and the abcess was first treated by a continuous lavage of the cavity through a nasocystic tube inserted during upper endoscopy. The patient became more and more septic and a second surgical drainage was performed through a posterior left laparostomy. An in-and-out lavage was then used for two weeks and the patient recovered perfectly well and is now totally asymptomatic. By reporting this case, the autors assess the role of imaging and the advantages of IRM, the different procedures of lavage reported in the litterature for the treatment of these large heterogenous collection following an episode of acute pancreatitis. They also overview the early and late consequences of this life-threating pancreatic pathology.

THREE YEARS FOLLOW-UP FOR INITIAL GERD PATIENTS INJECTED WITH EVOH POLYMER. H. Louis (1), D. Van Gansbeke (2), D. Silverman (3), J. Devière (1). Department of (1) Gastroenterology and (2) Radiology, Erasme Hospital, Free University of Brussels, 1070 Brussels, Belgium, and (3) Enteric Medical Technologies, Palo Alto, California.

Purpose : Results of previous endoscopic injection techniques for the treatment of gastroesophageal reflux disease (GERD) were short-lived because of sloughing or resorption of the implants. Enteryx™ is a liquid mixture of ethylene-vinyl-alcohol polymer (EVOH) with radiopaque tantalum powder in an organic solvent, which precipitates once injected *in vivo*. In a pilot study between 1999 and 2000, endoscopic implantation of EVOH polymer in the lower esophageal sphincter (LES) was performed in our center in 10 patients with GERD requiring daily PPIs to alleviate their symptoms.
Methods : Extension of follow-up during the 3rd year after the treatment was obtained to gather long-term safety and efficacy data. Questionnaires including SF-36 and GERD-HRQL, concomitant medications and adverse events were recorded. A spiral CT-scan with volumetric calculation of the amount of implant remaining was performed. Results. After 3 years of follow-up, one patient had died from unrelated cause and one patient was lost to follow-up. The remaining eight patients accepted to undergo extended follow-up. One patient without symptomatic improvement after EVOH polymer injection had a Nissen fundoplication. Five patients out of eight had stopped (n = 3) or reduced their anti-secretory medication to less than once a week (n = 2). Two patients were on daily ranitidine and cisapride, repectively. Six out of the eight patients reported improvement in their GERD symptoms when compared to before the endoscopic treatment. Spiral CT-scan revealed significant well-delineated implants in a circular or semi-circular fashion in most of the patients. The amount of remaining implant was calculated at 0.06 cm^3 (patient on daily ranitidine), and between 1.88 and 3.79 cm^3 for the other patients.
Conclusion : Three years after endoscopic EVOH polymer injection in the LES, most of the patients show a sustained improvement in their GERD symptoms, and the persistence of the implant at the gastroesophageal junction.

- G01 -

HEPATOCYTE TRANSPLANTATION IN A 4 YO GIRL WITH REFSUM DISEASE : TECHNIQUE, SAFETY AND EFFICACY. E.M. Sokal (1), F. Smets (1), A. Bourgois (1), L. Van Maldergem (2), T. Detaille (1), S. Clement de Clety (1), Ph. Clapuyt (1), Ch. St Martin (1), J.P. Buts (1), R. Reding (1), J.B. Otte (1), V. Evrard (1), D. Latinne (1), M.F. Vincent (1), A. Moser (3), H.E. Soriano (4). (1) Univ Cathol Louvain, St Luc Hosp, Brussels ; (2) Inst Génét, Loverval ; (3) Kennedy Krieger Inst, Baltimore ; (4) Children's Memorial Hosp, Chicago.

Background : Liver transplantation may clear toxic circulating metabolites associated to liver based inborn errors of metabolism. Aim : To evaluate safety and efficacy of hepatocyte transplantation as an alternative to orthotopic liver transplantation (OLT). Patient & methods : A 4 YO girl with severe psychomotor retardation, deafness and blindness due to infantile Refsum disease was refused for OLT. After extensive discussions and ethical board approval, she was accepted for an experimental treatment using hepatocyte transplantation. A Broviac catheter was inserted surgically and placed at the spleno mesaraïc confluent level. She received a total of 8 cell infusions, each performed over ± 30 minutes : Cell doses in millions were : d1 : 2 × 550, d3 : 80 , d4 : 140 & 90, d5 : 184 & 243 and d6 : 200. Day 1 cells were fresh and the rest were cryopreserved. Results : Portal pressure gradient increased from 12 to 26 mm Hg, returning to basal within 30 minutes after infusion. Doppler ultrasound showed no significant decrease in portal flow velocity. Blood saturation decreased temporarily to 95% after the first two infusions, but not subsequently upon reduced infusion rates. Immunosuppression included 10 mg of Basiliximab (chimeric anti-CD25 receptor monoclonal antibody, Simulect®, Novartis SA) and tacrolimus (Prograf ®, Fujisawa) to reach through blood levels of 6 to 8 ng/ml. Circulating metabolites showed a progressive decrease of the pipecholic acid (µmol/gr creat D0 : 32.6, D120 : 22.2, D534 : 17.6) ; of C26/C22 ratio (0.34, 0.26, 0.20) ; of the bile salts (µmol/l 8.4, 0.9, 0.7). Donor Y chromosome sequences were detected by PCR in biopsy from day 7, but not in biopsy at month 4 (sampling phenomenom ?) .The child tolerated well the procedure and started walking, with improved apetite and weight gain. Evoked auditive potentials showed similar tresholds. Liver function showed only transient mild GGT elevation.
Conclusion : Hepatocyte transplantation is feasible and safe in children with metabolic diseases with evidence of engraftment. Persisting metabolic benefit remains at 18 months indicating repopulation.

- G02 -

HYPERPLASTIC-INFLAMMATORY POLYPS OF THE OESOPHAGOGASTRIC JUNCTION : AN UNUSUAL MANIFESTATION OF GASTRO-OESOPHAGEAL REFLUX DISEASE IN CHILDREN. B. Hauser, Y. Vandenplas. Dpt Pediatric Gastroenterology, AZ-VUB, Brussels, Belgium.

Hyperplastic-inflammatory polyps of the oesophagogastric junction (HIPOGJ) are rare among adults and exceptional in children. They are characterised by hyperplastic epithelium (foveolar, squamous or both) with variable amounts of inflamed stroma. They occur predominantly in association with gastro-oesophageal reflux disease (GORD). We recently observed HIPOGJ in three children. A 9-year-old boy known with a psychomotor delay presented with anorexia. An oesophagogastroduodenoscopy (OGD) showed an ulcerative oesophagitis and a polyp at the oesophagogastric junction (OGJ). Biopsies of the polyp showed cardia-type mucosa with foveolar hyperplasia and inflammation of the lamina propia. A treatment with proton pump inhibitors (PPI) did not result in clinical nor endoscopic improvement. Antireflux-surgery was performed with clinical and endoscopic improvement (no oesophagitis, no polyp). A 13-year-old girl presented with epigastric pain and pyrosis. An OGD showed an erosive oesophagitis and a polyp at the OGJ. Biopsies of the polyp showed cardia-type mucosa with foveolar hyperplasia and inflammation of the lamina propia. A polypectomy was performed with clinical but no endoscopic improvement (persisting oesophagitis and residual polyp). Additional treatment with PPI was started with endoscopic improvement (no oesophagitis, no polyp). A 11-year-old girl presented with epigastric pain and pyrosis. An OGD showed an ulcerative oesophagitis and a polyp at the OGJ. Biopsies of the polyp showed hyperplastic cardia-type and squamous mucosa. A treatment with PPI was started with clinical and endoscopic improvement (no oesophagitis, no polyp). HIPOGJ is an unusual finding in children and a rare manifestation of GORD. In the three patients described, clinical, endoscopical and histological evidence of GORD was present, and treatment of this reflux resulted in a disappearance of the oesophagitis and the polyps.

- G03 -

HEPATIC HISTIOCYTOSIS. F. Motte, F. Smets, S. Gosseye, E. Sokal. Pediatric Hepatology and Pathology Department, Saint-Luc University Hospital, Brussels.

A 3 month-old boy develops fever with hepatosplenomegaly. Biology shows severe thrombopenia (10.000 plat/mm^3) and abnormal liver test (ALT = 138 U/ml, ALT = 217 U/ml). Soon after admission on our department, cholestasis progress (Bilirubine Tot/dir = 11,6/7,1) and liver function (INR > 7.0) deteriorates rapidly. Microbiologic and serologic testing are negative. A first bone marrow biopsy is normal but hemophagocytosis is found on a further control. Surgical liver biopsy shows a wide proliferation of histiocytes in the portal area, hepatic parenchyma and biliary ducts. Histology, histiocytes cell markers, elevated NSE (16,9 U/ml), elevated ferritine (1390 U/ml) and elevated triglycerides (868 mg/dl) leads to the diagnosis of hemophagocytic lymphohistiocytosis. Distinction between the familial form (Familial Lymphohistiocytosis) and the acquired form (Secondary Lymphohistiocytosis) is made by searching mutation in the perforin gene or by finding any pathogenic agent able to induce such a secondary histiocytes proliferation. Corticosteroids are started after the result of the liver biopsy to reduce the inflammatory storm of the disease. An impressive improvement of the INR and the cholestasis is noticed short after the beginning of the therapy. Chemotherapy under the HLH-94 protocol is added to the steroid regimen. Hepatic infiltration by histiocytosis is seen in different form of histiocytosis. The clinical picture, age of the child and liver biopsy histology differentiate the type of histiocytosis. For each form, a specific treatment exists, leading to a more or less complete recovery.

- G04 -

GASTRO-OESOPHAGEAL REFLUX ACCORDING TO AGE. S. Salvatore, B. Hauser, Y. Vandenplas. Clinica Pediatrica di Varese, Università dell'Insubria ; Academisch Ziekenhuis, Vrije Universiteit Brussel.

Gastro-oesophageal reflux in infants is considered as a common and benign phenomenon with resolution of regurgitation by 12-18 months of age. However subsequent feeding problems and impaired quality of life have been reported. Furthermore 5-9% of infants have troublesome GER-disease. In school-age, GER symptoms seems to occur in 1-8% of children causing oesophagitis in 15-62% of symptomatic subjects albeit the estimation of the real prevalence is limited by common self-treatment or lack of medical referral. Individual natural history of GER is largely unpredictable although congenital gastro-intestinal malformations, neurological disorders and cystic fibrosis favour persistent and complicated reflux. Compared to adults, children present more regurgitation and emesis and less heartburn, dysphagia and chest pain. Persistent crying, irritability, back-arching, feeding and sleeping disturbances have been proposed as equivalents of heartburn in young patients. Failure to thrive, apnoea, ALTE and coexisting cow's milk allergy seem exclusive for paediatric age, whereas recurrent respiratory infections, cough and unresponsive asthma are associated with GER at any age. The negative impact of GER on quality of-life is well proved in adults but still neglected in children and their parents. Age, symptoms, presence of complications and availability of diagnostic and therapeutic options influence the investigational approach. Different to adults, oesophageal biopsies are always indicated in children to detect oesophagitis and identify different oesophageal disorders. Empirical medication is increasingly used but carries the risk of delayed diagnosis of complications and overtreatment. Mostly infants may benefit from parental reassurance, dietary treatment and prokinetics. In adults, proton pump inhibitors (PPI) are now considered the treatment of choice for GER-disease. In children H2-antagonists are still widely used, despite PPI showed superior efficacy with great tolerance and safety.

- G05 -

EVOLUTION OF 6 PATIENTS WITH BRONCHIECTASIS (BE) AND GASTRO-ESOPHAGEAL REFLUX (GERD) AFTER ANTIREFLUX SURGERY (ARS). Tania Mahler°, Tyl Jonckheer*, Koen Schwagten**, Gigi Veereman°, Arnold Verhelst**, Micheline VanCaillie-Bertrand. Depts of Paediatric Gastroenterology and Nutrition, *Pneumology, and **Surgery, Queen Paola Children's Hospital – AZ Middelheim, Antwerp, Belgium.

Introduction : Although it is accepted that GERD is present in patients with BE, little literature is available on the natural evolution and the impact of ARS in this pathology.
Aim : To evaluate the efficacy of ARS on GERD in 6 patients with BE after long-term follow-up.
Patients and methods : 6 patients, partially responsive to medical treatment (Cisapride, Ranitidine, Omeprazole) with BE {diagnosed by CT thorax} and GERD {diagnosed by pHmetry, esophago-gastro-duodenoscopy (EGD), scintigraphy were referred for an adapted Nissenfundoplication {anterior partial wrap 180° with approximation of anterior crucia of diaphragm}. After ARS, patients were followed at the out-patient clinic. Control pHmetry, EGD, SCAN were done if necessary to adapt treatment. 8 patients with respiratory disease (asthma, recurrent infections) and GERD, needing ARS, served as control group.
Results : 1) After ARS 2 of the 6 patients tested with pHmetry and/or SCAN still had GERD. Of the 4 patients without GERD after ARS 2 had reappearance of GERD. So 2 patients remained GERD free (respectively 20 and 30 months after intervention). 2) After a mean follow-up of 28 months all patients have stabilisation of their clinic and BE (CT Thorax), but 4/6 still need antireflux medication to achieve suppression of GERD. 3) The control patients remained GERD free after a mean follow-up of 12 months.
Conclusions : 1) In 2/3 of our patients with BE , GERD could not be controlled with ARS alone and needed medical therapy, while in the control group of uncomplicated respiratory complaints operation was 100% successful. 2) Two patients had no reflux, 2 and 10 months after surgery, suggesting that the operation was initially successful. 3) We propose that in these patients a 360° Nissenfundoplication should be done, as disturbed intrathoracic pressure, continues to induce GERD after a 180° ARS.

- G06 -

RESULTS OF THE TREATMENT OF CHRONIC FUNCTIONAL CONSTIPATION. M.H. Suijker (1), A.J.R. Deprettere (2), J. Weyler (2), A.-M. Van de Sompel (4). (1) SFG Rotterdam, The Netherlands ; (2) Dept Pediatrics Univ Hosp Antwerp ; (3) Departement Epidemiologie Univ. Antwerp, (4) Div. Clinical Nutrition Univ Hosp Antwerp, Belgium.

