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HBV-HCV Coinfection: Insights from a Novel Model System

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Background: Coinfection with hepatitis B virus (HBV) and hepatitis C virus (HCV) has been associated with severe liver disease and frequent progression to liver cirrhosis and hepatocellular carcinoma. Clinical evidence suggests reciprocal replicative suppression of the two viruses (‘viral interference’). However, virtually nothing is known about molecular interactions between HBV and HCV due to the lack of appropriate model systems.

Methods: A tetracycline-regulated gene expression system was used to generate a panel of stable Huh-7 cell lines stably replicating HBV. These cell lines and control Huh-7 cell lines inducibly expressing the green fluorescent protein (GFP) were transfected with selectable HCV replicons or infected with cell culture-derived HCV (HCVcc). In these cell lines, it is possible to regulate the expression of HBV proteins, HBV genome replication, and infectious viral particle formation by the concentration of tetracycline in the culture medium while HCV proteins are expressed and HCV RNA replicated constitutively. The presence or absence of replicating HBV did not significantly affect gene expression, replication and release of the other. Experiments using HCVcc did not reveal any significant superinfection exclusion of HCV by HBV. Finally, cell culture-adapted HCVcc isolated from long-term cultures did not display any HBV-specific adaptation.

Conclusion: HBV and HCV can replicate in the same cell without any significant direct interaction. Therefore, the viral interference observed in vivo in coinfected patients is likely due to innate and/or adaptive host immune responses. These findings provide new insights into the pathogenesis of HBV-HCV coinfection and may contribute in the future to its clinical management.

Inactivation of Cardif, an Essential Adaptor Protein in the RIG-I Antiviral Pathway, in Patients with Hepatitis C

In the presence of interferon-alpha against HCV. In addition, specific inhibition of Cardif, an essential adaptor molecule Cardif in the RIG-I antiviral pathway. The aim of this study was to extend these experimental observations to patients with hepatitis C. Methods: Polyclonal and monoclonal antibodies against Cardif were generated in mice and in liver biopsies from patients expressing Cardif. In contrast, adenosine A3 receptor expression was significantly lower in easy-to-treat genotypes 2 and 3 as compared to difficult-to-treat genotypes 1 and 4. The amount of full-length or cleaved Cardif did not correlate with Cardif mRNA levels, necro-inflammatory activity, fibrosis stage or treatment outcome.

Conclusions: Cardif is cleaved and thereby inactivated specifically in patients with chronic hepatitis C. Increased Cardif cleavage in patients infected with HCV genotypes 2 and 3 may be related to the less frequent precipitation of interferon-alpha stimulated genes recently reported in these patients. However, a significant correlation with treatment outcome was not observed at the sample size examined in this study. Therefore, Cardif cleavage in the liver reveals insights into the pathogenesis of hepatitis C but does not provide an easily applicable predictor of treatment response.

Modulation of the inflammatory reaction by granulocyte-macrophage colony-stimulating factor improves mucosal repair in a mouse model of acute colitis

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Background: Innate immune cell subsets infiltrating inflamed and/or severely injured tissues are critically involved in the maintenance of inflammation.

Methods: Mice were exposed for 7 days to 4% dextran sulfate sodium (DSS) to induce colitis. Kinetic analyses of the inflammatory cell infiltrate, inflammatory mediator release and mucosal repair processes were comparatively assessed in untreated wild-type mice versus phagocyte-depleted wild-type mice or mice deficient for GM-CSF receptor. Moreover, the impact of GM-CSF administration on colitis was evaluated.

Results: Dysregulation of GM recruitment in phagocyte-depleted wild-type mice or mice deficient for GM-CSF receptor exacerbated ulcer numbers and fecal blood during DSS colitis. In contrast, adoptive transfer of CD11b-positive GM isolated from the spleen of GM-CSF-competent mice were protective. GM-CSF therapy elicited recruitment of anti-inflammatory monocytes and promoted prorepair factor expression. This resulted in reduced late inflammatory reactions, prevention of body weight loss and diarrhea, and a clear acceleration of ulcer healing.

Conclusions: Our study shows that CD11b-positive GM-CSF-responsive GM are critically involved in ulcer repair during DSS colitis and, by extension, suggests that enhanced mucosal healing might contribute to the mechanisms of action of GM-CSF treatment in Crohn’s disease.

Dysregulation of glucose homeostasis in chronic hepatitis C: The role of Protein Phosphatase 2A

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Background: Insulin resistance development and type 2 diabetes mellitus are metabolic disorders induced by the hepatitis C virus. They are considered as risk factors for fibrosis progression and nonresponse to antiviral therapy in chronic hepatitis C. The molecular mechanisms of insulin resistance development in HCV remain to be elucidated. Glucose homeostasis is tightly regulated by different signalling pathways that regulate glycogen synthesis and gluconeogenesis. We have shown that protein phosphatase 2A (PP2A) is overexpressed in HCV transgenic mice and in liver biopsies from patients with chronic hepatitis C. PP2A overexpression inhibits insulin signaling and AMPK phosphorylation. We therefore tested if HCV induced hepatic PP2A overexpression interferes with gluconeogenesis and thereby inducibly insulin resistant phenotype.

Methods: Insulin sensitivity was studied in HCV transgenic (BBHC) and in control mice by measuring fasting glucose and insulin levels for calculation of HOMA and by glucose and insulin tolerance tests. Expression levels of gluconeogenic key enzymes such as...
**ORAL PRESENTATIONS**

**Schweiz Med Forum 2008;8:(Suppl. 41)**

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### 5

**Restoration of HBV-Specific T Cell Responses in LamivudineLong Term Responder**

Florian Bihl1, Elisabetta Loggi2, Cinzia Fortini1, Carmela Cursaro1, Elena Grandini1, Lorenzo Micco1, Christian Brander3 and Pietro HBV-specific immune responses were detected in all LAM-R LTR (100%) and in eight of the 13 subjects with LAM-R (61%). The PBMC, p=0.03). Polymerase-specific responses dominated the T cell repertoire in both groups of patients, although LAM-LTR LTR (median 5 vs 1, respectively, p=0.001). LAM LTR (range: 7–11) and 13 LAM treated patients with viral breakthrough yet been analyzed.

**Conclusions:** ed the T cell repertoire in both groups of patients, although LAM-LTR SFC/106PBMC, p=0.03). Polymerase-specific responses dominated the T cell repertoire in both groups of patients, although LAM-LTR (100%) and in eight of the 13 subjects with LAM-R (61%). The frequency of HBV-specific T cell responses was higher in LAM-LTR compared to LAM-R (median 5 vs 1, respectively, p=0.001). LAMLTR presented stronger IFN-g responses (median: 2793 vs 1774 SFC/106PBMC, p=0.03). Polymase-specific responses dominated in both groups of patients, although LAM-LTR presented multiple responses to all four HBV proteins.

**Conclusions:** LAM-LTR are characterized by a multi-specific pattern of HBV-specific T cell responses. The HBV-specific cellular immunorepertoire restores in terms of both frequency and magnitude in LAM-LTR.

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### 6

**Hyperimmune anti-HBs plasma for the prevention of HBV recurrence after liver transplantation: efficacy, safety, kinetics and economics in 21 patients during a 13-year experience of two centers**

Florian Bihl1, Stefan Russmann2, Vanina Gurtner2, Loriana Di Giammarino Bihl1, Loredana Pizzi-Bosman3, Andreas Cerny1, Pietro Magno1, Antoine Hadengue1, Emilianno Giorstra1, Darniano Castelli1, Gilles Mertha4

**Background:** Commercial hepatitis B immune globulin (HBIG) products in combination with nucleos(t)ide analogues (NA) are effectively used for the prevention of HBV recurrence after liver transplantation (LT). However, associated treatment costs are exceedingly high.

**Methods:** Hyperimmune anti-HBs plasma (HIP) is obtained from blood donors vaccinated against HBV with high anti-HBs titer (>15’000IU/L). 21 HBV-related LT recipients received HIP starting at baseline cytometry as add-on to standard histology in surveillance of patients with Barrett’s esophagus Vogt, Nicole; Schönewe, René; Gschossmann, Juergen M.; Borovicka, Jan

**Division of Gastroenterology, Kantonsspital St. Gallen. Institute of Pathology, Kantonsspital St. Gallen. Division of Gastroenterology, University Hospital Bern**

**Background and Aims:** The current gold standard in the surveillance of Barrett’s esophagus (BE) is the Seattle four quadrant biopsies protocol (4-QB) every 1 to 2 cm. Using endoscopic brush cytology we studied prospectively whether digital image cytometry (DICM) is of additional benefit to regular histology as a predictor for progression to high-grade dysplasia (HGD) or cancer during a surveillance of at least 3 years.