Aim : Long-term results of treatment of chronic functional constipation.
Patients and methods : 145 patients with chronic functional constipation, treated between 1983 and 1999, were questioned by mail and/or by phone about residual defecation problems. Median age at start of therapy 5.4 yr (2mnths to 13.4 yrs). Stool frequency less than 3 / week : 37% ; never on toilet : 11% ; soiling : 58% ; primary encopresis 18% ; 73% already treated elsewhere.
Treatment protocol : information + demystificatoin, desimpaction (80%), chronic laxatives, toilet training (73%), biofeedback training (23%), dietary measures. Outpatient follow-up : 10 mnths (max 9.6 yr), mean 7.2 visits per patient (max 21). Cured = stool frequency at least 3 / week ; no soiling or encopresis ; no medication.
Results : Respons rate 92 (63%). M/F : 47/45. Actual age 11.5 yr (2.6-21.9 yr). The response group was statistically not different from the initial group. Stool frequency less than 3 / week in 3% ; encopresis or soiling in 21% ; still on laxatives in 16%. Sixty seven percent were cured.
Conclusion : Intensive and sustained treatment with intensive follow-up gives results comparable with the figures in the literature*. Still 1/3 remains constipated. No single item in the treatment protocol is significantly more contributing to the positive results.

* Staiano (1994) ; Abrahamian (1984) ; Loenig-Baucke (1993) ; Keuzenkamp (1996).

- G07 -

A GROUP OF 6 CHILDREN WITH HEPATIC HEMANGIOMA WITH NEONATAL EXPRESSION.
M. Vanderborght, C. Debauche, S. Gosseye, E. Sokal. Cliniques Universitaires St Luc, UCL, Brussels.

We describe a group of 6 children with hepatic hemangioma with neonatal expression. Two of them were affected by a single hepatic hemangioma (SHH), while the four others presented a diffuse hepatic hemangiomatosis (DHH). A Kasabach-Merritt syndrom was fund in one case of DHH. Corticosteroïds was used as first treatment in two cases of SHH with a 50% outcome. The second was cured by surgery due to easy surgical approach and to avoid corticosteroïds side effects. One of the DHH died of multisystemic failure after surgery. Another DHH was treated first with Interferon alpha instead of corticosteroïds because of cardiac failure. The outcome was good. Two patients affected by DHH (pathology of hemangioendothelioma) with hepatic failure went for liver transplantation and were followed by carcinomatous dissemination.
Conclusions : Hemangioma has a variable presentation : single or diffuse. A local ressection is possible for SHH. If not, corticosteroïds or Interferon alpha are a therapeutic approach. DHH can degenerate in generalized angiosarcoma, perhaps due to the immunosuppression.

- G08 -

EVEN WITH NEGATIVE FAMILIAL ANTECEDENTS, GENETICS ARE NEEDED FOR DIAGNOSIS OF HERIDITARY PANCREATITIS AS A FORM OF ATYPICAL CYSTIC FIBROSIS.
Z. Yüksel, T. Mahler, G. Veereman-Wauters, M. Van Caillie-Bertrand* E. Van Hollebeke**. *Department of Paediatric Gastroenterology, Hepatology and Nutrition. Queen Paola Children's Hospital-AZM, 2020 Antwerp, Belgium ; **General Paediatrics, St Elisabeth Hospital, Turnhout, Belgium.

Cystic fibrosis (CF) is an autosomal recessive disorder caused by mutation in the CFTR gene and is associated with abnormal sweat electrolytes, sino-pulmonary disease, congenital absence of vas deferens and exocrine pancreatic insufficiency. We present an atypical form of cystic fibrosis. We describe a 13 year old male with recurrent abdominal pain and vomiting since a massive gastroenteritis two month earlier with each time elevated pancreatic enzymes in serum and urine. On physical examination there was a diffuse tenderness of the abdomen. The diagnosis of chronic pancreatitis has been made. There was no evidence for trauma, infection, inflammatory, toxic or metabolic disorder. First screening test for CF showed 54 mmol Cl/l on Macroduct sweat test, this result was considered to be normal. Endoscopy showed hypertrophic mucosa with lymphoid hyperplasia but no distinctive ampulla of Vater. MRCP was then repeated and provided the diagnosis of pancreas divisum. Despite stenting the ampulla of Vater, abdominal pain (with elevated pancreatic enzymes) re-occurred. Sweat test has been repeated and showed borderline sweat chloride (60 mmol CL/l). Genetic analysis for hereditary pancreatitis was performed and showed a heterozygous mutation on the CFTR gene : delta F 508 mutation and T5/T9 mutation on intron 8. Genetic work-out of the parents showed that the mother was carrier of T5/T7 mutation on intron 8 and the father of delta F 508 on exon 11 and T7/T9 mutation on intron 8. Mutations of the CFTR gene lead to dysfunction of lung, sweat glands, vas deferens and pancreas. Severe mutations in both CFTR gene can lead to the classical CF and pancreatic insufficiency. There are also "atypical" mild CFTR associated mutation that are responsible for so-called monosymptomatic diseases such as late onset pulmonary disease, congenital bilateral absence of vas deferens and idiopathic pancreatitis (IVS8 – T5/T7/T9 on intron 8). The link between mutations of the CFTR gene and idiopathic pancreatitis has been proved earlier. Recently the association between mutations of the CFTR gene and T5 genotype has been demonstrated.(Sharer et al, New Engl J Med, 1998) The diagnosis of "atypical "cystic fibrosis must be considered when a patient presents with idiopathic chronic pancreatitis and genetic analysis for hereditary pancreatitis has to be done even if the parents do not have antecedents of pancreatitis.

- G09 -

NUTRITION OF YOUNG CHILDREN (0-2 YEARS) IN FLANDERS. Ph. Alliët, M. Raes, I. Goffin, S. Lenaers. Virga Jesse Hospital Hasselt and SEIN - Limburgs Univeritair Centrum.

In order to influence and improve nutrition in childhood, it is important to have an idea about the current practices. This study was ordered by “Kind en Gezin”. A questionnaire about e.g. the composition of feeding, feeding supplements and eating habits was sent to parents of infants aged 3, 6, 12 and 24 months old. The response rate was 71% (2925/4000 questionnaires). Infants were breastfed in 66.5, 59, 38.9, 15.5 and 3.9% at birth and age 1 week, 3, 6 and 12 months resp. Important differences in breast-feeding percentages were seen between the different provinces in Flanders. A higher parental educational level was positively correlated with breastfeeding. Smoking during pregnancy and a higher child ranking were negatively correlated with breastfeeding. Parents had chosen the type of feeding for their child before pregnancy in 71.9% and during the first part of pregnancy in 15,8%. Cessation of breast-feeding was due to infant complaints mainly during the first 13 weeks of age (30,5% and 19,4% during the period 0-6 and 7-13 weeks vs 11,6 and 10,2% at 14-26 and 27-52 weeks). Maternal reasons became more important with increasing age of the baby. Succesful breast-feeding at day 6 was correlated with the interval between birth and the first feeding : exclusive breastfeeding was discontinued in 16.1 and 29.6% of the infants receiving the first feeding 2-12 and > 12 hrs after birth. Beikost was introduced before the age of 4 months in 22% of infants. Vegetables and fruit were first started in resp 39 and 37%, with important regional differences. At the age of 6 m, oil or margarine were never added to the vegetable meal in 29%. 10% of infants at age 6 m were getting cottage cheese. Many parents do not know at what age gluten was introduced. At the age of 12 and 24 m, resp 9 and 24% of infants were drinking a - not for their age suitable - milk. Snacks were more frequently taken at the age of 24 m (38% “often to every day”). The use of candies, fruit juice, soft drinks and sweet milk drinks especially became more popular. Although nutritional habits in general were quite adequate, aberrations were at all ages more often seen in young parents with a lower educational level and/or having a first child.
Conclusion : This study describes the feeding habits of 0-2 year old children in Flanders. An insight in current practices makes intervention for improvement possible.

- G10 -

DYSPHAGIA AND GERD IN CHILDREN. G. Veereman-Wauters, N. Rommel*, T. Mahler, M. Van Caillie-Bertrand. Pediatric Gastroenterology, Hepatology and Nutrition, Queen Paola Children’s Hospital-AZM, Antwerp and Centre for Paediatric & Adolescent Gastroenterology * Women’s and Children’s Hospital, Adelaide, Australia.

In order to determine the frequency of GERD in young children presenting with severe feeding difficulties or dysfagia we reviewed our experience obtained over a 5,5 year period with a Pediatric Multidisciplinary Feeding Clinic (UZ Gasthuisberg, Leuven). 700 children under 10 years of age presented with feeding difficulties severe enough to interfere with growth. Of these patients 86% were diagnosed with an underlying medical condition, 61% had a motor or sensitive oral dysfunction, 18% were found to have a behavioural problem, 1,6% remained unexplained. Half of the patients (48,5%) had a combination of medical and oral problems. Gastrointestinal diseases were the most frequent medical diagnoses, with 60% of them being GERD. GERD was diagnosed in 228 children and thus may account for about 30% (228/700) of severe feeding problems or dysfagia. Treatment of GERD but also of the accompanying oral problems is indicated in this group. Clearly other underlying medical causes need to be ruled out.

- G11 -

OESOPHAGEAL MOTILITY PATTERNS IN CHILDREN WITH DIGESTIVE AND RESPIRATORY SYMPTOMS OF GORD. M. Scaillon (1), M. Fotoulaki (2), S. Cadranel (1). (1) Queen Fabiola Children's Hospital, Free University of Brussels ; (2) AHEPA Hospital. Aristotle University. Thessaloniki.

Gastrooesophageal reflux disease (GORD) symptoms can be oesophageal or respiratory.
Aim : Compare the long-term ambulatory oeophageal manometry (LTAOM) motility patterns in children with digestive (D) or respiratory (R) symptoms of GORD to controls (C).
Material and methods : Group D, 12 children (median 5.3 y ; range 1-14 y) ; Group R, 9 children (median 5.8 y ; range 1.5-11y) ; Group C, 8 children (median 9 y ; range 5.3 -14 y) suspected of GORD, found normal and with a normal follow up. Oesophagitis was ruled out by endoscopy and all 28 children were investigated in LTAOM using a probe with 4 electronic pressure transducers (Gaeltec Ltd), recording simultaneously from 3 sites separated either at 2.5 cm or at 5 cm apart depending on the stature of the child ; a probe with a pH antimony electrode ; a Microdigitrapper 4-Mb portable digital data logger with 1 channel devoted to pH-metry and the 3 others to manometry. Data were analysed at the proximal, mid and distal levels during the total recording time (T) and selected periods defined as reflux (G), meal (M), standing (U) and sleep (S) using a Multigram-Synectics software.
Results : statistically significative differences ($p < 0.001$ to 0.003) were observed : $R < D < C$ for the mean amplitude of proximal contractions during T, M, U and S ; $R < C$ for the percentage of effective sequences during U ; $R < C$ for the percentage of peristaltic sequences during U ; $D < R$ for the percentage of possibly effective sequences during G ; $R < D$ for the percentage of proximal contractions with > 25 mm Hg amplitude.
Conclusions : Oesophageal motility patterns in children with GORD seem more impaired proximally than distally and also more pronounced in R than in D especially during the U period.

- G12 -

ABNORMAL GUT FLORA AND LIVER DYSFUNCTION IN CHILDREN WITH REGRESSIVE AUTISM. S.L.M. Rosseneu, Centre for Paediatric Gastroenterology ; H.K.F. van Saene, Department of Medical Microbiology ; R. Heuschkel, S.H. Murch, Centre for Paediatric Gastroenterology, Royal Free University Hospital , London, United Kingdom.

Background : Children with late-onset or regressive autism often suffer gastrointestinal (GI) symptoms including severe constipation. Non-specific enterocolitis and complex immunopathology of the gut mucosa have been described in this group of patients. We recently reported that almost 60% of children with regressive autism and GI pathology had bacterial overgrowth. Bacterial overgrowth is defined as the presence of $\geq 10^5$ colony forming units of AGNB per ml of saliva and/or g of faeces. AGNB overgrowth is known to impair the liver function ; directly via endotoxin or indirectly via cytokine mediation. We prospectively investigated a possible association between AGNB overgrowth and liver dysunction in children with regressive autism and gut disease.
Patients and methods : Liver function and gut flora were measured in 62 patients diagnosed with regressive autism and GI-symptoms. The liver function tests included serum aminotransferases (AST, ALT) and bilirubin. Normal values for the liver tests are AST : < 40 IU/l, ALT : < 40 IU/l, bilirubin : < 17 micromol/l. None of the patients had a history of liver disease and none of the patients showed signs of liver disease on clinical examination. Surveillance cultures of throat and rectum were processed on a MacConkey agar plate using the four-quadrant method to detect the level of AGNB.
Results : 32 (52%) patients acquired AGNB with a median growth density of $\geq 10^7$ AGNB per ml of saliva and /or g of faeces. 17 individuals had transaminitis reflected by AST ≥ 40 IU/l (median 44 IU/l, IQR 26-52). Bilirubin was normal in all patients. 13/32 patients (41%) had transaminitis whilst only 4/30 (13%) patients with normal flora showed liver dysfunction (41% vs 13%, $p < 0.005$).
Conclusion : This observation that AGNB overgrowth is associated with transaminitis, supports the gut flora - liver link in children with regressive autism and gastrointestinal symptoms.

AN UNUSUAL CAUSE OF ACUTE PANCREATITIS IN A CHILD. B. Hauser, Y. Vandenplas. Dpt Pediatric Gastroenterology, AZ-VUB, Brussels, Belgium.

Acute pancreatitis in children can be caused by trauma, infection, biliary tract disease, drugs, hereditary predisposition, congenital anomalies, hypercalcemia, hypertriglyceridemia and a variety of less common factors including cystic fibrosis. We describe one child with an acute pancreatitis in whom Crohn's disease (CD) was diagnosed. A 14-year-old girl presented with epigastric pain, vomiting, fever, fatigue and weight loss lasting for two months. The history was negative for abdominal trauma, alcohol use or drug intake. There was no family history of pancreatitis or biliary tract disease. Serum amylase was 232 IU/l (< 113) and lipase was 2394 IU/l (50-200). Inflammatory parameters were moderately increased. Serum electrolytes, calcium, cholesterol, triglycerides, transaminases, bilirubine, alkaline phosphatase, gamma glutamyl transpeptidase, lactate dehydrogenase, ureum, creatinine, glucose, iron, ferritine, antinuclear factor, viral serologies and sweattest were normal. Abdominal ultrasound, CT scanning and MRI with MRCP were normal. CD was suspected and lower and upper gastrointestinal endoscopy were performed. Gastric, duodenal and colonic manifestations of CD were observed. Ileal involvement could not be demonstrated. Patient was initially treated with corticosteroids and mesalazine ; the latter was continued. During the one year follow-up, she had one flare-up of pancreatitis for which she received a short course of corticosteroids. The association of acute pancreatitis and CD is well known. The pancreatitis can be due to biliary lithiasis, drug toxicity from drugs used in the treatment of CD, duodenal involvement of CD, association of CD with pancreatic duct anomalies or can be idiopathic. In our patient a duodenal involvement may have played a role as a duodenitis was present. We conclude that pancreatitis can be the initial manifestation of CD.

- N01 -

DEVELOPMENT OF A MALNUTRITION SCREENING TOOL FOR ADULT HOSPITALIZED PATIENTS. M. Gouthière, J.M. Ketelslegers, J.P. Thissen. Div. of Diabetes and Nutrition Unit, Catholic University of Louvain, and St-Luc Academic Hospital, 1200 Brussels, Belgium.

Protein-energy malnutrition is common in hospitalized patients. Although malnutrition is associated with high morbidity and mortality, the nutritional status is rarely assessed. The aim of this study was to develop a practical tool for the screening of hospital malnutrition. To answer this question, we assessed the nutritional status of 505 adult patients within 48h of admission in the Academic St-Luc Hospital. The nutritional status of each patient was determined by performing Subjective Global Assessment (SGA), anthropometry, electric bioimpedance, and measuring plasma circulating proteins (albumin, transthyretin, IGF-I- n = 320). SGA was chosen as the “gold standard” for defining malnutrition. Our results show that malnutrition is as frequent in St-Luc Hospital as other academic hospitals. Based on the SGA, 34% of patients were recognised as malnourished (score B or C), with 23% moderately (score B) and 11% severely malnourished (score C). The nutritional status, as determined by the SGA, was tightly correlated with several objective nutritional parameters reflecting body composition (fat-free mass and fat-mass assessed by anthropometry and impedance). In contrast, circulating concentrations of plasma proteins did not correlate well with the nutritional status as determined by SGA. To develop a malnutrition screening tool, nutrition screening questions were selected from literature and from clinical experience. Each question was tested individually against SGA for possible association using the chi-square test. The two questions with the highest sensitivity and specificity were : “Have you lost weight recently without trying?” and ”Have you been eating poorly because of a decreased appetite ?”. With the addition of the question : ”How much weight have you lost ?”, we developed a score system based on the one described by Ferguson *et al.* (1999). Subjects obtained a score between 0 and 5. The cut-off value with the highest sensitivity and specificity determined by ROC analysis was 2. Subjects with a score of 2 or more were subsequently classified as at risk of malnutrition. The sensitivity of the screening tool was 75% and its specificity 78%. Whereas the positive predictive value was 63%, the negative predictive value was 86%. Subjects with a score of 2 or more had significantly worse values for the objective nutritional parameters compared with subjects with value less than 2. The Malnutrition Screening Tool and the Subjective Global Assessment are simple, reliable and valid to respectively screen and diagnose malnutrition in hospital.

- N02 -

PREVALENCE OF MALNUTRITION IN HOSPITALIZED PATIENTS WITH GASTROINTESTINAL DISORDERS. C. Montoisy, L. Drumel, M. Arvanitakis, K. Buedts, S. Vereecken, A. Van Gossum. Brussels, ULB.

Background : Malnutrition is frequent in hospitalised patients in industrialized countries. However the prevalence of malnutrition in Belgium is not known.
Protocol : A prospective study was designed to define the prevalence of malnutrition in patients that were admitted for GI disorders in the Medico-surgical Department of Gastroenterology (Erasme Hospital). The prospective study was performed by 2 independent observers. All the patients newly admitted during 6 consecutive weeks were included. The following parameters were assessed the day of admission : weight (usual, actual,% of loss), subjective global nutritional assessment, handgrip dynamometry and a dietary intake inquiry. These parameters were re-evaluated when the patients were discharge.
Results : 170 patients were evaluated. A severe malnutrition was detected in approximatively 20% of the cases. Details will be provided further.
Conclusion : Malnutrition is frequent in hospitalised patients with GI disorders. A systematic and simple assessment should be systematically performed.

- N03 -

NUTRITION ASSESSMENT IN ICU PATIENTS. F. Colardyn. Department of Intensive Care, Ghent University Hospital, De Pintelaan 185, 9000 Gent.

As malnutrition is frequent on admission in the hospital (up to 40%) the problem for the ICU patient is even more important as the nutrition status will rapidly deteriorate due to the catabolic state and protein malnutrition, which calls for an immediate action.
Methodology : survey of the literature over the last 10 years on the topic of nutrition assessment in the ICU.
Results : very few data have been found on nutrition assessment in the ICU. Anthropometry : the interpretation is controversial, for example creatinine height index (relying on 24 h urinary creatinine excretion) is hampered by : common kidney dysfunction, stress, immobilisation and feeding. The hepatic secretory proteins : interference of various half-lives, hepatic dysfunction, protein losses and inflammation with a shift of protein synthesis. Cellular immunity or delayed cutaneous hypersensitivity : most ICU patients are immune depressed by infection, injury, burns and medication. Also technical problems with the skin in the ICU patient. Multiparameter nutritional indexes, for example the Maastricht index : not very well evaluated in the ICU patients. Muscle function tests : most ICU patients are not fully cooperative, metabolic factors and medications interfere with the readings. Due to these difficulties most intensivists rely on nomograms for the estimation of caloric expenditure with an expected percentage of the RME, increased by stress, sepsis, pain and decreased by sedation and paralytis. But there is a high variability in the estimation of the stress factor. Two authors found the MAC a useful parameter in the prognosis of the ICU patient.
Conclusion : Nutrition assessment in the ICU is very important, due to the catabolic state and eventually previous malnutrition. The classical measures are hampered by the sickness of the patient, the treatment (for example positive fluid balance) and the lack of cooperation of the patient. Nutrition assessment can be used as a prognostic index, but up to now has not been proven to be of value in the outcome of the patient.

- N04 -

SURVEY ON THE USE OF PARENTERAL NUTRITION IN ADULT PATIENTS. L. Amininejad, M. Arvanitaki, V. Lievin, M. Perremans, A. Van Gossum. Brussels, Belgium.

A study has been designed to control the quality of the use of PN that has been recommended by the nutritional team. A survey of the use of PN was performed within a period of 4 months by an independent observer. The following parameters were recorded : number, age, sex, care units, underlying diseases, indications, subjective global assessment (SGA), median time of PN, iv intakes (A : 1500 kcal – 50 g prot ; B : 1800 kcal – 60 g prot ; C : 2200 kcal ; 70 g prot), clinical and nutritional outcome, complications, reasons for discontinuation PN. This study included 82 consecutive patients receiving PN (1% of the admissions), 49 males and 33 females with a mean age of 57 years (from 19 to 84). PN was initiated in 50% medical patients and in 50% surgical patients. SGA was considered to be A : 49%, B : 32%, C : 19% with a recent weight loss > 20% in 9 (11%). Median time for PN was 10 days (from 1 to 37). PN was exclusive in 68%, combined with enteral feeding in 9% or oral in 23%. Intakes were A in 66%, B in 3%, and C in 1%. Change in iv intake was done in 10%. On PN, 39% of patients were septic but only 4 experienced PN-related sepsis. Hyperglycemia (> 126 mg/dl) was observed in 32 patients and cholestasis in 11 patients, but responsible for discontinuation of PN in only 1 patient with cholestasis. 77% proceeded to oral nutrition, 9% to enteral, 1 patient to home PN and 11% died. The survey revealed that : 1-Low proteino-caloric intake was mostly used ; 2-Rate of PN-related complications was low (may be related to 1.). 3-Adaptation of iv intakes was uncommon. 4-Duration of PN was less than 7 days in 25% of the cases.5-Estimation for the need of PN should be improved for avoiding very short-time PN.

- N05 -

PITFALLS OF ORAL MEDICATION AND TUBE FEEDING. E. Herbots, H. De Bosscher, M. De Clercq, P. Bruyneel, D. Ysebaert. Hospital Pharmacy and Nutrition Team, University Hospital of Antwerp.

Nursing and medical staff are confronted with theoretical and practical problems concerning the administration and possible interactions of (intended) oral medication and enteral tube feeding. In daily practice it is not always evident to give an optimal pharmaceutical treatment in patients with total enteral nutritional support. A survey conducted at several care units a lot of questions from the nursing staff regarding technique of administration, timing and problems of tube obstruction. Almost no specific information is available from literature or pharmaceutical companies, leading to “trial and error” behaviour of nursing staff, with possible consequences of underdosing which is problematic in case of critical medication. Special product formulations (controlled release, enteric coated, long acting, retard preparations, etc…), interaction with food elements, tube adherence and location (in GI tract) of tube tip, all have to be taken into consideration when considering “oral” medication in patients with enteral nutritional support. Guidelines on tablet crushing technique, timing of administration (fasting or not), knowledge of the special drug formulations, together with consulting the hospital pharmacists on a structural basis, are the keystones in successful delivery of critical oral medication in these nutritionally supported patients. A web-supported updated database could be a useful tool and is under construction.

- N06 -

THE BENEFICIAL EFFECTS OF SUPPLEMENTARY GLUTAMINE ON EXPERIMENTAL IRRADIATED COLONIC ANASTOMOSIS ; HISTOLOGICAL AND MORPHOLOGICAL EVALUATION. M. El-Malt (1), P. De Metter (2), C. van den Broeke (2), W. Ceelen (1), C. Cuvelier (2), B. de Hemptinne (1), W. De Neve (3), P Pattyn (1). (1) Dpt of Gastrointestinal Surgery ; (2) Dpt of Pathology ; (3) Dpt of Radiotherapy, UZ-Ghent, Ghent University, Belgium.

Purpose : To investigate the effects of adding glutamine to total partenteral nutrition on the histology and morphology of irradiated colonic anastomosis.
Methods : The rectosigmoid colon in male Wistar rats was irradiated up to a total dose of 25 Gy (5 Gy daily for 5 consecutive days). Five days after the end of RT, side-to-side anastomosis was constructed between the irradiated rectosigmoid and the non-irradiated caecum. Postoperatively, animals were divided randomly into 3 groups ; group I was fed orally (lab chow), group II received TPN and group III received TPN enriched with 2% glutamine (Gln-TPN). One week after surgery animals were sacrificed.
Results : Mucosal morphometric measurements and mucosal regeneration were improved with the addition of glutamine to TPN. Crypt depth at the anastomotic site was significantly more in group III in comparison to group II ($p = 0.04$) and it was comparable to goup I. Mucosal ulceration was less in group III in comparison to group I ($p = 0.005$) and group II ($p = 0.05$). The mucosal ulcers that penetrate deeply into the serosa were also less in group III (54%) compared to group I (91%) and group II (70%). The radiation effects on the submucosal arteries were significantly less in group III in comparison to group I ($p = 0.001$) and group II ($p = 0.001$). No differences were observed between the three groups regarding the inflammatory reaction in the submucosa or the serosa. E-cadherin expression was upregulated at the edge of the ulcerations. However, reparative epithelium showed downregulation of E-cadherin.
Conclusion : Supplementary glutamine promotes mucosal regeneration and diminishes the radiation effect on the submucosal blood vessels which can be beneficial for the healing of colon anastomosis after radiation therapy.

- N07 -

LIPID EMULSION PARTICLES AS EFFICIENT SUPPLIERS OF ALPHA-TOCOPHEROL TO PLASMA LIPOPROTEINS AND BLOOD CELLS IN VIVO. I.E. Dupont, O. Scruel, Y.A. Carpentier. Laboratory for Experimental Surgery, Université Libre de Bruxelles, Brussels.

Alpha-tocopherol (a-toc), the major liposoluble antioxidant of cell membranes, is largely transported in plasma lipoproteins. The oxidative stress associated to several acute situations often leads to a-toc deficiency. Oral supplementation may not promptly restore a-toc status in acute phase patients. The aim of the study was to determine the rate and extent of a-toc enrichment in plasma lipoproteins and blood cells following the injection of an a-toc rich lipid emulsion (LE). Six healthy volunteers were injected (within 2 min) with 20 ml LE supplying 200 mg a-toc. Alpha-toc was measured by HPLC in LDL, HDL, WBC, platelets and RBC after 0.5, 1, 2, 4, 6 and 24h. Values (mean ± SD, *Student t test : $p < 0.05$) are expressed as µmol/mmol cholesterol in lipoproteins and µmol/mmol cell phospholipids. All clinical and biological parameters of tolerance were unchanged. Within 30 min following injection, a-toc content significantly raised in LDL (+ 35%) and HDL (+ 29%). Enrichment continued to reach 59% in LDL and 41% in HDL at 6h and was still significant at 24h. Of interest, a-toc enrichment in LDL was correlated to a prolonged lag phase using the Esterbauer peroxidation test ($R^2 = 0.98$). The injection also induced a prompt a-toc increase in blood cells, noticeable at 30 min, to reach 57% in WBC, 44% in platelets, and 38% in RBC at 6h ($p < 0.01$), an effect that subsisted at 24h. In conclusion, marked enrichment of a-toc can be achieved in lipoproteins and target cells within 30-120 min following injection of a-toc-rich LE. This safe treatment could be used prophylactically to protect against oxidative stress towards lipid membranes.