**Methods:** In this prospective cohort we included 74 patients (85% male) with BE and baseline endoscopies with at least one DICM in addition to 4-QB. A minimal endoscopic surveillance follow-up of at least 3 years at the time of analysis was requested. HGD and adenocarcinoma (AC) were defined as primary endpoints. DNA patterns were defined as diploid (2c), intermediate and aneuploid.

**Results:** Patients received on average 8.2 HIP transfusions per year (range 5.8–11.4). Anti-HBs terminal elimination half-life after HIP administration was determined in 5 patients with a mean of 20.6 days, which is comparable to commercial HBIG products. All patients remained free of HBV recurrence during follow-up. Seven patients developed reversible mild transfusion reactions and were switched to commercial HBIG. Any transfusion-transmitted infection or other serious transfusion complication was observed. The cost for one HIP unit is 140 US$ with an average yearly treatment costs of 1'148 US$ per patient, which compares to 25'000–100'000 US$ for treatment with commercial HBIG.

**Conclusions:** HIP is an effective, safe and inexpensive treatment for the prevention of HBV recurrence after LT. It can be easily produced and may be an attractive alternative to commercial HBIG products.
Results: 8 of 74 patients with diagnosis of HGD or AC at baseline endoscopy were excluded from follow-up analysis. 66 patients were analyzed after a mean follow-up time of 44 months (range 36-72). Ten of 66 patients (15%) had low-grade dysplasia (LGD) at baseline endoscopy. One of two patients with LGD and aneuploid DICM showed HGD on follow-up whereas none of 8 patients with LGD and diploid DICM developed HGD. 56 of 66 patients (85%) had either no dysplasia (49) or indefinite for dysplasia (5) at baseline endoscopy. One of 6 patients with no dysplasia and intermediate/aneuploid DICM developed HGD. None of those with negative or indefinite for dysplasia and diploid DICM had HGD on follow-up, at baseline and no patient with LGD at baseline endoscopy were excluded from follow-up analysis. 66 patients were assessed additionally.

Conclusion: DICM from brush cytology as add on to histology appears to be of additional benefit during surveillance of BE. While aneuploidy warrants an early reendoscopy a diploid result of DICM underscores the low-risk status in patients with low-grade dysplasia. Studies with larger patient arows at low-risk are therefore encouraged.

Active intravenous drug use during chronic hepatitis C therapy does not have sustained virological response rates in adherent patients

Philip Bruggmann1, Luis Falcato1, Beat Helbling2, Olivia Keiser3, Francesco Negro4, Daniel Meili1 on behalf of the Swiss Hepatitis C Cohort Study

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Background: Reluctance has been expressed about treating hepatitis C (HCV) in active IV drug users in both guidelines and clinical practice. IV drug users make up the largest risk group in HCV patients. The literature offers no evidence for a general exclusion of this high risk group. The aim of this study was to evaluate the direct influence of active IV drug use on the efficacy of HCV treatment.

Methods: In this retrospective study 2535 patients were analysed. To study the direct influence of IV drug use on treatment outcome we selected all patients who were adherent enough to have their serum HCV RNA tested 6 months after the end of treatment and to attend at least one cohort follow-up visit during HCV therapy, documenting the drug use status.

Results: The proportion of patients with a sufficient antiviral drug exposure (>80% of the scheduled cumulative dose) and treatment duration (>80% of the scheduled duration) was comparable in the two groups: 66% of the patients with active IVDU during therapy and 65.5% in non-IVDU group. The SVR rate was 69.3% in the IVDU group and 59.8% in the non-IVDU group. The multiple logistic regression analysis showed that the only independent predictors of SVR were HCV genotype, age whereas active IVDU during therapy did not have a significant influence on treatment outcome.

Conclusions: IV drug use does not have a negative direct influence on the efficacy of HCV treatment in patients adherent to antiviral therapy. Our study results should encourage physicians not to exclude IVDU per se from HCV treatment. Based on our experience adherence in IV drug users can be improved by a comprehensive care setting and by interfacing opioid maintenance treatment with HCV therapy.

Alcohol consumption during Hepatitis C therapy in patients of the Swiss hepatitis C cohort study

Philipp Bruggmann, Magdalena Dampz, Luis Falcato ARUD Zurich

Background: Usually clinicians demand complete abstinence for at least 6 months before treating alcoholics for hepatitis C (HCV). There is only few data on the effect of ethanol consumption during HCV therapy. This evaluation uses the data of the Swiss Hepatitis C cohort study (SCCS) to examine the effect of ongoing alcohol intake on sustained virological response (SVR).

Methods: Patients were eligible for the study if they had their HCV RNA tested 6 months after the end of treatment and at least one cohort follow-up visit during HCV therapy, documenting the consumed amount of alcohol. They were assigned to three groups: abstinence, 124g alcohol per day and 25g more per day. The type of interferon and the cumulative dose of interferon and ribavirin were assessed additionally.

Results: At the time of the analysis, 2535 people were included in the SCCS. 368 patients were included, 236 (64%) indicating no alcohol consumption during HCV therapy, 190 (27%) with 1-24g/d and 32 (9%) with 25g and more ethanol a day. Neither the type of interferon used nor the rate of patients with at least 80% of the scheduled cumulative dose (59.5% vs. 65.7% vs 59.4%) did significantly differ between the three groups. 93% of all patients were treated with peginterferon. The SVR rate at 1-24g group 61% and ≥25g/d group 50%. No significant negative influence of alcohol consumption during therapy was observed in the multiple regression analysis for treatment success (OR 1.16 for >24g/d, 95% CI 0.72-3.66).

Conclusion: Alcohol seems not to have a relevant direct influence on the efficacy of anti HCV drugs, as drinkers reached similar rates of SVR and sufficient cumulative doses to non drinkers. Previous studies described a negative influence of a recent history of alcoholism on the compliance to HCV therapy, a factor which was not studied in this evaluation. Future efforts in care of patients not able to abstain completely from alcohol should attempt to improve compliance. This could be reached for example by comprehensive care with high frequency contact settings during HCV treatment.

Prognostic influence of immunohistochemically detected lymph node micrometastasis and histological subtype in pN0 oesophageal cancer

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Introduction: Differences in frequency and clinical impact of lymph node micrometastases between histological subtypes of oesophageal cancer have not been determined.

Methods: 1204 lymph nodes from 32 squamous cell carcinomas and 54 adenocarcinomas with complete resection and pN0 status were re-evaluated using a serial sectioning protocol including immunohistochemistry. Intra-nodal tumor cells were classified as micrometastases (0.2-2 mm) or isolated tumor cells (<0.2 mm).

Results: No significant difference in the frequency of micrometastases between adenocarcinoma and squamous cell carcinoma (11.3% vs. 3.1%, p=0.247) occurred. Kaplan-Meier curves showed a significantly prolonged 5-year survival (p=0.017) and disease free interval (p=0.006) in immunohistochemically negative patients with squamous cell carcinoma compared to adenocarcinoma, no difference (p=0.404 and p=0.092, respectively) was seen. Patients without pre-treatment and adenocarcinoma showed a significant 5-year survival (85% vs. 53%, p=0.028 and disease free interval (83% vs. 58%, p=0.048) advantage compared to squamous cell carcinoma. After pre-treatment, no difference between the histological subtypes could be detected. Regression analysis showed no factor influencing overall survival significantly in this nodal negative collective, whereas four factors influenced disease free interval significantly: pretreatment (HR 3.3 [95% CI 1.2-9.1], p=0.020); micrometastasis (HR 0.3 [95% CI 1.1-19.7], p=0.012); UICC stage II vs. 0/I (HR 2.2 [95% CI 1.1-4.4], p=0.032); adenocarcinoma (HR 0.3 [95% CI 0.1-0.9], p=0.028).

Conclusion: The differences in frequency and clinical impact of immunohistochemically detected micrometastases may indicate that adenocarcinoma and squamous cell carcinoma should not be treated as one entity.
Factor(s) responsible for the conditioned medium induced steatosis

Conditioned medium of human white adipose tissue products of white adipose tissue on hepatocytes. In contrast, little is known about the interactions of white adipose tissue in the regulation of energy balance and other physiological processes (cytokines), an endocrine and paracrine role for white adipose tissue.

Background:
HCV is now considered as one of the causes of insulin resistance as it increases the homeostasis model assessment (HOMA) score in patients even in the early stage of liver disease, while HCV clearance leads to a decrease of the HOMA score. HCV infection leads mainly to insulin resistance through the down regulation of IRS1 via mechanisms that seem to be specific for each HCV genotype. In fact, IRS1 downregulation occurs through a decrease of the peroxisome proliferatoractivated receptor (PPAR) and the upregulation of suppressor of cytokine signaling (SOCS) in genotype 3a, and through the activation of mTOR for genotype 1b. Our goal in this study was double: (1) to study the mechanism leading to insulin resistance in other genotypes (namely 2a, 4h) and (2) to compare and analyze the sequence of the core protein of different genotypes in order to identify the amino acid residues responsible for insulin resistance.