	LDL	HDL	WBC	Platelets
0 h	3.27 ± 0.55	6.57 ± 0.71	5.37 ± 1.19	7.43 ± 0.75
2 h	4.72 ± 0.40* (p = 0.00076)	8.85 ± 1.23* (p = 0.0015)	10.35 ± 4.38* (p = 0.027)	10.51 ± 3.89 (p = 0.089)

- N08 -

PROBIOTICS IN PREVENTION AND TREATMENT OF ENTERIC INFECTIONS. Y. Vandenplas. ULB, Brussels.

The World Health Organization does not recommend the systematic administration of medication in acute gastroenteritis. The pathogen involved is likely to – at least partially – determine the outcome. It is unlikely that the same degree of efficacy is valid for all strains of lactobacilli. And equally, it is unlikely that only lactobacilli are of benefit in diarrhoea related to infectious diseases. Dose-response studies have not been performed. Better knowledge about the pharmacokinetic and -dynamic mechanisms for bacterial probiotics is needed. Yeast biotherapeutic agents have been shown to be effective in the treatment of acute gastroenteritis, antibiotic associated diarrhoea, in the prevention of antibiotic associated diarrhoea, and in the treatment of Clostridium difficile colitis. Guidelines for the treatment of acute gastroenteritis should consider a cost-benefit analysis, and should also consider the risk for side-effects. The effect of prebiotics, in combination with oral rehydration solution, has not been studied thoroughly. There are no reports on the efficacy of a combination of therapeutic possibilities such as the combination of biotherapeutic agents with anti-peristaltic or anti-secretory medication. The conclusion of Van Niel that “a 48-hour course of a Lactobacillus product is commercially available for $ 10 and on an average could save about 17 hours of caring for a sick child with diarrhoea and 1 to 2 diapers” illustrates the role of biotherapeutic agents in improving patient comfort. However, the effects of biotherapeutics in the developing world may be more obvious. What is relevant, is not so much whether the biotherapeutic agent reduces the duration and severity of diarrhoea, but whether the biotherapeutic agent reduces mortality, relapse or re-infection, chronic diarrhoea, malnutrition, (re)hospitalisation and thus whether there is a significant “saving” in severe disease and thus long-term cost of health care by investing in short-term.

- P01 -

CHOLANGIOCARCINOMA : PREDICTIVE VALUES OF CLINICOPATHOLOGIC FEATURES. M. Praet*, P. Demetter*, L. Ferdinande*, T. Botelberghe**, H. Van Vlierberghe***, I. Colle***, R. Troisi****, B. De Hemptinne****. *Dpts of Pathology, **Radiotherapy, ***Gastroenterology, ****Livertransplantation, University Hospital Gent, De Pintelaan 185, 9000 Gent.

Background : according to the literature the macroscopic types of the intrahepatic cholangiocarcinoma determine the prognosis of the patient. The intrahepatic cholangiocarcinomas can be classified into the following growth types : mass forming, periductal-infiltrating, mass forming plus periductal infiltrating, intraductal. Intrahepatic cholangiocarcinoma is different from the hepatocellular carcinoma and from the hilar cholangiocarcinoma (Klatskin tumor).
Patients and methods : 12 patients underwent right leverlobe (n = 6) and left liverloge (n = 6) resection. 2 patients received a livertransplantation. Three patients underwent palliative surgery with resection of stenosing tumor masses. The clinical data were collected including cholestasis and serum levels of Ca 19.9. The macroscopy of the resected tumor was compared with the ERCP findings.
Results : out of the clinical data we could not predict the cellular behaviour nor the extend of the neoplastic process. The macroscopical approach of the tumor provides no adequate information about the anaplasia of the tumor. The comparison between the tumorgrowth and the ERCP findings discloses major differences s.a. presence of metastatic nodules and perinervous infiltrations in the vicinity of the tumormass.
Conclusion : Microscopical more than macroscopical evaluation of the tumor provides adequate information of the to be expected outcome.

- P02 -

ABSENT FDG-AVIDITY IN ADENOCARCINOMAS OF THE ESOPHAGUS AND CARDIA HAS A HIGH SPECIFICITY AND POSITIVE PREDICTIVE VALUE FOR POOR DIFFERENTIATION. H. Alaerts, J. Van Riet, A. Driessen*, P. Nafteux, T. Lerut, L. Mortelmans, P.N. Ectors Flamen. University Hospitals Leuven, Belgium ; University Hospital Maastricht*, The Netherlands.

Oesophageal cancer has a poor prognosis, which is related to the advanced stage of disease and the presence of lymph node metastasis. Preoperative staging is essential as treatment modalities are chosen in function of this. Positron emission tomography (PET) with 18F-labeled fluorodeoxyglucose (FDG) increases preoperative staging accuracy. However, reduced or absent FDG avidity of some carcinomas has been reported. The aim of our study was to compare the FDG uptake intensity as measured by dedicated PET with different histopathological features of the primary tumour. Therefore, a series of distal oesophageal and cardia adenocarcinomas (n = 96, 65 yr, 37 - 83 yr, M/F = 6) treated by primary surgery were classified according to their differentiation grade (well 21%, moderate 36%, poor 43%), the Lauren-classification (intestinal 84%, diffuse 16%) and the Goseki-classification (I = 45%, II = 36%, III = 7%, IV = 11%). Histology was performed on formol-fixed paraffin-embedded samples of resection specimens. Patients underwent FDG-PET prior to surgery. The FDG-uptake of the primary lesion (T) were classified as T0 = negative due to small size of tumour (< 10mm) (n = 12), T1 = intense hot spot (n = 61), T2 = limited positivity (n = 5), T 3 = inhomogeneous labelling (n = 6), and T4 = no detectable FDG uptake (n = 12). The results show that a T4 PET score frequently corresponds to a poorly differentiated tumour (82%). Furthermore, T4 has a high positive predictive value for a poorly differentiated tumour (PPV 75%) and an even higher specificity (96%). In case of T1 signal the PPV for intestinal type (Lauren) and type I + II (= glandular differentiation in Goseki) of carcinoma was 87% and 85% respectively. In conclusion, absence of FDG uptake as measured by PET in an adenocarcinoma of the oesophagus or cardia of sufficient volume is highly predictive for poorly differentiated tumours. This result maybe useful in the choice of therapy.

- P03 -

A RARE PRESENTATION OF MYELOID SARCOMA. M.-C. Nollevaux (1), A. Sonet (2), A. Rosière (3), G. Müller (4), P. Hoang (5), I. Théate (6), M. Delos. (1) Dpts of Pathology, (2) Haematology and (3) Surgery, Cliniques universitaires UCL de Mont-Godinne, 5530 Yvoir, Belgium ; (4) Institut de Pathologie et Génétique, 6280, Loverval, Belgium ; (5) Gastroenterology, Clinique Ste Elisabeth, 5000 Namur, Belgium and (6) Dpt of Pathology, Cliniques universitaires St-Luc, UCL, Brussels, Belgium.

Myeloid sarcoma, also called granulocytic sarcoma or chloroma, is an extramedullary tumour composed of myeloblasts or immature myeloid cells and is most often associated with acute leukaemia or with chronic myeloproliferative/ myelodysplastic disorders. In rare cases, the tumor arises in absence of leukaemic features in peripheral blood and bone marrow, leading to diagnostic difficulties, especially when it occurs in uncommon sites such as the gastrointestinal tract. Indeed, the most common sites of involvement are skull, paranasal sinuses, sternum, ribs, vertebrae, pelvis but also lymph nodes and skin. We describe the case of a 60 year-old woman who complained from abdominal pain and constipation. Coloscopy revealed a thickening of caecal mucosa and computed tomography showed a diffuse circumferential extension of the caecal wall. Histological examination of colonic biopsies let to the diagnosis of myeloid sarcoma of the caecum. Bone marrow biopsies showed no morphological abnormality and karyotype was normal. The patient was treated by systemic chemotherapy, including aracytine and daunorubicine. After the first course of induction, massive bleeding resulting from tumoral necrosis required surgical resection. The surgical specimen revealed a large tumoural mass of 16 cm large. The caecal wall was diffusely infiltrated by myeloid atypical cells, which expressed myeloperoxidase, lysozyme and CD 15 in immunohistochemistry. Unfortunately, severe post-operative renal failure let the patient to a fatal issue, three months after the diagnosis. This observation describes a very rare location of an aleukaemic form of myeloid sarcoma. Non-Hodgkin's lymphoma represents the most striking diagnostic challenge of this lesion, for which immunohistochemical studies are mandatory.

- P04 -

METAVIR FIBROSIS SCORE OF CHRONIC HEPATITIS : PRACTICAL GUIDELINES. Tania Roskams. Dept of Morphology and Molecular Pathology, University of Leuven, Leuven, Belgium.

Classification of chronic hepatitis is based on etiology (viral, auto-immune, drug-induced,…), grade of inflammatory activity and stage of progression of the disease (degree of fibrosis). Grading and staging of chronic hepatitis can be done in a descriptive way (mild moderate, severe) or can be done, using numerical scores. There are several scoring systems : Knodell scoring system, Scheuer scoring system, Ishak scoring system, Metavir scoring system, each of which has advantages and disadvantages…Since August 2002, a treatment with Pegylated interferon can be only reimbursed from a Metavir score of fibrosis grade 2 onward. Therefore, the Metavir scoring system of fibrosis will be explained and practical guidelines will be given. Many examples will be shown, illustrating also the pitfalls of scoring.

- P05 -

EMPHYSEMATOUS GASTRITIS AFTER ENDOSCOPIC SCLEROSIS FOR HAEMORRHAGIC PEPTIC ULCER. P. Fajardo-Mostenne , A. Grauls, O. Plomteux, B. Moreau-Massart, F. Corhay-Abraham, B. Bastens, C. Jehaes, F. Fontaine, C. Wahlen. Services de Gastroentérologie, de Chirurgie Digestive et d' Anatomopathologie, Les Cliniques Saint Joseph, 75 rue de Hesbaye, Liege.

Emphysematous gastritis is a rare and severe disease caused by gas-producing organisms. We report a 67-years old man hospitalised for a recurrent haemorrhagic peptic ulcer who developed an emphysematous gastritis after endoscopic sclerotherapy. In the following hours after sclerotherapy, he rapidly deteriorated and developed an acute abdomen. Computorised tomography scanner of the upper abdomen revealed a large collection of gas within the stomach wall and emergency laparotomy showed a complete necrotized anterior and posterior stomach wall filled with air. A total gastrectomy was performed with successfull outcome. The histopathological examination of the stomach revealed a severe emphysematous gastritis. This is the first case of emphysematous gastritis after endoscopic sclerosis described in the literature. The authors discuss ethiopathogenesis, treatment, prognosis and review the literature of this uncommon condition.

- P06 -

INVASIVE GASTROINTESTINAL ZYGOMYCOSIS IN CROHN'S DISEASE. E. Van den Heuvel, R. Salgado, H. Demey, E. Van Marck, J. Bogers. Department of Pathology and Intensive Care, University Hospital of Antwerp, Wilrijkstraat 10, 2650 Edegem, Antwerp, Belgium.

Zygomycotic infection of the gastro-intestinal tract is a rare, but often fatal disease in routine clinical practice presenting as vague abdominal symptoms in patients with diabetes mellitus, neutropenia, sustained immunosuppresive therapy, iron chelation therapy, broad spectrum antibiotic use, severe malnutrition or chronic corticosteroid use. A 82-year old patient with a history of Crohn's disease treated with corticosteroids presented with sustained fever, vague abdominal discomfort and melena. Endoscopy showed a 3.5 cm ulcer in the body of the stomach, highly suspicious for malignancy. Biopsy specimens demonstrated superficially invasive, broad, non-septated and thin-walled, often bent hyphae in a prominent neutrophylic infiltration in the lamina propria. The epithelium at the borders of the ulcer showed severe reactive atypia but no clear malignancy. Rapid clinical deterioration occurred and the patient died despite supportive therapy. Post-mortem investigation showed a large gastric ulcer invaded by hyphae throughout all layers of the stomach, but no malignancy. The occurence of zygomycotic infection and lethal sepsis in this patient was possibly exacerbated by chronic corticosteroid use for Crohn's disease and severe malnutrition. This case illustrates that zygomycotic infection of the gastro-intestinal tract is a rare but life threatening complication in patients with Crohn's disease, possibly mimicking malignancy. The diagnosis is dependent on histology, stressing the importance of adequate biopsy material from the border and the center of the ulcus.

- P07 -

SMALL BOWEL PSEUDO-OBSTRUCTION, A RARE COMPLICATION OF MULTIPLE MYELOMA. N. Nagy, P. Feron, R. Chamlou, A. Van Gossum, C. Moreno, A. Kadhim, C. Deprez, I. Salmon. Dpt of Pathology and Gastroenterology, Erasme University Hospital, Free University of Brussels, Brussels. Dpt of Pathology, Brugman Hospital, Brussels.

Small bowel pseudo-obstruction due to AL-amyloidosis is an extremely rare complication of multiple myeloma. Pseudo-obstruction in patients with amyloidosis is caused by either myopathy or neuropathy. The chemical type of amyloid determines which of the two factors affect the bowel function. We report the case of a 76 year old man who develops abdominal pain due to acute small bowel pseudo-obstruction, 6 months ago, associated with a progressive axonal polyneuropathy. Despite conservative treatment and total parenteral nutrition, the pseudo-obstruction persists. Firstly, the patient was treated by adhesiolysis, and secondly, 4 months later, he undergo a jejunal resection for necrosis. Pathological examination reveals complete destruction of the muscularis propriae due to extensive infiltration by AL type amyloid deposits. Such a pathological diagnose induce the clinicians to diagnose a multiple myeloma.

- P08 -

SEGMENTAL ABSENCE OF SMALL INTESTINAL MUSCULATURE : AN IMPORTANT CAUSE OF NEONATAL INTESTINAL OBSTRUCTION AND PERFORATION. G. De Hertogh, P. Van Eyken, K.P. Geboes, M. Miserez, H. Devlieger, K. Geboes. Dpt of Pathology, University Hospitals K.U. Leuven, Minderbroedersstraat 12, 3000 Leuven, Belgium.