Methods:
Using a lentiviral system, we expressed the HCV core protein of genotypes 2a, 4h and chimeric constructs and we measured the expression levels of IRS1 and several SOCS family members, involved in the insulin signal pathway in a human hepatoma cell line (HuH7).

Results and Conclusions:
Our results show that while HCV core protein of different genotypes induced downregulation of IRS1, mechanisms involved different actors and pathways in each case. In addition, investigations with chimeric constructs give the first indications regarding the sequence involved in these processes.

Monococyte Chemoattractant Protein1 Secreted By Adipose Tissue Induces Direct Lipid Accumulation In Hepatocytes

Sophie Clément1, Cristiana Juge-Aubry2, Antonio Sgroi3, Sophie Conzelmann1, Lucien Deplano1, Stéphanie Pascarella1, Kévin Guilloux1, Sophie Clément1

Background:
Since the discovery that adipocytes may secrete cytokines/chemokines shown to be secreted by white adipose tissue. In contrast to interleukin-8 and -6, the monocyte chemoattractant protein (MCP) was identified as a powerful attractant for monocytes, macrophages and T lymphocytes. MCP-1, also known as CCL2, is encoded by a gene located on chromosome 17. In fact, MCP-1 is a member of the C-C chemokine family.

Methods:
We investigated the effect of conditioned medium (CM) of human white adipose tissue on the uptake of fatty acid labeled with C14. The effects of CM on the expression of FAS and PPARgamma were also measured.

Results:
The expression of MCP-1 was increased in the adipocytes after 24 hours of incubation with CM. The uptake of fatty acid labeled with C14 was increased in hepatocytes treated with CM. The expression of FAS and PPARgamma was decreased in hepatocytes treated with CM.

Conclusions:
Our results suggest that MCP-1 may play a role in the development of steatosis in hepatocytes.

Sorafenib treatment for advanced HCC prior to surgery:
Should we stop?

JF. Dufour1, P. Romand1, S. Wilhelm1

Institute of Clinical Pharmacology, Bern University 1, Switzerland, Bayer HealthCare Pharmaceuticals, Inc. USA 2, Medicine Faculty, University of Chile, Santiago, Chile 3

Background:
HCC is the third most common cause of cancerrelated death. Therapeutic options depend on the stage of the tumour, but only patients with small HCCs are amenable to curative treatments. Sorafenib is a multiple kinase inhibitor which blocks the receptor tyrosine kinases VEGF/K, PITDGFb and the ser/thr kinase RAF. Sorafenib has been approved by the EMEA and the US FDA for the treatment of unresectable HCC. Another potential indication for Nexavar® is neoadjuvant therapy for patients with advanced disease, who are candidates for surgery. No preclinical studies of sorafenib on liver regeneration have been conducted, which was our aim.

Methods:
C57BL/6 mice received oral BAY 54-9985, sorafenib tosylate, 50 mg/kg/day for 14 days before undergoing 2/3 hepatectomy. Treatment was stopped the day before surgery (group B) or given continuously for up to 120h post hepatectomy (group C). For both groups the time points 24, 72 and 120 hours after hepatectomy were investigated. Liver, scar tissue and blood samples were taken at endpoints. Results are presented as Mean ± SD.

Results:
When animals received continuous sorafenib treatment (group C) impaired liver regeneration was observed at 120h, which was statistically significant compared to control groups. (C=0.52±0.06, n=8 vs. vehicle=0.72±0.1, n=4 p=0.001, One way ANOVA and Newman-Keuls). No significant differences in liver weight at the endpoint were observed when the treatment is stopped the day before surgery. Side effects such as diarrhoea, wound healing complications and bleeding during surgery were observed in few cases. Weight loss of about 10% occurred in animals treated with the drug. Additional studies to examine the effects of sorafenib treatment on BrdU incorporation and growth factor expression in this liver regeneration preclinical model are ongoing.

Conclusion:
Our study indicates that when administered before surgery sorafenib therapy should be stopped before the resection.
Stage IV colorectal cancer treated with neoadjuvant chemotherapy: a comparison of histological response in liver metastases, primary tumors and regional lymph nodes

Background: We report herein the histopathological results of a novel “inverted” strategy designed to manage CRC patients presenting with synchronous liver metastases using chemotherapy first, liver surgery second, and resection of the primary tumor as a final step. The aim of this study was to assess and to compare the response to chemotherapy in the resected liver metastases, in the primary tumor and in the locoregional lymph nodes.

Methods: 27 patients with stage IV CRC were initially treated with a combination of oxaliplatin, irinotecan, 5-fluorouracil and leucovorin (OCFL) for 3-4 months. Histological response to chemotherapy was assessed using a tumor regression grading (TRG) score based on the presence of residual tumor cells and the extent of fibrosis. TRG1 corresponded to absence of tumor cells replaced by abundant fibrosis; TRG2 to rare residual tumor cells scattered throughout abundant fibrosis; TRG3 to more residual tumor cells throughout a predominant fibrosis; TRG4 to large amount of tumor cells precluding over fibrosis; and TRG5 most exclusively to tumors without fibrosis.

Results: Median age of patients was 56 (range 37-69) years. Primary tumor location was: right colon (4); left colon (7); and rectum (16 patients). Median number of liver metastases was 5 (range 1-21). The median delay between surgery and resection of the primary was 45 (range 2-280) days. Complete tumor response (pT0N0M0) was achieved in 2 patients. The majority of patients (81%) demonstrated identical (48%) or better (33%) response in the liver metastases than in the primary tumors. Complete absence of response (TRG5) was documented in the lymph nodes of 3 out of 18 (16%) patients with N+ tumors.

Conclusion: Colorectal cancer is chemosensitive, whether it is primary or metastatic to the liver. Complete pathologic response, however, rarely occurs, and the most chemoresistant location appears to be the locoregional lymph nodes. These data indicate that oncologically adequate lymph node and primary tumor resection is still warranted after OCFL neoadjuvant chemotherapy for metastatic CRC.
Results of in situ adult-child split liver transplantation in a Swiss program
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Background: To share the results of in situ split liver transplantation in a mixed adult and pediatric program while this procedure is to some extent controversial in the opinion of adult transplant centers.

Patients and methods: Since November 1999, 27 in situ splits for 7 adult and 20 pediatric recipients have been performed in our center.

Results: Pediatric patients were between 6 months and 15 years old (median 1.6 years), adult recipients were between 33 and 66 years old (median 50 years). After a median follow-up of 3.5 years, overall patient survival was 90% for pediatric patients (one death from massive pulmonary embolism in a patient with Budd-Chiari syndrome and a child with graft-versus-host associated to recipient’s bone marrow aplasia accompanying fulminant hepatic failure) and 86% for adult patients (one death due to local anesthesia, and a biliary fistula that resolved spontaneously). For P-LDLT, donors were discharged after 6-10 days without major complications. The 17 adult recipients were between 29 and 58 years old (median 53y), there were 6 women and 11 men. Median graft to recipient weight ratio was 1.5% with 2 cases below 0.8%. The middle hepatic vein was harvested with the graft and in 3 cases avenoplasty with the hepatic venous branches to segment 5 and 8 was done. Vascular complications occurred in two patients, both having required interposition grafts (portal and arterial), and biliary complications in 6 patients, (2 leaks and 4 strictures), none leading to graft loss. Three patients died: one patient at two months from MOF; another at 11 months because of tumor recurrence (sarcomatous hepatocellular carcinoma), and one patient at 4 years because of HCV recurrence. All P-LDLT recipients are alive with a functioning graft (follow up 6-44 months). After a median follow-up of 48 months, (range 1 to 104 months), actuarial patient and graft survival were 85% at 1 year, 78% at 3 years and 72% at 5 years.

Conclusions: In the current era of graft shortage, in situ SLT appears justified despite the increased work burden inherent to the procedure, as it generates grafts of superior quality. For adults in particular, patient and graft survival figures are excellent and should encourage promoting of the technique in other centers.

Alterations of the mitochondrial functions by the HIT protein Hint2
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Background: We identified previously Hint2, a protein expressed predominantly in the liver and the first human HIT protein to be localized in mitochondria. We previously reported that over-expression of Hint2 resulted in enhanced apoptosis after treatment with anti-Fas/actinomycin D and that the expression of Hint2 was down-regulated in hepatocellular carcinoma. The aim of this study was to investigate the effects of Hint2 expression on mitochondrial function.

Methods: HepG2 cell lines over- or under-expressing Hint2 and their respective controls were studied. The activity of the complexes I to IV of the respiratory chain was determined, O2 consumption and ATP content may represent an advantage for tumoral cells having less Hint2.

Conclusions: The level of expression of Hint2 affects the mitochondrial network and its functional capacity. The decrease in O2 consumption and ATP content may represent an advantage for tumoral cells.
mTOR Activation by HCV Core Protein Protects Hepatoma Cells from TGF-β-Induced Apoptosis

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Background and aims: Several HCV proteins have been shown to affect the interferon signaling and the pathways leading to apoptosis in vitro. Modulatory effects may represent a key mechanism to circumvent host innate and adaptive immune responses in order to establish persistent infection. In addition, they may promote HCV-associated tumorigenesis, leading to hepatocellular carcinoma and Bclllymphomas.

Methods: We used a human hepatocyte hepatoma cell line transiently expressing the HCV core protein 1b to 3a to investigate their effects on interferonalpha signaling and hepatocyte apoptosis induced by a variety of stimuli (IFN-α, TNF-α, and TGF-β). SMAD3 and SMAD4

Results: HCV core proteins of both genotypes 1b and 3a failed to increase SMAD3 mRNA levels (1b vs 1b+TGF-β: 86.57 ± 0.04%; p= NS). In parallel, in Huh 7 cells expressing the HCV 1b core protein, the nuclear translocation of SMAD3 increased to levels comparable to controls (83.55 ± 0.05%; p= 0.048). However, when hepatocytes expressing the HCV 1b core protein (but not 3a) rendered Huh7 cells resistant to apoptosis induced by TGF-β-1 (1b vs 1b+TGF-β: p= NS, GFP vs GFP+TGF-β: p= 0.014). To test whether mTOR activation induced by HCV 1b core was involved in the resistance to apoptosis, we coinubated transfectected cells with TGF-β and rapamycin, which resulted in a ~100% increase in the number of apoptotic cells (tested by FACS). TGF-β-induced nuclear translocation of SMAD3 was significantly reduced in cells transfected with HCV core protein 1b (52.66 ± 0.08%) as compared to those expressing only the GFP protein as control (63.55 ± 0.05%; p> 0.048). However, when hepatocytes expressing the HCV core protein 1b were coinubated with TGF-β and rapamycin, the nuclear translocation of SMAD3 increased to levels comparable to controls (65.57 ± 0.04%; p= NS). In parallel, in Huh7 cells expressing the core protein 1b, the SMAD3 mRNA expression levels increased after coinubation with TGF-β and rapamycin (1b vs 1b+TGF-β+rapamycin p= 0.038) whereas the TGF-β-1 alone failed to increase SMAD3 mRNA levels (1b vs 1b+TGF-β: p= 0.25432).

Conclusion: The HCV 1b core protein activates mTOR in Huh7 cells: this results in decreased sensitivity to TGF-β-1-induced apoptosis.
**Increased intrabolus pressure: a novel pathophysiologic factor in nonobstructive dysphagia?**

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*Background:* There are only limited data on the pathophysiologic mechanisms esophageal dysphagia in the absence of structural lesions or major motility abnormalities. The aim of our study was therefore to compare intrabolus pressure in patients with dysphagia, gastro-esophageal reflux (GERD) symptoms and non-cardiac chest pain.

*Methods:* Patients referred to our laboratory underwent combined impedance-manometry testing using 10 saline (Sn) each and 10 bread swallows in recumbent position. Manometric and impedance data were recorded at 5, 10, 15 and 20 cm above the LES. In each channel intrabolus pressure (IBP) was calculated as average pressure measured during the time interval elapsed between bolus entry and exit. Results: 3) In 58 patients (34 females, mean age 47, range 23-81; 18 dysphagia, 17 chest pain and 12 GERD) intrabolus pressure was higher during bread compared to saline swallows (p<0.01). Dysphagia patients had lower IBP during saline (p<0.05) and bread (p<0.05) swallows compared to chest pain and GERD patients. Patients with dysphagia had shorter LES relaxations compared to chest pain patients (p<0.01) during bread swallows.

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<td>IBP 5cm above LES (mm Hg)</td>
<td>10.5 ± 0.3</td>
<td>9.1 ± 0.2</td>
<td>7.76 ± 0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LES relaxation duration (sec)</td>
<td>7.9 ± 0.2</td>
<td>8.2 ± 0.1</td>
<td>8.4 ± 0.1</td>
<td>0.089</td>
</tr>
<tr>
<td>IBP 10cm above LES (mm Hg)</td>
<td>16.4 ± 0.9</td>
<td>14.0 ± 0.5</td>
<td>12.2 ± 0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LES relaxation duration (sec)</td>
<td>8.0 ± 0.3</td>
<td>8.2 ± 0.2</td>
<td>9.1 ± 0.3</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

**Conclusion:** Increased intrabolus pressure might be a key factor in the pathophysiology of non-obstructive dysphagia. Providing pressure and bolus presence data combined impedance manometry (MII-EM) is an ideal tool for monitoring IBP.

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**Hepatitis Delta Virus Inhibits Alpha Interferon Signaling**

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1 Divisions of Clinical Pathology and 2 Gastroenterology and Hepatology, University Hospital, Geneva, Switzerland

*Background:* Hepatitis delta virus (HDV) can cause severe acute and chronic liver disease in patients infected with hepatitis B virus. Interferon (IFN) alpha is the only treatment reported to provide some benefit in chronic hepatitis D. Unfortunately, only a minority of HDV-infected patients respond to IFN therapy. The molecular mechanisms underlying resistance to therapy are unclear. IFN-induced activation of the Janus kinasesignal transducer and activator of transcription (Jak-STAT) signaling cascade is essential for the induction of an antiviral state. Interference of HDV with the JakSTAT pathway could be responsible for the observed IFN resistance in patients with chronic hepatitis delta.

*Methods:* We analyzed IFN-induced signal transduction through the JakSTAT pathway in human hepatoma cells. The expression of IFN-stimulated genes was investigated with reverse transcription real-time PCR. STAT1 and STAT2 activations were examined by immunofluorescence and Western blots.

*Results:* We observed that the expression of the interferon stimulated genes coding for the antiviral proteins myxovirus resistance A (MxA), dsRNA-dependent protein kinase (PKR) and oligoadenylate synthetase (OAS2) were downregulated in HDV-infected hepatoma cells in response to IFN treatment. We provide evidence that HDV inhibits the type I interferon signaling by severely impairing the phosphorylation of both STAT1 and STAT2 and consequently blocking their translocation from the cytoplasm to the nucleus.

**Conclusions:** IFN alpha induces intracellular signaling is impaired in HDV-infected human hepatoma cells. HDV subverts the JakSTAT pathway by selectively preventing activation and translocation to the nucleus of STAT1 and STAT2. Interference of HDV with IFN signaling could represent an important mechanism of viral persistence and treatment resistance.

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**Decreased levels of liver specific microRNA miR-122 in hepatitis C patients with poor response to interferon therapy**

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*Background:* Liver-specific microRNA miR-122 is important for efficient replication of HCV RNA in Huh7 cells stably expressing anHCV replicon. This observation raised much interest in a role of miR122 in HCV infection and as potential therapeutic target. Furthermore, it was reported recently that levels of miR-122 and several other miRNAs are regulated by interferon (IFN) in Huh7 cells and that miRNAs might mediate at least some effects of IFN on HCV RNA replication in vitro.

*Methods:* We measured IFN-mediated regulation of six miRNAs (miR1, miR-122, miR-196, miR-296, miR-351, and miR-448) in Huh7 cells. We then analyzed levels of these miRNAs and of known IFN stimulated genes in livers of IFNα-treated mice and in paired biopsies of patients with chronic hepatitis C (CHC) undergoing pegIFNα/ribavirin therapy. Measurements were performed by quantitative PCR.

*Results:* Four miRNAs were induced by IFN in Huh7 cells. The miR122 level was decreased in response to IFN, but only 20 to 40% rather than 4-fold as previously reported. There was either no significant expression or no significant regulation of any of these miRNAs in the livers of IFNα-treated mice. None of these miRNAs were regulated in human liver after pegIFNα administration. Unexpectedly, miR-122 expression levels were significantly lower in pre-treatment biopsies of patients with a primary non-response to treatment (P<0.001) than in patients with a complete early virological response (cEVR).

**Conclusions:** Our analysis of miRNAs revealed only limited IFN-induced changes, inconsistent with a major role of miRNAs in mediating anti-viral effects of IFN. Low miR-122 expression levels are negative predictors of response to pegIFNα/ribavirin treatment.

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**Stepwise Radical Endoscopic Mucosal Resection for Complete Removal of Barrett’s Esophagus with Early Neoplasia**

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*Background:* Endoscopic mucosal resection (EMR) of high-grade intraepithelial neoplasia (HGIN) or intramucosal cancer (IMC) in Barrett’s esophagus (BE) is an effective and safe alternative to surgical treatment. However, after localized EMR metachronous lesions may develop in the residual BE. Stepwise radical endoscopic mucosal resection (SRER) aims at removing the entire BE. This study aims to evaluate the safety and efficacy of the concept of SRER.