Background : Neonatal intestinal obstruction and perforation can be due to a variety of causes, e.g. atresia and necrotizing enterocolitis (NEC). We observed 25 cases of segmental absence of the bowel musculature (SAM) causing either obstruction or perforation in premature newborns.
Objectives : To describe the clinicopathologic features of SAM. To emphasize the histologic characteristics that are helpful in the recognition of the condition by routinely available methods. To stress the differential diagnosis with NEC. To evaluate the presence, abundance and location of the interstitial cells of Cajal (ICC).
Methods : We reviewed surgical files and histologic material from 60 infants indexed as “intestinal obstruction” or “intestinal perforation” between 1991 and 2002.
Results : Twenty-six patients had NEC, 25 had SAM and 9 had various other forms of bowel myopathy. Patients with SAM had a lower gestational age and birth weight and presented with abdominal distension with few systemic symptoms. Patients with NEC were seriously ill at presentation and radiography showed pneumatosis intestinalis or portal venous air. At histologic examination, cases of NEC were characterized by necrotizing inflammation of the bowel with or without pneumatosis intestinalis. In contrast, the bowel of patients with SAM was not necrotic and showed little inflammation. It had always a defect of the internal layer of the muscularis propia while the plexus of Auerbach and the ICC were normally developed.
Conclusions : Segmental absence of intestinal musculature and necrotizing enterocolitis differ in their clinical and histopathologic characteristics. Segmental absence of intestinal musculature is an important cause of neonatal intestinal obstruction and perforation.

- P09 -

FOLLICULAR DENDRITIC CELL SARCOMA OF THE STOMACH : CASE REPORT AND REVIEW OF THE LITERATURE. P. Demetter, A. Geerts (1), E. Lagae (2), K. Dhaene, M. Peeters (1), A. Waeytens, L. Defreyne (3), M. De Vos (1), P. Pattyn (2), C.A. Cuvelier. Departments of Pathology, (1) Gastroenterology, (2) Surgery and (3) Radiology, Ghent University Hospital, 9000 Gent, Belgium.

Follicular dendritic cell (FDC) sarcoma was first described in 1986 on the basis of a series of four cases, all of which occurred in lymph nodes. Recently, there has been a surge of interest in this tumour because of the ability to confirm FDC lineage by more sensitive markers. Today, approximately 65 cases of FDC sarcoma have been reported, mainly affecting the lymph nodes. However, in about one third of cases extranodal sites are involved, mostly intra-abdominal organs, oral cavity and tonsils. The gastrointestinal tract location is rare, and only three cases are described : one case involving the small intestine, one the colon and one presenting as a submucosal tumour of the stomach. As a result FDC sarcoma is an entity rarely listed in the differential diagnosis of spindle cell neoplasms of the gastrointestinal tract. The only identified predisposing factor is hyaline-vascular Castleman's disease, found in a minority of cases. Epstein-Barr virus has been demonstrated in a few FDC sarcomas, but does not appear to play a significant role. We report a case of a 40-year-old woman presenting with severe asthenia, nausea, back pain and loss of weight. Upper gastrointestinal tract endoscopy revealed a proliferating tumour in the stomach, of which biopsies were taken. A CT-scan of the abdomen showed a lobulated multinodular mass situated between the left liver lobe and the stomach, with compression of stomach and pancreas. A solitary nodule in the lobus quadratus of the left liver lobe was noted. Light microscopical examination showed a poorly differentiated tumour. A tentative diagnosis of gastrointestinal stromal tumour (GIST) was made. The tumour was resected en bloc. Histopathological examination of the resection specimen showed tumour cells with indistinct cytoplasmic outlines and ovoid vesicular nuclei with one or more eosinophylic nucleoli. These cells were positive for CD21, CD35, KI-M4p and vimentin, but negative for CD31, CD34, F VIII, CEA, CKs, EMA, SMA, MSA, myoglobin, desmin, c-kit, S-100, CD68, CD1a, myeloperoxidase, LCA and HMB-45. In situ hybridisation could not detect Epstein-Barr viral DNA. Based on histological and immunohistochemical findings, the diagnosis of FDC sarcoma was made – the second known case of FDC sarcoma presenting in the stomach.

- P10 -

UPREGULATED EXPRESSION OF VEGF AND CA IX CORRELATE WITH THE VASCULAR METASTASIS PATTERN OF INTESTINAL TYPE CARCINOMA. A. Driessen°, W. Landuyt, L. Goethals, S. Pastorekova*, V. Winnepenninckx, K. Haustermans, P. Nafteux, E. Van Cutsem, T. Lerut, L. Filez, F. Penninckx, N. Ectors. °University Hospital Maastricht, The Netherlands ; *Slovak Academy of Sciences, Bratislava, Slovak Republic ; °University Hospitals Leuven, Belgium.

Hypoxia is a major drive in tumour progression. Growth factors involved in angiogenesis, such as Vascular Endothelial Growth factor (VEGF) are upregulated. Carbonic anhydrase IX (CaIX), a marker for chronic hypoxia, has multiple functions in oncogenesis as it is involved in cell-to-cell communication, pH-regulation of the microenvironment and cell proliferation in tumours. The aim was to evaluate 1) the expression of VEGF and CaIX in carcinomas situated at the distal esophagus (n = 60, X = 65 yr, M/F = 5.89), the cardia (n = 52, X = 63 yr, M/F = 4.2), and the distal stomach (n = 48, X = 73 yr, M/F = 1.67), 2) the relationship to the microvessel density (MVD) and necrosis. The adenocarcinomas were subtyped in intestinal (52%) and diffuse type (38%) (Lauren-classification). Immunohistochemistry was performed on formol-fixed paraffin-embedded material : CaIX (clone M75, 1/20), VEGF (SantaCruz, 1/100), CD31 (Dako, 1/50). CaIX-positivity : membranous positivity in ≥ 30% of tumour cells, VEGF-positivity : semiquantitative analysis based on extent (< 25% : 1 ; 25-50% : 2 ; 50-75% : 3 ; > 75% : 4) and intensity (1-3). The MVD (vessels/mm?) was determined according to Gundersen (CD31). Necrosis, defined as continuous areas of cell necrosis, were assessed as present and absent. Statistical analysis : Chi?-test, t-test, Spearman's correlation. The overall expression of CaIX and VEGF was 67% and 47% respectively. CaIX-expression showed a positive correlation with VEGF (52%, r = 0.1642, p = 0.04). 22% of tumours were negative for both markers. VEGF- and CaIX-expression were independent of the tumour localization. However VEGF (95% vs. 29%, $p = 10^{-6}$) and CaIX-positivity (56% vs. 33%, p = 0.005) were both significantly higher in intestinal than in diffuse type carcinomas. Whereas the VEGF-expression was associated with a higher MVD ($p = 10^{-6}$), the CaIX-expression was related to tumour necrosis (p = 0.004). In conclusion, our study shows that angiogenic (VEGF) and hypoxia-related oncogenic mechanisms (CaIX) are involved to a variable extent, especially in intestinal type of adenocarcinomas.

- P11 -

ROLE OF THE PATHOLOGIST IN COLORECTAL CANCER : RELATION WITH MOLECULAR BIOLOGY. Jean-François Fléjou. Service d'Anatomie Pathologique, Hôpital Saint-Antoine, AP-HP, Paris, France.

The molecular alterations involved in colorectal carcinogenesis are well described, with two pathways, LOH for Loss of Heterozygosity (80% of cases), and MSI for MicroSatellite Instability (15% of cases). These two mechanisms are involved both in sporadic cancers and in hereditary cancers (familial adenomatous polyposis for familial LOH tumours and HNPCC syndrome for MSI tumours). This genetic classification of cancers will probably become more and more important, in terms of treatment (surgery +/- chemotherapy), of prognostic evaluation, and also to detect familial forms of tumours. Although the gold standard to classify the genetic pattern of colorectal cancer remains molecular biology, the pathologist is now involved in this "molecular" classification, especially to detect MSI+ tumours. These tumours have a peculiar morphological aspect (poorly differentiated or mucinous pattern in numerous cases, with numerous intraepithelial lymphocytes), resulting in typical cases in a "medullary" pattern of differentiation. However, this histological pattern is not sensitive enough to detect all tumours belonging to this group. Immunohistochemistry is a sensitive and specific method to detect MSI+ tumours, as in almost all cases these cancers loss the expression of MMR (Mismatch Repair) proteins, either hMLH1 or hMSH2. Moreover, the loss of hMSH2 is only observed in HNPCC tumours with a germinal mutation of the corresponding gene, but loss of hMLH1 can be observed both in HNPCC cancers (germinal mutation of the *hMLH1* gene) and in sporadic MSI+ cancers (hypermethylation of the promoter of the *hMLH1* gene). It is potentially useful to determine the immunohistochemical MSI pattern of colorectal cancer in terms of therapeutic and prognostic evaluation of the patients, and this technique can also be used to help to find the mutation on the corresponding gene in case of HNPCC syndrome. However, the main role of Pathology in colorectal cancer at the present time remains to make the diagnosis of cancer on biopsies, and to establish the stage of the disease on the surgical specimen. This result will determine the indication of an adjuvant chemotherapy. Therefore, it is mandatory to examine and report the surgical specimen with validated guidelines, and especially to obtain a sufficient number of lymph nodes to stage the cancer.

- P12 -

PERCUTANEOUS, TRANSHEPATIC BILE TRACT CYTOLOGY. M. Praet*, L. Defreyne**, P. Vanlangen-Hove**, A. Janssens***, H. Van Vlierberghe****, B. De Hemptinne****. *Dpts of Pathology, **Radiology, ***Hematology, ****Gastroenterology, University Hospital Gent, De Pintelaan 185, 9000 Gent.

Percutaneous transhepatic bile duct intervention has undergone many refinements during the last years. The technique allows the possibility to get cytology and biopsies from difficult areas in the intrahepatic and extrahepatic tree and from the pancreatic ducts.This technique is regularly performed in patients suffering from severe cholestasis due to stenotic lesions of the biliary tract. Selective cytological approach of the stenotic segments happens by selective brushing of the wall. The cytological diagnosis will eventually determine the ultimate therapeutic strategy.

Patients and methods : we analysed the cytological results of selective bile duct brushing obtained by an 8 French Cytomas II, Cook catheter in 14 patients.

Results : no adequate cytological (3 pat) was made due to poor cellularity and blood contamination, these patients suffered from advanced metastatic disease. In 2 patients with metastases, normal bile duct cytology consisting of long slender cylindrical cells with regularly shaped nuclei was seen in 1 patient and the other patient demonstrated a combination of normal billary cells and carcinomatous cells. Inflammation was diagnosed in one patient with in a background of debris and bile, pycnotic nuclei, inflammatory cells and foamy, lipid-laden macrophages. Some groups of normal mucosal epithelial cells with long slender cytoplasm were also found. The surgical resection contained a bile duct cystocoele surrounded by a chronic aspecific inflammation. Selective bile duct brushing in primary stenosing neoplastic processes revealed a heterogeneous spectrum of cell clusters with three-dimensional arrangement and crowding of the nuclei. Some cases contained isolated atypical cells with a poor amount of cytoplasm and irregularly shaped hyperchromatic nuclei. The nucleolus was often prominent. In one neoplastic process the cylindrical cells appeared pseudostratified with some irregularities of the nuclei. Mucin accumulation was occasionally seen. Comparing the tissue blocs with the cytology of the cytospins revealed a higher cellular yield with more defined cytological criteria in the tissue blocks.

Conclusion : bile tract cytology remains a difficult task for cytopathologists because of the degeneration action of bile on the cellular compound. We studied 14 selective cytology brushings of stenotic bile duct processes with inclusion of tissue blocks for the final diagnosis. In metastatic disease this technique was often disappointing. In inflammatory conditions and primary bile duct neoplasms sufficient cellular material was obtained.

- P13 -

DIEULAFOY'S LESION. A BRUSH UP FOR THE PATHOLOGIST. APROPOS OF THREE CASES. R. Croes, N. Ectors, K. Geboes. Pathologishe Ontleedkunde, UZLeuven, 3000 Leuven, Belgium.

Introduction : Massive gastrointestinal (GI) haemorrhage is a major and uncommon clinical problem that can be caused by several conditions such as bleeding ulcers and varices. Usually the pathologist is not involved in the diagnosis and treatment because of the emergency nature of the condition. However, the pathologist needs to know the different entities because of medicolegal reasons and when the etiologic diagnosis has not been made earlier. The aim of this report is to brush up the awareness of the pathologist of one particular and uncommon cause of massive GI haemorrhage known as Dieulafoy's ulcer or *exulceratio simplex*.
Materials and methods : Surgery was performed in three male patients (mean age of 52,6 y) who presented with massive GI haemorrhage persisting after unsuccessful endoscopic hemostasis. A total colectomy was performed in a patient of 26 years because of a fulminant course of ulcerative colitis with fresh blood in the stool. After sampling one gastrectomy, one right hemicolectomy and one total colectomy specimen routine histology was done.
Results : Microscopic examination revealed in each specimen an unusually large and tortuous submucosal muscular artery with a small mucosal erosion over the point of rupture. Except for thrombosis of the anomalous calibre artery additional abnormalities were not encountered. No inflammation, no wall malformation in particular. In the patient with severe active ulcerative colitis (UC) a bleeding Dieulafoy's lesion on the iliocaecal valve was encountered. The valve was not involved in the inflammation of UC.
Conclusion : Although diagnosis and treatment of bleeding Dieulafoy's lesion is usually achieved endoscopically, the pathologist has to be aware of this seldom cause of severe GI haemorrhage since endoscopic approach can be difficult and surgery a therapeutic issue. Awareness is the key to an accurate diagnosis. Dieulafoy's lesions occur most commonly in the proximal stomach but the pathology is essentially the same throughout the GI tract. The etiology and pathogenesis are still unclear. A combination of predisposing factors as decreased perfusion of the overlying mucosa with an eliciting minor mucosal injury that finally unmasks the silent *caliber-persistent artery* is supposed. Local anatomic factors, such as the normal blood supply, are supposed to predispose some parts of the GI tract to develop Dieulafoy's lesion, e.a. the proximal lesser curve of the stomach. Association with UC has never been reported before which makes this report unique.