*Methods:* Patients with HGIN/IMC in BE <5cm, without submucosal infiltration were included. EMR was performed using simple snare resection technique or multiband ligation technique (Duette, Cook Endoscopy). In patients with Short Segment Barrett’s Esophagus, the whole Barrett’s epithelium was removed in one session. Otherwise, subsequent resections were performed with intervals of 4 weeks until complete eradication of all visible BE.

*Results:* Fifty seven patients with HGIN/IMC, treated between Jan. 2000 and Sept. 2006 were included. Complete eradication of HGIN/IMC was achieved in 56/57 patients (98%) after a median number of two EMR sessions (IQR 2-3). Perforation was noted in 1 patient. Complete eradication of BE was achieved in 56/57 patients (98%). During a median FU of 18 months (IQR 7-31),
1 patient (1.7%) had recurrence of HGIN and 4 patients (7%) had recurrence of BE detected on FU biopsies and were successfully treated with repeat EMR. There were no patients with “buried glands” noted. Symptomatic stenoses occurred in 34/57 patients (59.6%) which were effectively treated with bougienage. One patient developed a huge tear with a suspected perforation during bougienage. He was subsequently sent to surgery. Histopathological evaluation of the operative specimen showed no perforation.

Conclusion: SREP by RFA ± previous localizing HGIN and/or IMC is an effective treatment modality with a low rate of recurrence. SREP is however associated with esophageal stenosis in more than half of the patients and is frequently managed by bougienage. None of the patients showed dysphagia after completion of treatment.

First Experiences with Radiofrequency Ablation (BARRX®) in Patients with Barrett's Esophagus
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1 Department of Interdisciplinary Endoscopy, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, 2 GastroZentrum, Klinik Hirslanden, Zürich, Switzerland

Background: Stepwise circumferential and focal ablation using radiofrequency ablation [RFA] BARRX® HALO system is a relatively new endoscopic treatment option for Barrett’s esophagus (BE) without the known drawbacks of other ablation techniques. In patients with BE containing high-grade intraepithelial neoplasia (HGIN) or intramucosal cancer (IMC), endoscopic mucosal resection (EMR) is the first-line therapy. However, after localized EMR metachronous lesions occur frequently in the remaining BE. Treatment of the residual BE by RFA could be a potential treatment option. We report our initial experiences with RFA in patients with BE + previous localized EMR of HGIN/IMC as part of an ongoing study.

Methods: Patients with BE ± previous localized EMR of HGIN/IMC in which treatment was completed was included in the analysis. All visible lesions were resected prior to ablation. A balloon-based electrode (HALO®) or an endoscopic currettage electrode (HALO®) was used for circumferential and/or focal ablation of the remaining BE. Eradication of dysplasia, IMC or BE was the main outcome measure.

Results: RFA treatment was completed in 7 patients with a median BE length of 5cm (3-12cm). In 6 patients, localized EMR (median EMR session: 1 [1-7]) was performed before RFA (Histology of EMR: IMC:4 HGIN:2). Biopsy of the remaining BE showed HGIN in 1 patient and BE with no dysplasia in 5 patients. One patient was treated for BE with no dysplasia. A total of 19 RFA sessions (median: 3 [1-6]) were performed (HALO 360°: 8 times, HALO 90°: 11 times). Ablation occurred in 1 patient. None of the patients developed stenosis. After a median follow-up of 5 months (range 3-12), 6 of 7 patients showed neither recurrent HGIN/IMC nor recurrent Barrett’s or “buried glands”. One patient had a recurrence of HGIN after 4 months and is presently undergoing RFA re-treatment.

Conclusions: RFA seems to be a safe and effective method for the ablation of Barrett’s metastasia. Interestingly, neither stenosis nor buried glands were observed in a short term follow-up. Scarring after extensive EMR may lead to severe laceration during RFA. In patients with long segment Barrett’s esophagus containing HGIN/IMC, the combination of localized EMR and RFA seems to be an effective treatment approach. Prospective randomized controlled trials are warranted.

Loss of Notch-1 signaling leads to portal hypertension and dedifferentiation of the adult hepatic sinusoidal microvasculature
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1 Department of Interdisciplinary Endoscopy, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, 2 GastroZentrum, Klinik Hirslanden, Zürich, Switzerland

Background: The diagnosis of hepatic vascular steatosis (ASH) is based on histology (hepaticcellular damage with ballooning, Mallory’s bodies; steato-changes; inflammation with predominance of neutrophils; pericellular fibrosis). Additional features include bile pigment accumulation, iron deposition, and some degree of ductular reaction. Whether the intensity of histological damage is of clinical significance is ill-defined. We studied the prognostic value of individual features on liver biopsy, as well as other parameters (age, MELD and MAddrey) to predict the 90-day mortality in patients with ASH.

Methods: 138 patients (age > 35; gender: 55% male; biopsy proven ASH (no associated viral hepatitis or infection at admission) admitted over a 3-year period were studied. Clinical scores were calculated at time of biopsy (median time of 3 days [0-10] after admission). All patients with MAddrey > 32 (= 73 %) received steroids. A semi-quantitative evaluation of the findings was performed, while blinded to patients’ outcome: macrovesicular steatosis (>50%); +1; microvesicular steatosis (present; +1); hepatocellular damage (numerous Mallory: +1; frequent ballooning: +1); neutrophilic infiltration (severe: +1); iron deposits (moderate/severe: +1); ductular reaction (marked: +1); and bile pigment accumulation (moderate/severe: +1). Fibrosis was not scored as almost all patients had cirrhosis. The 3-month survival status was based on hospital records and phone calls.

Results: Survival was 74%. Sixty patients died (median time 26 days [1-88]; at univariate analysis, age > 50 yrs, MAddrey > 32, MELD > 19, bile pigments accumulation (all p<0.001), marked iron deposits (p<0.015), were associated with death. Bilirubin showed a weak but significant correlation with bile pigments (Kendall tau = 0.45, p<0.0001). On multivariate analysis (OR [95% CI]), an age > 50 yrs (3.8 [1.35-10.9]; a MAddrey > 32 (5.7 [1.7-19.7]; and bile pigments on biopsy (2.5 [1.25-2.2) were independent predictors of death.

Conclusions: A part from the description of features for the diagnosis of ASH, histology identifies bile pigments accumulation with a prognostic significance, together with an age > 50 yrs and a MAddrey’s score > 32.
Budesonide as Induction Treatment for active Eosinophilic Esophagitis in Adolescents and Adults: A randomized, double-blind, placebo-controlled Study (BEE Trial)

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Background: Eosinophilic Esophagitis (EE) is a clinicopathological defined condition characterized by PPI-refractory esophagus-related symptoms in combination with a dense eosinophilic eosinophilia. Topical corticosteroids have shown to be an efficient therapy in children with EE and, on an anecdotal base, in adults. The purpose of this study is to assess the efficacy of budesonide in adolescents and adults with active EE and to analyze the reversibility of symptoms and signs in EE.

Methods: In this randomized, double-blind trial, 36 adolescent or adult patients (n=1=31/5; mean age 35.7yrs, range 17-65) with active EE (≥20 eos/hpf and dysphagia) swallowed either nebulized aqueous budesonide suspension formulation (Pulmicort® Respules 0.25 mg/ml) at a dose of 1 mg (4 ml) twice daily or placebo twice daily for 15 days. Pre-and post-treatment the activity of the disease was assessed clinically, endoscopically, histologically and via biomarkers in the blood and in the tissue. Symptoms were recorded with a diary. The primary endpoint was histological reaction, defined as remission (max <5 eos/hpf), response (max 5-20 eos/hpf) or persistent active inflammation (max >20 eos/hpf).

Results: At baseline, both groups were histologically comparable (p=0.52, Wilcoxon test). After the 15-day induction therapy, the remission rates were 61.1% (11/18 patients) in the budesonide group as compared with 5.7% (1/18 patients) in the placebo group (p=0.0009). The rates of response were 11.1% (2/18 patients) in the budesonide group and 5.7% (1/18 patients) in the placebo group. The inflammation was still active in 27.8% (5/18 patients) of the budesonide group and in 88.9% (16/18 patients) in the placebo group. The treatment was well tolerated and no serious adverse events occurred. The course of symptoms reflected fairly well the activity of the inflammation. Among the endoscopical sings, white exudates and red furrows disappeared in parallel with the eosinophilic infiltration, whereas corrugated and solitary rings persisted.

Conclusions: A 15-day course with the topical corticosteroid budesonide is highly effective in inducing a remission in adolescent and adult patients with active EE. Symptoms correspond fairly well with degree of inflammation. White exudates and red furrows are associated with active inflammation and are reversible, whereas corrugated and solitary rings do not respond to anti-inflammatory therapy and likely reflect fibrosis. However, the long-term management of this chronic-inflammatory disease remains further investigation. (ClinicalTrials.gov number NTC00271348)

Reversibility of esophageal dysmotilities after conversion from gastric band to gastric bypass

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Division of Gastroenterology Kantonsspital St.Gallen; Department of Surgery, Kantonsspital St. Gallen; Division of Gastroenterology University of Zurich

Background: Recent studies report on esophageal motility disorders induced by gastric banding, on occa-sions severe enough to mimic pseudoachalasia. To date there are insufficient data whether these changes are reversible or not.

Aim: Evaluate changes in esophageal symptoms, peristalsis, bolus transit and clearance be-fore and 3 months after conversion from gastric ban-ding to gastric bypass.

Methods: Patients scheduled for conversions from gastric banding to gastric bypass were evaluated before and 3 months after con-versions. Clinical assessment included 7-point Likert scale rating of dysphagia, heartburn, regurgitation and chest pain. Esophageal peristalsis and bolus transit were assessed using combined impedance-manometry. Esophageal emptying was assessed using a modified timed barium swallow.

Results: Twenty-four patients (20 F, mean age 45, range 28-61 years) completed pre- and post-operative (average 98, range 63-186 days) evaluations. Conversion from gastric banding to bypass improved esophageal symptoms, esophageal bolus transit (impedance) and clearance (timed barium swallow) while there was only a trend in improved esophageal peristalsis (manometry).

Conclusions: Conversion from gastric band to gastric bypass improves esophageal symptoms and function. Abnormal motility caused by gastric banding may persist in some patients after to gastric bypass. However few of these patients are symptomatic and have abnormal bolus transit.
Significance of serum adiponectin levels in patients with chronic liver disease
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Institute of Clinical Pharmacology, University of Berne, Berne, Switzerland

Background: Adiponectin plays a pivotal role in metabolic liver diseases. It increases fatty acid beta-oxidation, decreases hepatic triglyceride content and hepatic insulin resistance. Recent studies reported reduced serum levels of adiponectin in patients with non-alcoholic steatohepatitis. The aim of this study was to establish a correlation between adiponectin and metabolic, laboratory and diagnostic findings in patients with liver disease.

Methods: Adiponectin serum concentrations were measured by enzyme-linked immunoassays in 208 fasting patients (118 men, 90 women) with chronic liver disease: 31 non-alcoholic fatty liver disease (NAFLD), 53 HCV, 16 HBV, 38 biopsy-proven cirrhosis.

Results: Circulating adiponectin levels were significantly increased in patients with cirrhosis compared to those with simple steatosis or other chronic liver diseases (19 ug/ml vs. 5.4 ug/ml vs. 10.3 ug/ml, p=0.00000017). Serum adiponectin concentrations positively correlated with serum bile acid levels (r=0.12), serum hyaluronan acid (r=0.00000363), fibroscan values (r=0.00013) and negatively with BMI (r=0.0029). Analysis by gender revealed further sex-related differences in the correlation of adiponectin with BMI, hyaluronic acid and elastography.

Conclusion: Adiponectin levels are decreased in patients with NAFLD and do not help to separate patients with NASH from those with steatosis. Serum adiponectin levels decrease with BMI in other chronic liver diseases (19 ug/ml vs. 5.4 ug/ml vs. 10.3 ug/ml, p=0.07 and 0.05 respectively). Serum adiponectin concentrations positively correlate with metabolic, laboratory and diagnostic findings in patients with liver disease.

Is a sustaining rod necessary for diverting loop ileostomy?
Vanessa Banz, Lukas Brügger, Christian Eggli, Hans Gelpke, Marco Decurtins, Daniel Candinas

Objective: The presence of a loop ileostomy (LI) facilitates clinical management after leakage following distal colorectal anastomosis. Generally, diverting LI are secured at skin level with a supporting device in order to prevent retraction of the ostomy. A supporting rod may result in difficult stoma bag application and leakage of faeces even with correct elevation of the limbs. We compared morbidity and time to self-sufficient stoma-care in patients having a LI with rod to those without rod.

Methods: 60 patients requiring LI (30 with rod, 30 rodless) were analyzed for morbidity according to a scoring system ranging from 0 to 4 points for bleeding, necrosis, skin irritation, abscess, retraction, fistula, prolapse, parastomal hernia, inhomplete diversion, where 0 = no complication and 4 = severe complication. Continuous variables were expressed as median (95% CI). Inter-group comparisons used the Mann-Whitney U test, categorical variables the χ² test.

Results: There were no differences in age, gender, rate of emergency-operations, number of diabetics and hospital stay length between the two groups. The total morbidity score also was not significantly different (p=0.5), but severe complications (score≥5) occurred significantly more in the rod group (p=0.04). Although not significant, patients having a LI with rod had a tendency towards more stoma-related reoperations. There was no significant difference in time to self-sufficient stoma-care between the groups (p=0.88). However, the number of patients reaching total self-sufficiency regarding stoma-care was higher after rodless LI (26 v. 20 regarding changing the stoma-bag respectively 24 v. 17 patients for changing of the stoma plate; p= 0.07 and 0.05 respectively).

Conclusions: According to our data, rodless LI seem to fare just as well as those with a supporting rod, with the rodless group having lower severe morbidity rates and more patients reaching self-sufficient stoma-care. Therefore routine application of a rod for diverting LI seems unnecessary.
In Vietnam HBV and HCV prevalence is higher in urban setting than in rural areas.

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Background: Vietnam has a very high prevalence of HBV of 10 to 20% in three community based studies. HCV prevalence is reported at 1% in rural areas and estimated over 5% in Ho Chi Minh City (HCM). In urban areas the higher prevalence of HBV and HCV may be due to increased healthcare related risk factors. Results recorded in a hospital in HCM are reported.

Methods: 1) HBV and HCV serology was done during a World Digestive Health Day 2007 campaign in patients coming to the hospital 2) two cohorts of HBV and HCV patients were studied from May to August 2007.

Results: 1) serology in 378 Vietnamese attending a city hospital: mean age 36.5 y, HBsAg+: 105 (27.7%), anti-HBc+: 145 (38.3%), anti-HCV+ 27 (7.1%), co-infection HBV/HCV 21 (5.6%), negative serology:122 (32.3%), 2) HBsAg+ cohort (397 patients): 57.2% men, HBsAg+ 29% with 93.4% HBV-DNA>104 IU/ml, HBeAg-71% with 39.7% HBV/DNA>104 IU/ml, HBeAg-71% with 39.7% HBV/DNA>104 IU/ml. HCV cohort (228 cases): 47.4% men, 68.2% genotype 1, 12.9% genotype 2, 18.1% genotype 6.

Conclusions: 1) in a patient population attending a hospital in HCM the prevalence of HBV was higher than that reported in rural zones. HBsAg was found in 29% and high HBV-DNA in 58.4%. The prevalence of HCV was 7.1%. Genotype 1 and 6 were the most frequent (86.3%). Preventive measures are being promoted as a huge liver disease related burden is projected in Vietnam.

Health care related risk factors, difficult genotypes and moderate fibrosis underlie the management of hepatitis C in the south of Vietnam

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Background: Few reports are published on hepatitis C in Vietnam and none with liver biopsy. We aimed to fully characterize clinical factors and liver histology in a setting with high prevalence in order to base clinical management.

Methods: a series of 100 consecutive liver biopsies performed in HCV+ patients attending an hospital in Ho Chi Minh City was studied, and epidemiological and biochemical factors are analyzed in order to find predictors of advanced fibrosis.

Results: The group included 50% men, 98% Vietnamese, mean age was 47.5 years, BMI was +23 in 63%. Risk factors were: previous invasive medical procedure in 48%, blood transfusion in 25%, acupuncture in 18%, heroin injection in 2%. Only 17% drank more than 20 g of alcohol per day. HCV genotypes were: 66% genotype 1, 7% genotype 2, 1% type 3, and 23% type 6. Metavir scores of fibrosis were F0/F1 in 69%, F2/F3/F4 in 31%. Sex, age, BMI, alcohol, viral load, and others risk factors were not predictive of advanced fibrosis. APRI score was the only independent variable predictive of advanced fibrosis.

Conclusions: There is predominance of genotype 1 and high frequency of genotype 6 in this series of patients. Liver biopsy showed that benign histological forms were more frequent than severe. Risk factors for infection were related to healthcare and risk factors for progression of fibrosis such as alcohol and overweight were found only in a minority. This background of moderate fibrosis on histology and difficult to treat genotypes underlies clinical management of hepatitis C in the south of Vietnam.

BCRP deficiency in human colorectal adenomas and in the Apc Min mice promotes accumulation of the colon carcinogen PhIP and may represent an acquired susceptibility factor for colon carcinoma

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1 Klinikum Aschaffenburg, Med. Klinik II, 2 Universitätsklinikum Aachen, Med. Klinik III, 3 Universitätsklinikum Giessen, Med. Klinik II, all in Germany, 4 Universitätsklinik Zürich, DIM, Gastroenterologie & Hepatologie

Background: Several molecular changes in colorectal adenomas provide the basis of the adenoma-carcinoma sequence. We investigated the expression of transporters for xenobiotics, which confer cellular toxicological resistance, in humans and in Apc Min mice and conducted functional studies estimating the importance of the expression changes.