- P14 -

SEVERE AND RARE COMPLICATIONS OF RECREATIONAL DRUG USE : ABOUT TWO CASES. N. Nagy, A. Mathieu, N. Bourgeois, M. Adler, M. Gelin, N. Nagy. Dpt of Pathology and Gastroenterology, Erasme University Hospital, Free University of Brussels, Brussels.

The first one is a case of thromboangeiitis obliterans involving visceral vessels associated with cannabis use. We report the case of a 23 year old male smoker and daily cannabis user. He presented brutal abdominal pain with vomiting. The arteriography revealed occlusion of the inferior mesenteric artery treated by low weight molecular heparin. Two months later same symptoms recurred. Colonoscopy revealed stenosis of the sigmoid and CT-scan demonstrates aspecific colitis. The treatment consisted in segmental colectomy. The microscopic examination showed an ischemic mucosa with segmental Buerger's like lesions i.e. organized and recanalized thrombus of middle arteries and vasculitis lesions of small arteries ans veins. The second case illustrates adverse effects of 3,4-methylenedioxymethamphetamine (Ectasy) in a 25 year old male who had developed hepatic failure after using Ectasy two months before. Hepatic biopsy showed toxic acute hepatitis. One month later he developed encephalopathy with reduced hepatic coagulation factors and icterus. Orthotopic liver transplantation was carried out. Histopathological examination of the hepatectomy specimen revealed massive necrosis with regenerative hepatic nodules.

- R01 -

BILE DUCT CYSTS : VALUE OF MRI IN DIAGNOSTICS AND COMPLICATIONS. M. van Weerelt (1), B. Op de Beeck (1,2), K. Vanderdood (1), L. Tappeniers (1), M. Osteaux (1). (1) Dpt of Radiology, University Hospital Brussels VUB, Laarbeeklaan 101, 1090 Brussel, Belgium ; (2) Dpt of Radiology, University Hospital Antwerp UZA, Wilrijkstraat 10, B-2650 Edegem, Belgium.

Purpose : iconography of MR-findings in bile duct cysts and their complications.
Materials & methods : A total of 8 patients with bile duct cysts underwent MRI. The examinations were performed between 1996 and 2002. All cases are surgically proven. MRI was done on a 1.5-T unit (Magnetom Vision, Siemens, Erlangen ; Germany) with phased array coil. The study included axial GRE T1-weighted and HASTE T2-weighted sequences. Additional breath-hold thick-slab RARE (30mm slice thickness) and multislice HASTE sequences (4 and 6mm slice thickness) were performed in the coronal and the paracoronal plane.
Discussion : Although bile duct cysts are still rare conditions, their possible complications necessitate detection in a early state. A meticulous description of the anomaly is mandatory when surgical intervention is considered. The bile duct cysts are subdivided in five types according to the Todani modification of the Alonso-Lej classification. Complications of bile duct cysts include stone formation, pancreatitis, biliary cirrhosis, cyst rupture, liver abscess and cholangiocarcinoma. The relevant diagnostic clues on MRI are discussed and compared with our own experience in our patients.
Conclusion : Although bile duct cysts are rare, it is important to detect them in a early stage. MRI offers the opportunity to visualize the biliary system and is the screening method of choice. The knowledge of this anomaly is mandatory to prevent inadvertent injury during surgical or interventional procedures.
Learning objectives : To recognize the range of imaging characteristics of bile duct cysts and their complications.

- R02 -

ASSESSMENT OF THE HEPATIC FLOW WITH MR IMAGING AND DOPPLER SONOGRAPHY IN PATIENTS WITH CHRONIC LIVER DISEASE. L. Annet, R. Materne, E. Danse, J. Jamart, Y. Horsmans, B.E. Van Beers. Dpt of Radiology, St-Luc University Hospital, 1200 Brussels, Belgium.

Purpose : To compare the results of MR imaging and Doppler sonography in the assessment of parameters of the hepatic flow in patients with chronic liver disease.
Method and materials : Forty-six consecutive patients referred for measurements of portal pressure (3 patients with normal liver, 12 with non-cirrhotic chronic liver disease, 31 with cirrhosis (Child A : 10, Child B : 13, and Child C : 8)) were included in the study. Dynamic contrast-enhanced MR images of the liver were obtained to generate signal-intensity versus time curves. These curves were converted to relative concentration versus time curves. The curves were fitted to a dual-input, one-compartmental model to calculate the total liver inflow, portal fraction, distribution volume, and mean transit time. Measurements of portal velocity, portal flow, congestion index, resistance index of the hepatic artery, and modified hepatic index (portal flow velocity/resistance index of right hepatic artery) were obtained with Doppler sonography.
Results : With MR imaging, all flow parameters, except the distribution volume, were significantly different between patients with and without cirrhosis. There was a significant correlation between all flow parameters measured with MR imaging and the portal pressure. The arterial fraction and mean transit time were correlated to the Child score. The flow parameters measured with Doppler sonography did not differ significantly between patients with and without cirrhosis. Only the hepatic arterial resistance and the portal flow were correlated to the portal pressure. No Doppler parameter was significantly correlated to the Child score.
Conclusions : The hemodynamic changes associated with chronic liver disease are better assessed with MR imaging than with Doppler sonography.

- R03 -

COMPUTED TOMOGRAPHIC AND MAGNETIC RESONANCE IMAGING FEATURES OF BUDD-CHIARI SYNDROME. B. Op de Beeck (1), R. Salgado (1), E. Ooms (1), A. Sermeus (3), D. Ysebaert (2), A. De Schepper (1). (1) Depts. of Radiology and (2) Surgery, University Hospital Antwerp UZA, Wilrijkstraat 10, B-2650 Edegem ; (3) Dept. of Gastroenterology, University Hospital Brussels VUB, Laarbeeklaan 101, 1090 Brussel, Belgium.

Purpose : To analyse the computed tomographic and magnetic resonance imaging features of Budd-Chiari syndrome.
Materials & methods : Imaging findings of 15 patients with hepatic vein thrombosis or Budd-Chiari syndrome were retrospectively reviewed. Special focus on pathophysiologic manifestations and spiral multiphasic CT and MRI findings were performed.
Results : The radiographic “gold standard” for hepatic vein thrombosis has been hepatic venography and cavography. These procedures are not suitable for screening patients with non-specific signs and symptoms. Color Doppler imaging combined with pulsed Doppler should be used in the first line. CT and MRI features of Budd-Chiari syndrome depend on the age and extend of the obstruction and the presence of coexisting changes in portal venous blood flow. In patients with chronic Budd-Chiari syndrome, benign regenerative nodules are often detected on CT or MR imaging. In the acute phase of the disease, liver enlargement and ascites are noticed. Intravascular thrombus is best seen in the acute phase. Comma-shaped intrahepatic collateral vessels and marked constriction of the inferior vena cava are also often detected as well as enlargement of the caudate lobe. After I.V.-contrast injection, decreased enhancement during arterial and portal-parenchymal contrast phase is seen. Increased enhancement is noticed on delayed imaging.
Conclusion : Multislice spiral CT and MRI are excellent imaging techniques for the diagnosis of Budd-Chiari syndrome, especially for the subclinical forms.

- R04 -

SPONTANEOUS DISSECTION OF THE SUPERIOR MESENTERIC ARTERY : AN UNUSUAL CAUSE OF ACUTE ABDOMINAL PAIN. E. Danse, E. Ketelslegers, B. E. Van Beers, F. Vershuren, F. Thys , P. Goffette , F. Hammer, M. Mukolo-Ndjolo, E. Coche. Departments of Radiology, Emergency Medicine and Critical Care. St-Luc University Hospital, Université Catholique de Louvain, B-1200 Bruxelles.

Objectives : to describe the clinical and computed tomographic (CT) signs in patients with spontaneous dissection of the superior mesenteric artery.
Material : Review of the clinical and radiological data of four patients admitted in the emergency room of our hospital for acute abdominal pain, during a 18-month period, and for whom the final diagnosis was spontaneous dissection of the superior mesenteric artery. In the four cases, a multidetector spiral CT examination of the abdomen was performed, to find the cause of the severe abdominal pain without abnormalities of blood tests and plain films series.
Results : In the four cases the CT examination was considered to be normal at the initial analysis performed by the attending radiologist. A second interpretation performed by a senior radiologist permitted to detect a limited dissection of the main trunk of the superior mesenteric artery, related to a localized thrombosis of jejunal branches in one case. In the four cases, clinical follow-up was obtained. Fibrinolytic therapy was performed in two cases, combined with endovascular treatment in one patient.
Conclusion : Spontaneous dissection of the superior mesenteric artery should be included in the differential diagnosis of unexplained acute abdominal pain.

- R05 -

COMPUTED TOMOGRAPHIC COLONOGRAPHY : A FOUR YEARS EXPERIENCE. S. Gryspeerdt (1), Ph. Lefere (1), M. Baekelandt (1), B. Van Holsbeeck (1), J. Dewyspelaere (1), R. Deman (2), L. Rutgeerts (2). (1) Departments of Radiology and Gastroenterology, Stedelijk Ziekenhuis ; (2) H. Hart Ziekenhuis, 8800 Roeselare, Belgium.

Purpose : To retrospectively evaluate a four years experience with computed tomographic colonography (CTC). Materials and Methods In a four years period, we performed 506 CTC's. In 118 patients, CTC was performed after incomplete conventional colonoscopy (cC). This group is not included in this retrospective analysis. In 120 patients, CTC was performed in the setting of a study comparing CTC and cC. This group is reported as study group (stG). Based on the experience from this stG, the CTC technique was optimised. In 268 patients, using the optimised CTC technique, CTC triggered 72 cC. This group of 72 patients is referred to as the screening group (scrG). In the stG, 20 patients had standard colonoscopic preparation (ScCl) , 50 patients had a reduced preparation (RcCl) , and 50 patients were prepared with dietary fecal tagging (FT). In the scrG the colon cleansing technique was FT for all patients. In 12 patients in the scrG, CO2 instead of room air was used. In both groups of patients, sensitivity and specificity were calculated for polyp detection using cC as the gold standard. In the stG we also evaluated patient acceptance.
Results : Results of the stG showed that : A/ ScCl results in a clean colon, but produces fluid levels which hamper a complete CTC, resulting in false negative diagnosis (3 of 20 patients). Sensitivity and specificity were respectively 77% and 57%. B/ RcCl reduces the problem of fluid levels, but is then faced with the problem of fecal residues, resulting in false positive diagnosis (7 of 50 patients). Sensitivity and specificity were respectively 85% and 77%. C/ FT offers the possibility to obtain a dry colon, with tagged fecal residues, reducing false negative (2 of 50 patients) as well as false positive diagnosis (4 of 50 patients). Sensitivity and specificity were 88%. Optimisation of the diet and replacement of PEG by magnesium citrate in FT reduces the preparation related discomfort and improves final opinion (FT significantly better than RcCl : $p = 0.03$). Results of the scrG showed that : A/ cC confirmed all polyps, and additionally showed 9 polyps smaller than 1 cm in 7 patients ; B/ using optimised CTC technique, a total of 8 false positive diagosis were found in 6 patients ; with 5 being caused by diverticular disease ; C/ CO2 reduces dyscomfort during CTC.
Conclusion : Optimised CTC technique encompasses FT as preparation technique, and use of CO2 to inflate the colon. CTC results in acceptable sensitivy and specificity for detecting the clinically significant polyps. Diverticular disease remains a challenge to CTC.

- R06 -

INTESTINAL INVOLVEMENT IN ACUTE PANCREATITIS : CT FINDINGS. E. Pelzers (1), A.I. De Backer (l), B. De Keulenaer (2), L. Henkaerts (2), K.J. Mortele (3), P.R. Ros (3). (1) Department of Radiology and (2) Internal Medicine (2), Algemeen Centrumziekenhuis Antwerpen, Campus Stuivenberg, Lange Beeldekensstraat 267, B-2060 Antwerpen, Belgium ; (3) Department of Radiology, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, USA.

Purpose : To review the spectrum of CT findings in acute pancreatitis complicated by intestinal involvement.
Materials and methods : In a retrospective study over a seven-year period (between 1995 and 2001) we reviewed the files of 19 patients with diagnosis of acute pancreatitis complicated by intestinal involvement.
Results : The second and third part of the duodenum was involved in 4 patients. Inflammatory thickening of the wall with subsequent stenosis and gastric dilatation was noted in two patients. A duodenopancreatic fistula was present in two. Small bowel abnormalities were seen in 3 patients. In one patient ascites and paralysis was associated with diffuse thickening of the small bowel wall with increased contrast enhancement. In another patient prolonged hypotension resulted in shock bowel. A third patient developed an inflammatory mass extending into the mesenterium and bowel wall and resulted in small bowel stenosis with obstruction. Colonic involvement was noted in 12 patients. The left colon was involved in 10 patients, the right colon in one. In one patient diffuse colonic involvement was noted. Infected pancreatic necrosis resulted in pancreatocolonic fistula in one patient. Ischaemic colitis and colonic necrosis with perforation was seen in one patient respectively. Retroperitoneal and (peri)colic inflammation resulted in colonic stenosis in nine patients. In four of them pancreatic abscess with compression on the colon was noted.
Conclusion : Intestinal involvement is an uncommon but potentially lethal complication of acute pancreatitis. CT scan may accurately demonstrate intra- and peripancreatic inflammation and also extension through the intestinal tract. Our experience illustrates the diverse types of intestinal involvement that may occur. Colonic involvement was the predominant presentation.

- R07 -

PANCREATIC PERFUSION MEASUREMENTS USING A 3D GRADIENT-ECHO MRI-SEQUENCE WITH BOLUS-INJECTION OF GD-DTPA : COMPARISON OF PERFUSION PARAMETERS IN NORMAL VOLUNTEERS AND PATIENTS WITH CHRONIC PANCREATITIS. K. Coenegrachts(1), W. Van Steenbergen(2), D. Vanbeckevoort(1), D. Bielen(1), C. Feng(1), G. Marchal(1), H. Bosmans(1). Dpt of Radiology(1) and Hepatology(2), Catholic Universities of Leuven, 3000 Leuven, Belgium.