Methods: 30 adenomas from 25 patients and 8 adenomas from 4 Apc Min mice were analysed regarding the expression of Breast Cancer Resistance Protein (BCRP/ Bcrp) using Western Blotting and quantitative RT-PCR. In a functional study, Apc Min mice received radioactively labelled PhIP, a heterocyclic amine and food colon carcinogen, by oral gavage, later analyzing adenomatous tissue regarding PhIP accumulation.

Results: BCRP was significantly downregulated in human colorectal adenomas (35 ± 30 % compared to adjacent healthy tissue). This was in line with data from Apc Min mice adenomas, where downregulation was significant as well (98 ± 34%). In parallel, quantitative RT-PCR showed mRNA downregulation in human adenomas (17 ± 31 %), 48 h after oral gavage of PhIP; we could demonstrate a higher carcino genesis concentration in adenomas of Apc Min mice (181 ± 113 % when compared to normal tissue). Other xenobiotics transporters (MRP2/Mrp2 and MDR1/Mdr1) were unchanged.

Conclusions: Significant transcriptional downregulation of BCRP/Bcrp leads to higher carcino genesis concentrations in colorectal adenomas. This might promote the adenoma-carcinoma sequence by higher genotoxic effects. The results indicate a possible role of transporter deficiencies in susceptibility for colon carcinoma. Further studies regarding the impact on DNA adduct formation of PhIP in adenomas are ongoing.

A biphasic response with enhanced transcription and subcellular shutting of Y-box protein 1 to inflammatory signals regulates hepatic Mrp2 gene expression

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1,2 Universitätsspital Zürich, DIM, Gastroenterologie & Hepatologie, 3 Universitätsspital Zürich, DIM, Gastroenterologie & Hepatologie

Background: Expression of hepatobiliary transporters is decreased during endotoxemia. Reduction of Mrp2 is mediated by IL-1ß-dependent signals but the underlying mechanism is still unclear. YB-1 is a predominantly cytoplasmic protein which translocates to the nucleus in response to various insults. Consequently, we characterized the mechanisms of YB-1 activation and its potential role as a regulator of hepatic acute phase genes.

Methods: Liver sections from LPS-injected rats (20h) were stained with YB-1-specific antibodies. RT-PCR quantification was performed for Mrp2, MMP-2 and YB-1. YB-1 protein was quantified from IL-1ß- or TNFα-stimulated FAO cells and the localization of a CFP-YB-1-YFP fusion protein was visualized by confocal microscopy. CHP assays and EMSA were performed analyzing YB-1 DNA-binding.

Results: In endotoxemic livers Mrp2 mRNA was down-regulated to 20%, while YB-1 mRNA expression increased 2.5-fold. Immunohistochemical staining showed a marked up-regulation and predominant nuclear localization of YB-1 protein. In FAO cells IL-1ß caused an increase in cytoplasmic YB-1 protein up to 16 hours. As a rapid effect within 90 min, IL-1ß-stimulation resulted in a 6-fold up-regulation of Mrp2, MMP-2 and YB-1. YB-1 protein was quantified from IL-1ß- or TNFα-stimulated FAO cells and the localization of a CFP-YB-1-YFP fusion protein was visualized by confocal microscopy. CHP assays and EMSA were performed analyzing YB-1 DNA-binding.

Conclusions: YB-1 is activated during the hepatic acute phase response by time-dependent cellular changes: a IL-1ß-mediated rapid nuclear shutting within 90 minutes and a transcriptional induction thereafter. This biphasic response now explains the IL-1ß-mediated suppression of Mrp2 in endotoxemic rats.
Beware of Colophos® in the elderly! Gerber L., Meyer-Heim T., Heuss L.T., Bleisch J.A. Spital Zollikerberg, CH-8123 Zollikerberg, a Medizinische Klinik, b Nephrologische Abteilung

Background: Phosphate-containing purgatives for bowel cleansing before colonoscopy are popular. The potentially hazardous side effects are still underestimated.

Case study: A 73-year-old woman was referred to our nephrological ambulatory due to an acute and progressive worsening of a previously mildly impaired kidney function of unknown origin. There was no history of hypertension or diabetes. A pre- or postrenal kidney disease could be excluded. Extensive serum and urine analysis didn’t reveal any cause. The kidney biopsy finally showed a distinct phosphate nephropathy. We identified Colophos®, a phosphate-containing purgative as the causing agent, which the patient had received for bowel cleansing before a colonoscopy one day before the detection of the acute kidney failure. During the following months the kidney function initially declined further (Peak Serumkreatinin 284 μmol/l) and then improved (Serumkreatinin 124 μmol/l one year later).

Discussion: Phosphate nephropathy is a rare but underestimated cause of an acute renal failure. Most cases are associated with the ingestion of phosphate-containing purgatives. Persons at risk are women, elderly persons, patients with impaired kidney function, hypotension, and dehydration. The consequence is sometimes an irreversible tubulo-interstitial injury that can lead to end-stage renal disease in a minority of the cases. Therefore gastroenterologists should be cautious to prescribe phosphate-containing purgatives in this risk group and should favour safer alternatives.

Treatment of HCV in HCV mono-infected and in HIV-HCV co-infected patients: an open-labeled comparison study Wagner G., Oneta C., Gonvers J.-J., Heim M., Cavassini M. Laboratory of Internal Medicine, Department of Infectious Diseases, Geneva University Hospitals, Switzerland

Background and aims: The treatment of chronic HCV infection has become a major public health issue in the last decade due to its propensity to develop into end-stage liver disease. The primary endpoint of this study was to evaluate the antiviral efficacy of Peginterferon alpha 2a plus ribavirin in HCV mono-infected patients and in HIV-HCV co-infected patients, and to examine whether 6 months of therapy would suffice in HIV patients with favourable genotypes 2 and 3. Secondary endpoints were to evaluate predictors of response and frequency of side-effects.

Methods: Patients with genotypes 1, 4, 5 were treated for 48 weeks with Pegasa®180 μg per week plus Copegus® 1,000-1,200 mg daily. Patients with genotypes 2, 3 were treated for 24 weeks with Pegasa®180 μg per week plus Copegus® 800 mg daily.

Results: 132 patients were included in the study: 85 HCV mono-infected (38 with genotypes 1, 4, 5; 47 with genotypes 2, 3) and 47 HIV-HCV co-infected patients (p = 0.001). For genotypes 2,3 SVR was observed in 70% of HCV mono-infected and in 67% of HIV-HCV co-infected patients (p = 0.973). Absence of a 2-log drop in HCV-RNA or an undetectable viral load after 12 weeks was a potent negative predictor of treatment response in all patients. Undetectable HCV-RNA at week 4 had a high positive predictive value of SVR. The Study was not terminated in 22 patients (36%) with genotypes 1, 4, 5 and in 12 patients (17%) with genotypes 2, 3.

Conclusion: Genotypes 2,3 predict the likelihood of SVR in mono-and in co-infected patients. In conformed patients with genotypes 2,3 a 6-months treatment has the same efficacy as in mono-infected patients. To increase SVR it is crucial to avoid withdrawals/treatment-stops.

Value of spatiotemporal representation of manometric data Claudia Grübel1, 2, Richard Hiscock3, Geoff Hebbard1 1 Dept. of Gastroenterology, The Royal Melbourne Hospital, Australia, 2 Dept. of Gastroenterology, Kantonsspital St.Gallen, Schweiz, 3 Dept. of Obstetrics and Gynaecology, Mercy Hospital, Heidelberg, Australia

Introduction: High-resolution manometry with spatiotemporal representation of pressure data is a technique that has developed over the past 10-15 years. We compared spatiotemporal and traditional line plot representation of manometry data in a group of medical students in terms of the ability of the user to come to a rapid and accurate diagnosis, and evaluated user preferences for the two forms of data display.

Methods: Following standardised paper-based and electronic tutorials, sixty medical students classified 30 typical examples of a range of motility disorders in both line plot (10 sensors, including a ‘virtual sleeve’) and spatiotemporal plot format (derived from 16 sensors). Swallows were presented electronically in random order. The accuracy and speed of the assessment were compared between the two forms of data presentation, as well as a subjective rating of preference. Results are presented as mean ± SEM.

Results: Classifications based on data presented in spatiotemporal format were more often correct (89 % ± 1.2% vs. 86 % ± 1.3%, p = .002) and correct diagnoses were provided more promptly (25 ± 2.9 s vs 31 ± 3.2 s, p < .001), than in line plot format. 93 % of the study population preferred the spatiotemporal presentation.

Conclusions: The analysis of manometry data by manometry naïve individuals is faster and more accurate when data is presented in spatiotemporal than in line plot format. In addition, users preferred the spatiotemporal plots. Spatiotemporal presentation of manometric data is likely to be more easily understood by patients and the ‘non-expert’ physician community.