Introduction and objectives : In the early stage of chronic pancreatitis (CP), morphologic changes may be absent or discrete making the diagnosis difficult. In this study, we have explored a new approach using perfusion-weighted MRI. The purpose of this study was to compare perfusion-related data in volunteers (V) and in patients with proven CP.
Material and Methods : Thirty-one V (mean age 38 yrs) and 19 pts with moderate to severe CP (mean age 45 yrs) were imaged. Perfusion studies were performed with 1ml of Gd-DTPA/5kg b.wt. Signal enhancement curves at the level of the pancreatic head, body and tail were obtained. The following perfusion parameters (PP) were calculated : maximal enhancement (Enh_{max}) (defined in arbitrary units, a.u.), maximal relative enhancement ($RelEnh_{max}$), time of arrival of contrast inflow (T_0), time-to-peak (T-peak), wash-in (W_{in}) and wash-out (W_{out}) rates, and brevity-of-enhancement (time between point of wash-in and wash-out rate) (BrevEnh).
Results : PP for the pancreatic head are shown in the table.
Discussion : MRI-PP most representative for CP were T-peak, W_{in}, and BrevEnh. This is compatible with the hypothesis of an increased resistance to the normal parenchymal perfusion due to tissue ischemia. A limitation is that all patients had moderate to severe CP. The significant difference of PP in CP vs. normal volunteers is not yet proven in patients with mild forms of CP. Additional studies in patients with upper abdominal pain suggestive of CP are being performed.

	p-values	**Volunteers** *Mean ± S.D.*	**CP patients** *Mean ± S.D.*
$RelEnh_{max}$ (%)	0,23	124,8 ± 47,7	140,6 ± 39,5
T-peak (sec)	1,35E-12	15,4 ± 6,1	46,6 ± 16,6
W_{in} (a.u./sec)	7,09E-05	99,6 ± 39,5	58,8 ± 13,3
W_{out} (a.u./sec)	0,50	48,4 ± 25,5	42,3 ± 34,4
BrevEnh (sec)	2,59E-10	21,5 ± 12,3	53,3 ± 15,8

- R08 -

ROLE OF PERITONEOGRAPHY IN THE EVALUATION OF CHRONIC GROIN PAIN : A RETROSPECTIVE STUDY OF 112 PATIENTS. R. Salgado (1,2), M. Maes (1,2), P. Bellinck (1), J-L Termote (1), B. Op de Beeck (2), A. De Schepper (2). (1) Dpt of Radiology, Heilig Hart Ziekenhuis, 2500 Lier, Belgium ; (2) Dpt of Radiology, University Hospital Antwerpen, 2650 Edegem, Belgium.

Purpose : To assess the usefulness of peritoneography in the evaluation of patients with chronic undeterminate groin pain.
Materials & methods : 112 consecutive patients with groin pain who underwent a peritoneography examination during the period 1998-2002 were retrospectively reviewed. The procedure was performed with intraperitoneal injection of 90 cc water-soluble contrast. Subsequently PA and oblique conventional radiographs were obtained with the patient in the upright and semi-upright (upward examination table tilting of 20-30 degrees) position during valsalva manoeuvre. These results were compared, when available, with the surgical findings. The outcome of CT and ultrasound examination, when performed, is also reviewed.
Results : Peritoneography showed an occult hernia in 40/106 (38%) patients with a negative or inconclusive clinical examination. 24/40 (60%) of these patients underwent laparoscopic exploration, which confirmed the hernia on all occasions (100% positive predictive value). In 9 patients peritoneography also revealed an asymptomatic hernia on the contralateral side. Of the 58/106 (54%) patients who showed no abnormality on peritoneography, 41/58 (70%) improved clinically without surgical intervention. Eventually, no specific diagnosis could be found in 45/106 cases (42%). Three patients had a positive clinical examination for an inguinal hernia, which was on all cases confirmed during peritoneography. Alternative diagnoses in other patients include osteitis pubis, lipoma and adductor tendinitis. Intraperitoneal injection could not be accomplished in two patients due to obesity and procedural errors. One patient had injection of contrast in the colon, which required no significant intervention. An abdominal CT examination was performed in 22/112 (19,6%) patients, revealing an inguinal hernia on only one occasion. Thirty patients (26,7%) also underwent an ultrasound examination, clearly demonstrating an inguinal hernia in three patients.
Conclusion : peritoneography is a safe and reliable technique in ruling out or demonstrating an occult hernia in patients with chronic unexplained groin pain.

- R09 -

ABDOMINAL TUBERCULOUS LYMPHADENOPATHY DEMONSTRATED BY CT AND MRI. A.I. De Backer (1), L. Rappoort(1), P. Bomans(1), B. De Keulenaer (1), L. Henckaerts (1), D. Deeren (1), K.J. Mortelé (2), P.R. Ros (2). (1) Algemeen Centrumziekenhuis Antwerpen, Antwerp ; (2) Brigham and Women's Hospital, Boston.

Purpose : To assess the value of CT and MRI in abdominal tuberculous lymphadenopathy.
Materials and methods : CT and MRI studies of 10 patients with histologically proven abdominal tuberculous lymphadenopathy were reviewed with regard to anatomic distribrution, size, MRI signal intensities, pattern of contrast enhancement, the relation to adjacent structures, and the presence of extranodal manifestations of tuberculosis.
Results : CT and MRI of the abdomen were performed in nine and seven patients, respectively. The most common sites of involvement were the lesser omentum (n = 6), anterior pararenal space (n = 6), and upper paraaortic regions (n = 6), followed by mesenteric (n = 5), and lower paraaortic regions (n = 5), root of the superior mesenteric artery (n = 4), and greater omentum (n = 1). Lymph node size varied from 3 mm to 3 cm. On MRI, T1 hypointensity in relation to abdominal wall muscle was seen in two patients. In one of them a hyperintense rim was noted. T1 isointensity was noted in six patients and lymph nodes heterogeneity in one. Hypointensity (n = 1), isointensity (n = 1), and hyperintensity (n = 6) were noted on T2-weighted images. In all of them, peripheral enhancement was noted. A conglomerate group of nodes showing peripheral and central areas of enhancement was present in two. A homogeneous enhancement pattern was seen in three. On CT, peripheral enhancement was noted in five. A conglomerate group of nodes showing peripheral and central areas of rim enhancement was seen in four. Homogeneous enhancement was noted in seven. In four patients with periportal lymphadenopathy, the enlarged nodes encased major vessels and main bile duct without definite evidence of obstruction or invasion. Concomitant pulmonary tuberculosis was noted in six patients. Spondylitis and cervical lymphadenopathy was present in one patient. In all patients extranodal abdominal manifestations of tuberculosis were noted.
Conclusion : Abdominal tuberculous lymphadenopathy showed a variety of patterns of contrast enhancement on CT, even within the same nodal group. On MRI, lymphadenopathy with a peripheral enhancement pattern was noted in all patients. This enhancement pattern may suggest the diagnosis of tuberculosis in the appropriate clinical setting.

- R10 -

IMAGING OF GASTROINTESTINAL AND ABDOMINAL TUBERCULOSIS. F.M. Vanhoenacker (1,2), A. I De Backer (3), B. Op de Beeck (1), D. Vanbeckevoort (4), A.M. De Schepper (1). (1) Department of Radiology, University Hospital Antwerp, Wilrijkstraat 10, B-2650 Edegem, Belgium ; (2) AZ Sint-Maarten, Rooienberg 25, B-2570 Duffel, Belgium ; (3) Algemeen Centrum Ziekenhuis Antwerpen, Lange Beeldekensstraat 267, B-2060 Antwerpen ; (4) Universitair Ziekenhuis Gasthuisberg, Herestraat 49, B-3000 Leuven.

Purpose : to discuss the range of manifestations of tuberculosis (TB) of the abdomen, including involvement of the gastrointestinal tract, the peritoneum, mesentery, omentum, abdominal lymph nodes, solid abdominal organs, the genital system and the abdominal aorta.
Discussion : abdominal TB is a diagnostic challenge, particularly when pulmonary TB is absent. It may mimic many other abdominal diseases, both clinically and radiologically. An early correct diagnosis, however, is important in order to ensure proper treatment and a favourable outcome. Modern imaging is a cornerstone in the early diagnosis of abdominal TB and may prevent unnecessary morbidity and mortality. Generally, Computed Tomography (CT) appears to be the imaging modality of choice in the detection and assessment of abdominal tuberculosis, other than gastrointestinal TB. Barium studies remain superior for demonstrating mucosal intestinal lesions. Ultrasound (US) may be used for follow-up to monitor therapy response. The role of MRI has to be further defined. Ileocaecal involvement, free or loculated high density ascites with thin-mobile septa, omental thickening, a thickened and enhancing peritoneum, a misty mesentery and low density adenopathies, focal hepatosplenic lesions are suggestive imaging findings demonstrated by either gastrointestinal series, US, CT and MRI.
Conclusion : the diagnosis of abdominal TB should be considered if suggestive imaging findings are found in patients with a high index of suspicion.
Learning objectives :
1.To recognise the range of imaging characteristics of abdominal TB.
2.To define the strength of each imaging modality in detecting (specific) changes encountered in abdominal tuberculosis.

IS THERE A ROLE FOR CHEMOTHERAPY IN THE ADJUVANT TREATMENT OF RECTAL CANCER? E. Van Cutsem. University Hospital Gasthuisberg, Leuven, Belgium.

Radiation and chemotherapy, when used alone in addition to surgery, have failed to prolong survival in most studies. Combined modality treatment seems attractive in order to reduce the rates of recurrence both at the primary tumour site and outside the pelvis and hence to improve the survival. It has been shown that a combined postoperative chemoradiotherapy is superior to postoperative radiotherapy alone and that a protracted infusion of 5-FU is superior to bolus injections of 5-FU/FA when combined with postoperative radiotherapy. In Europe, almost all experts favour the use of preoperative radiotherapy. It has been shown that preoperative irradiation decreases the risk of recurrence, even if an optimal type of surgery (TME) is performed. This study as well as the Swedish studies, used the 'short' irradiation regimen (5 x 5 Gy). Others favour the 'long' regimen of irradiation (45-50 Gy ; 1.8 Gy/Fraction). This 'long' regimen has the advantage of downsizing the tumour and facilitating the resection and offering a greater chance to the patient of performing sphincter saving surgery compared to the 'short' regimen. Therefore the challenge is to demonstrate that the addition of chemotherapy further improves the results by increasing the rate of downsizing and thus offering a greater chance of complete resection and of sphincter saving surgery in low rectal cancers. The approach of combined preoperative chemoradiotherapy might also offer the hope of improving the survival by further decreasing the local recurrence rate and decreasing the rate of metastases. Several studies are still ongoing to prove this concept : the EORTC is randomizing patients between preoperative radiotherapy (45 Gy) +/- chemotherapy (5-FU/LV). In this study patients are also randomized postoperatively between adjuvant chemotherapy and no chemotherapy. A German study is randomizing patients with resectable rectal cancer between pre- and postoperative chemoradiotherapy. Several phase 1 and 2 studies have shown the feasibility and the promising activity of combination studies of the new drugs (irinotecan, oxaliplatin, capecitabine, UFT, raltitrexed) with radiotherapy in rectal cancer. Several phase 1 and 2 studies have shown the feasibility and the promising activity of combination studies of new drugs (irinotecan, oxaliplatin, raltitrexed, capecitabine, UFT) with radiotherapy in rectal cancer.

WHAT 'S NEW IN RECTAL CANCER IMAGING ? R.G.H. Beets-Tan. Department of Radiology, University Hospital Maastricht, The Netherlands.

Paramount for a differentiated treatment of rectal cancer is a reliable preoperative test that can distinguish between the different risk groups for local recurrences. There have been numerous reports on imaging with Ultrasound, CT or MRI, but most studies only focused on T and N stage determination, rather than the more relevant circumferential resection margin (CRM). Radiologists were not used to evaluate the mesorectal fascia as an anatomic border because it had not been visualized on planar imaging techniques until only very recently [1]. There is recent evidence suggesting that MRI can accurately predict the CRM at TME. The largest of these studies was published in the Lancet early 2001[1]. High resolution MRIs of 76 patients were evaluated by 2 observers with different MR experiences. The accuracy for T staging was 83% for the experienced observer 1 and 67% for the less experienced observer 2. For 12 T4 tumors that had an involved mesorectal fascia and thus a CRM of 0 mm the accuracy for predicting the CRM was 100% (12/12) for both readers. For 29 patients that had a wide circumferential margin (> 10 mm) the accuracy for predicting this wide margin was 97% (28/29) for reader 1 and 93% (27/29) for reader 2. For distances between 1 and 10 mm a linear regression curve showed that the crucial distance of at least 2 mm can be predicted with 97% confidence when the distance on MRI is at least 6 mm. An important finding was the high agreement of the measurements both within and between the observers (intraclass correlation coefficients 0.99&0.91 and 0.93 resp.) in contrast to the only moderate interobserver agreement for the T stage determination (kappa 0.53). This indicates that MRI is highly accurate and reliable for the prediction of the CRM. The prediction of the T stage however was less accurate and more affected by the experience of the observer. MRI therefore serves as a promising tool to preoperatively select rectal cancer patients with a high risk for recurrences, so that they can be treated more aggressively. New generation multislice spiral CT may compete with MRI because of its lower cost, faster acquisition and ability to stage for distant metastases and local tumor extent in one single examination. The role of CT in rectal cancer has however not yet been fully explored.

Reference :

Beets-Tan R.G., Beets G.L., Vliegen R.F. *et al*. Accuracy of magnetic resonance imaging in prediction of tumour-free resection margin in rectal cancer surgery. *Lancet*, 2001, 357 (9255) : 497-504.

(NEO)ADJUVANT TREATMENT IN RECTAL CANCER. K. Haustermans. Dpt of Radiotherapy, University Hospital Gasthuisberg, 3000 Leuven, Belgium.

The main objective in the treatment of rectal cancer is to cure the patient with a good quality of life. Locoregional control can usually be obtained with a combination of surgery and radiation. The macroscopic tumour can be removed by surgery, although microscopic disease may remain in the surgical bed and lead to 15 to 50% of patients developing a local pelvic relapse. While radiation alone is seldom able to cure the macroscopic tumour, it is successful in eradicating microscopic disease. These patterns of failure are the main reason why both modalities are combined in the curative treatment of rectal cancer. On a theoretical basis preoperative radiotherapy should be superior to postoperative radiation. Preoperative radiation is certainly more dose efficient and is also better tolerated by the patients. There are three randomised trials comparing preoperative radiation with postoperative radiation. Two trials closed recently while the third one showed that preoperative radiation leads to less local recurrences but doesn't translate into an improved survival. Most trials have evaluated the role of radiotherapy in combination with conventional surgery, which employs blunt dissection of the rectal fascia. With the introduction of TME (Total Mesorectal Excision) the incidence of local recurrences after surgery alone has decreased substantially. However, the Dutch TME trial showed that even in these patients preoperative radiotherapy using five big fractions the week before surgery is still useful in reducing the number of local recurrences. The choice of fraction size to be used and the interval between preoperative radiotherapy and surgery are the subjects of active debate. A better clinical response was observed in a preoperative trial comparing a short interval between radiation and surgery with a long one but the percentage of sphincter preserving procedures was not significantly different. Drugs are added to increase the effect of radiation. These cytostatic compounds do not only sensitise the tumour cells within the radiation fields but also treat distant microscopic disease. Combining both modalities in the preoperative setting downsizes the tumour, facilitates resection and increases the number of sphincter saving procedures.

SURGERY FOR RECTAL CANCER : NEW CONCEPTS. A. Kartheuser, R. Priso, S. Wese. Colorectal Surgery Unit, Cliniques Universitaires Saint-Luc, UCL, 1200 Brussels.

To date the mainstone of rectal cancer treatment is still surgery, which can not be considered without a multi- or interdisciplinary integrated approach. During the last decade, the widespread of the use of the total mesorectal excision (TME) with preservation of the genito-urinary innervation as described by Heald is certainly the main progress in reducing local recurrence rates after rectal surgery for cancer. Indeed, the reported reccurence rate of 15-40% has been decreased to 4-10%. In the mean time, the reported genito-urinary dysfunction of 40 to 100% has been decreased to about 15% (Tiret E. *et al.*, 1999). Since the improvement in stapling devices and the introduction of coloanal anastomosis with or without a colonic pouch, sphincter saving operations for low-lying tumors of the rectum have become more common. More recently, the concept of per anum intersphincteric rectal resection with a distal safety margin of 1 cm has become the "ultimate sphincter preserving operation" (Teramoto T. *et al.*, 1997). If abdominoperineal rectal resection or Miles operation is still required, the option of a total perineal reconstruction with double electrostimulated graciloplasty could be offered to a few highly selected and young patients (Cavina E. *et al.*, 1998). Regarding the laparoscopic approach for rectal cancer surgery, there are very few studies showing that the results are potentially as good as with open surgery (Lacy A.M. *et al.*, 2002). Classical transanal surgery, or transanal endoscopic microsurgery (TEM or Buess procedure) can be used for local excision of small rectal cancer (Kartheuser A. *et al.*, 1998), but the risk of lymph node metastasis left behind in T1 carcinoma can be as high as 13% (Nascimbeni R. *et al.*, 2002) and the recurrence rate at 10 years as high as 17% (Paty P.B. *et al.*, 2002). Palliative surgical options for advanced rectal cancer include endoscopic transanal resection of tumour (ETAR) using urologic resectoscopes (Sutton C.D. *et al.*, 2002) and rectal stenting (Khot U.P. *et al.*, 2002).

PATHOLOGICAL EVALUATION OF RECTAL CANCER SPECIMENS. C. Sempoux, Dpt of Pathology, Cliniques Universitaires St Luc, UCL, 1200 Brussels, Belgium and the Working Group of Pathologists on colorectal cancer (J.P. Bogers, C. Cuvelier, P. Demetter, N. Ectors, K. Geboes, A. Jouret, N. Nagy, C. Sempoux).

Pathological examination of rectal cancer specimen plays a primary role in determining the prognosis of the patient, therefore influencing the decision of further clinical management (1). The TNM stage of the tumor remains a good indicator of survival. However, in the absence of metastatic disease, the most powerful independent predictor of both local recurrence and overall outcome is the macroscopic quality of the mesorectum in the resected specimen (2) and the distance between the tumor and the circumferential resection margin (CRM) (3-6). A CRM of £2mm has been shown to be associated with a local recurrence risk of 16% (vs. 5.8% if > 2 mm) and a CRM of £1mm with an increased risk of distant metastases (37.6% vs. 12.7% if > 1 mm) and a shorter 2-year survival rate (67.9% vs. 90.0%) (7). The pathologists have thus to precisely assess the CRM with a standardized method that has been proven reliable (8). First, the fresh resected specimen must be examined macroscopically to evaluate the completeness of the mesorectal envelope. Then, it is opened, except for the area in which the tumor is present, and the mesorectum is inked in order to precisely localize the CRM. After fixation, the resected specimen is sliced transversely to provide multiple coronal sections through the tumor and the associated mesorectum and the CRM is measured macroscopically. When the tumor or a suspected lymph node approach the CRM (< 1 cm), blocks have to be taken to repeat the measurements microscopically. In case of preoperative chemo-radiotherapy, the macroscopic tumoral evaluation is often difficult. Furthermore, it might be hard to reach the ideal number (according to the TNM guidelines) of 12 lymph nodes. Several samples in the tumoral area as well as in its periphery must then be taken to assess the persistence of residual tumoral tissue and the clearance of the CRM.

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IMPACT OF NEW IMAGING MODALITIES ON DIAGNOSIS AND MANAGEMENT OF CHRONIC PANCREATITIS. C. Matos (Brussels, ULB).

Goals of imaging : Detect ductal abnormalities that confirm the clinical diagnosis ; detect and characterize parenchymal damage and evaluate the functional integrity of the gland ; delineate extrapancreatic extension of the inflammatory process and provide a ductal mapping for interventional procedures.
Contribution of imaging modalities : **Helical CT** : Advanced disease and complications are easily recognized and staged ; it is the best modality to demonstrate intrapancreatic calcifications ; less sensitive to detect the early stages in the absence of calcifications.
MRCP : Poor sensitivity to detect calcifications in the parenchyma ; the best non invasive modality for evaluating ductal morphology ; provides information on global or segmental pancreatic flow dynamics, and allows specific estimation of exocrine reserve (with secretin stimulation) before and after interventional procedures. Accuracy of 92% for the detection of the early stages of the disease. Allows functional evaluation of cystoenterostomies or pancreaticoenterostomies. **EUS** : Is invasive ; reported as accurate to diagnose, rule out and establish the severity of chronic pancreatitis found by ERCP. More and more used for therapy of complications (cystoenterostomies and pancreaticogastrostomies) and differential diagnosis with cancer and in the presence of single cystic lesions.
Clinical applications : Non enhanced helical CT and secretin enhanced MRCP provide all the information needed to establish the diagnosis and guide therapy of painful chronic pancreatitis. However, considering the still limited availability of MRCP, it seems more rationale to use it in those centers without advanced endoscopic skills, where a risk-free view of the ductal system in patients with ductal obstruction may be beneficial before therapy. In centers with a high degree of expertise in therapeutic endoscopic procedures, MRCP is less indicated in patients with obvious ductal obstruction on helical CT, for which therapeutic ERCP is the next step. However, it may help after ERCP failure and in patients who needed a functional evaluation of new therapeutic procedures.

ACUTE PANCREATITIS : ASSESSMENT AND MANAGEMENT IN PRACTICE. J.C. Debongnie, Gastroenterology, Clinique St-Pierre, 1340 Ottignies, Belgium.

Aim : To evaluate the practice in the initial assessment and subsequent management of acute pancreatitis by using questionnaire sent to all members of local groups of medical evaluation (GLEM).
Method : A questionnaire was established by four “experts” that included 11 questions from diagnosis to treatment, including the use of scores (Apache, Ranson – Glasgow – Balthazar) or classifications (Atlanta). The results were compared to recent consensus conferences or guidelines for management (UK 1998 – France 2001 – OMGE 2002).
Results : 107 individual answers collected in 15 groups were obtained. Overall, the practice seems to reflect the present scientific data. However, scores and classifications are underused, limiting comparisons between centers.
Future : A further step could include the collection of morbidity and mortality data from different centers. If the results confirm the use of present scientific date, this could confirm the impression of a low mortality in acute pancreatitis.

REPORT OF GLEMS’S QUESTIONNAIRE ABOUT HEPATITIS C. Ch. de Galocsy, E. de Goede, J.L. Coenegrachts, J.Cl. Debongnie.

A questionnaire on the current practice about hepatitis C was proposed to all the Glems-Loks in 2001-2002. From the (French-speaking) Glems, 90 individual answers were analyzed. Two Glems gave global answers, not taken into account. For nearly all answerers, the General Practioners should be more involved in the diagnosis and follow-up of hepatitis C. Eighty-one percent did a liver biopsy only when a treatment was considered, and 40% for the follow-up of non-treated patients. Fifty-one percent did it in day-care, 82% after an ultrasound, 32% under US guidance. The use of qualitative and quantitative PCR and genotyping was generally correct but rather low compared to today’s standards. The follow-up of non-treated cases was in agreement with the consensuses, as well as the decision to treat “special cases” (cirrhosis, acute hepatitis, patients with normal transaminases). Seventy-six percent tended to include their patients into trials. Ex-drug addicts were treated often by only 30%, and sometimes by 51%. Alcohol was to be limited to 0 to 20 g/day by 73%. Seventy-eight percent said they adhered (always 29%, often 49%) to the guidelines of consensus conferences, and 64% knew where to find them. More answers will be detailed, and they will be compared to the latest consensus guidelines.

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ABSTRACTS

A01 — A14 Belgian Association for the Study of the Liver (BASL)
B01 — B18 Research Group "Gastrointestinal Regulatory Mechanisms (OG-NFWO)"
C01 — C06 Belgian *Helicobacter Pylori* Study Group
D01 — D69 Joint Meeting of Gastroenterology
N01 — N08 Research groups of Clinical Nutrition and Metabolism (SBNC and VVKVM)
R01 — R10 Research Group "Digestive and Abdominal Imaging"
G01 — G13 Belgian Group of Pediatric Gastroenterology and Nutrition
P01 — P14 Gastro-intestinal Pathology Club
S01 — S08 Symposium of the Five Societies "Multidisciplinary approach to digestive diseases: rectal cancer, chronic pancreatitis and GI bleeding"

Name	*Number*	*Comment*
A		
ADLER M.	A10, D02, D18, D22, D35, P14	
ALAERTS H.	D14, P02	
ALFIDJA AT.	D44	
ALLIËT PH.	G09	
AMININEJAD L.	N04	
ANNET L.	R02	
ARTS J.	D17, D39, D41	
ARVANITAKI M.	N04	
ARVANITAKIS M.	D09, N02	
ASSENE C.	A10	
B		
BAEKELANDT M.	D23, R05	
BAKARI S.	B01	
BALI M.	D09	
BAREA M.	A10	
BASTENS B.	A09, D68, P05	
BEETS-TAN R.	S02	Invited lecture
BELAICHE J.	D28, D31, D52, D61, D64	Moderator D21-27
BELGHITI J.	A12	
BELLINCK P.	R08	
BERGMANS A.	D53	
BIELEN D.	D10, R07	
BILLIET E.	D37	
BISSCHOPS R.	B04	
BODENHEIMER H.	A11	
BOGERS J.	P06	
BOMANS P.	D65, R09	
BOSMANS H.	D10, R07	
BOSSUYT X.	D32	
BOTELBERGHE T.	P01	
BOUDEREZ V.	D33	
BOURGEOIS N.	D02, D18, P14	Moderator A01-05
BOURGEOIS S.	D65	

DE BACKER A.	D65, R06, R09, R10	
DE BOCK W.	D62	
DE BOSSCHER H.	N05	
DE CLERCQ M.	N05	
DE CUYPERE G.	D03	
DE GALOCSY C.	S08	
DE GOEDE E.	S08	
DE HEMPTINNE B.	D03, D06, D20, D62, N06, P01, P12	Moderator D08-14
DE HERTOGH G.	P08	
DE HOOGT R.	B11	
DE HOON J.	D53	
DE JONGE F.	B15	
DE KERCHOVE D'EXAERDE A.	B06	
DE KEULENAER B.	R06, R09	
DE KONINCK X.	D18	
DE KOSTER E.	B01, C03	Moderator C01-06
DE LEPELEIRE I.	D53	
DE LEYN P.	D13, D16	
DE LOOZE D.	D57	Moderator Sympos.
DE MAEGHT S.	D19	
DE MAN J.	B05, B12, B15	
DE MAN M.	D33	
DE METTER P.	N06	
DE NEEF P.	B02, B03	
DE NEVE W.	N06	
DE RIDDER M.	D51	
DE RONDE T.	D40	
DE SAEGER C.	A01, A02	
DE SCHEPPER A.	R03, R08, R10	
DE SCHEPPER H.	B12	
DE VOS M.	A05, D31, D58, D59, D62, D63, P09	Moderator D21-27
DE VOS R.	A03	
DE VRIESE A.	D46	
DE VRIESE AS.	A05	
DE VRIESE C.	B02	
DE WINTER B.	A12, B05, B12, B15	
DEBAUCHE C.	G07	
DEBONGNIE J-CL.	S08	Moderator D35-42
DECKER G.	D13, D16	
DECRUYENAERE J.	D20	
DEELDER A.	B16, D44, D45	
DEEREN D.	D65, R09	
DEFREYNE L.	D58, D62, P09, P12	Symposium Invited lecture
DEGOTT C.	A12	
DEGREEF H.	D55	
DELAZZER S.	D08	
DELFORGE M.	D68	
DELHAYE M.	D02, D09	Symposium Invited lecture
DELOS M.	P03	
DELPORTE C.	B02	
DELRÉE P.	B01	
DELTENRE P.	D19	
DELVENNE P.	D28	
DELWAIDE J.	A09, A11	
DEMAN R.	D23, R05	

T

U

V