Anastomose colo-anale: Comparaison entre les anastomoses hautes et basses. Résultats péri-opératoires et qualité de vie. Marc-Olivier Guerin, Béatrice Kern, Ida Montal, Markus von Flie Allgemeinchirurgische Abteilung, St. Charles, 4068 Bâle, Suisse

Buts: Nous voulions évaluer, à l’aide de formulaires standardisés, pour les reconstructions colo-anales basse avec résection inter sphinctérienne, les résultats pér-opératoires et la qualité de vie post opératoire.

Patients et méthode: Entre 2000 et 2005, 69 patients ont subis dans notre clinique une résection antérieure basse avec anastomose colo- anale et stomie de protection. La fermeture de cette stomie a été effectuée entre trois et six mois plus tard. Chez 13 patients il s’agissait d’une anastomose très basse. On a relevé prospectivement la morbidité péri-opératoire. Le contrôle à long terme a été effectué à l’aide des formulaires standardisés selon Eypasch (Gastro-Intestinal Quality of Life score) et Wexner.

Résultats: Le groupe de patients comportait 32 femmes et 37 hommes. Chez 13 patients, une résections très basse avec anastomose manuelle intra anale a été effectuée; chez 56 patients, une résection antérieure basse avec anastomose colo-anale mécanique a été effectuée. La durée opératoire était de 330 min pour les reconstructions intra anales et de 261 min pour les anastomoses mécaniques. En post opératoire, 3 patients ont présenté une infection urinaire. Une infection de cathéter central a aussi été relevée. Aucune complication chirurgicale n’a été relevée La durée d’hospitalisation était de 17 jours. La mortalité n’a été nulle. Tous les patients encore en vie à l’heure actuelle ont reçu le formulaire de contrôle standardisé avec un taux de retour de 65%. La durée moyenne entre l’opération et la réponse au formulaire était de 1,98 ans. Le score d’Eypasch était de 101 pour les anastomoses manuelles respectivement de 112 pour les anastomoses mécaniques. Le score d’incontinence de Wexner était de 7 pour l’anastomose mécanique et de 8 pour l’anastomose après résection intersphinctérienne.

Conclusion: Les anastomoses colo-anales basses, compris lors de résections intersphinctériennes, sont une technique sûre. Les résultats péri-opératoires des deux techniques sont (hormis le temps opéra- toire) comparables. Lors du contrôle à long terme : – Les patients ayant subi une anastomose très basse présentent des résultats inférieurs pour ce qui est de la qualité de vie et de la conti- nence. Les anastomoses très basses sont faisable techniquement mais les patients devraient être informé des problèmes de continence et de la réduction de la qualité de vie qui en découle.
Acute Liver Failure Upon Insertion of Transjugular Intrahepatic Portosystemic Shunt in a Patient with Glycogenosis Type IIIb and Immediate Resolution after Shunt Reversal

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Background: Transjugular intrahepatic portosystemic shunt (TIPS) is successful in the management of recurrent variceal bleeding in patients with liver cirrhosis. Complications comprise hepatic encephalopathy, silent occlusion, and liver hydropsferation.

Case Report: A 51-year-old female patient with liver cirrhosis due to glycogenosis type IIIb was listed for liver transplantation with CHILD A and MELD 12 score because of recurrent variceal bleeding and a single episode of grade IV encephalopathy. During the elective TIPS shunt insertion the portovenous pressure gradient was 22 mm Hg and liver parameters were near normal (ASAT 49 U/L, INR 1.1, MELD-8). 48hr later hyperacute liver failure developed (ASAT 4802 U/L, INR 2.9, encephalopathy grade III, MELD 31) requiring mechanical ventilation and hemofiltration. Toxic, vascular, and infectious causes were ruled out. Portosystemic shunt volume was found at 1,600 ml/min with no evidence for hepatic hydropsferation. Emergency TIPS revision and reduction of stent diameter from 10 to 7mm was performed. Hepatic angiography revealed normal liver perfusion. Within 24hr, liver and kidney failure, and encephalopathy resolved. The patient successfully underwent liver transplantation 11 days thereafter.

Conclusion: Patients with glycogenosis type IIIb may be more susceptible to hepatic hydropsferation and acute hepatic dysfunction due to TIPS-related portosystemic shunting. In such cases, immediate reinsertion of TIPS diameter should be considered.

Radiochemotherapy for Locally Advanced Rectal Cancer

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Objective: Radiochemotherapy for locally advanced rectal cancer is currently the gold standard for patients with locally advanced adenocarcinoma of the middle and lower third of the rectum.

Methods: The clinical data of a prospective study on 79 patients was presented with special interest on downstaging, perioperative morbidity and short-term follow-up.

Results: Median follow-up was 16 months (1-33), mean age was 65 years (20-86). Mean tumor distance from anal verge was 6 cm (1-13). After RCT 51% were downstaged with MRI and 45% with endorectal ultrasound. Rectal amputation was performed in 25%, 75% had a sphincter preserving procedure. Major complications were seen in 5.8%, including 2 anastomotic leaks. On histopathologic analysis 21% of specimens were ypT0 ypN0 with tumor regression grade 4. One local recurrence and 3 distal metastases occurred 7 to 24 months after RCT.

Conclusion: Neoadjuvant radiochemotherapy (RCT) is effective with good downstaging and complete pathologic response in 21%. Surgery after RCT is well tolerated and can be performed with very low morbidity.

Radiochemotherapy for Rectal Cancer: A Predictor of Response to Neoadjuvant Treatment

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Objective: Predictors for pathologic complete response after neoadjuvant radiochemotherapy for locally advanced rectal cancer are currently unknown. The tumor suppressor gene p53 has been proposed to play a role in tumor response to RCT. The aim of this study was to examine the correlation between p53 expression before and tumor response after neoadjuvant RCT.

Methods: The study included 51 patients with rectal cancer stage T3 or T4 and neoadjuvant RCT. Immunohistochemistry was done for p53 before RCT. Tumor regression was graded according to Dworak (D0-D4). A semiquantitative grading system and the immune reactive score were considered in the staining system.

Results: p53 expression on tumor biopsies was positive in 40/51 cases (78%) and negative in 11/51 cases (22%). Correlation of p53 and tumor response to RCT.

Conclusion: Immunohistochemical expression of p53 on rectal cancer cells before RCT does not correlate with tumor regression grade. It is not helpful to identify patients with good response to the neoadjuvant treatment.
Incidence and treatment of incisional hernia after liver transplantation

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Background: The incidence of incisional hernia is a common complication in abdominal surgery. However, little data is available regarding incidence and treatment strategies in patients post orthotopic liver transplantation (OLT). Our study was performed to evaluate the outcome after open with laparoscopic incisional hernia repair in these patients. A prospective cohort of patients with OLT allows us to describe the incidence of incisional hernia.

Methods: Our study based on 225 patients who had undergone OLT. The demographic parameters like age, BMI and MELD score were similar in both groups. Different techniques/mesh were used in the open group whereas in the laparoscopic group a single type of mesh was used. The operative time in the laparoscopic group was significantly longer (p<0.001) compared to open surgery. No statistical difference was found for the median length of hospital stay (7 days in the laparoscopic group vs. 8 days in the open group). Postoperative complications were similar in both groups. Different techniques/mesh were used in the open group whereas in the laparoscopic group a single type of mesh was used. The operative time in the laparoscopic group was significantly longer (p<0.001) compared to open surgery. No statistical difference was found for the median length of hospital stay (7 days in the laparoscopic group vs. 8 days in the open group). Postoperative complications were similar in both groups.

Results: The incidence of incisional hernia after OLT in our study group was 25.8% (58/225), occurring after a mean of 29 months. Among these patients 44 underwent incisional hernia repair (31 patients received open and 13 laparoscopic surgery). The demographic parameters like age, BMI and MELD score were similar in both groups. Different techniques/mesh were used in the open group whereas in the laparoscopic group a single type of mesh was used. The operative time in the laparoscopic group was significantly longer (p<0.001) compared to open surgery. No statistical difference was found for the median length of hospital stay (7 days in the laparoscopic group vs. 8 days in the open group). Postoperative complications were similar in both groups. Different techniques/mesh were used in the open group whereas in the laparoscopic group a single type of mesh was used. The operative time in the laparoscopic group was significantly longer (p<0.001) compared to open surgery. No statistical difference was found for the median length of hospital stay (7 days in the laparoscopic group vs. 8 days in the open group). Postoperative complications were similar in both groups.

Conclusion: The incidence of incisional hernia post OLT is high. Laparoscopic incisional hernia repair in patients post OLT is safe and associated with a trend towards a lower rate of complications and recurrence rate.

Predictive factors for morbidity and mortality in patients undergoing laparoscopic paraesophageal hernia repair

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Background: Patients undergoing laparoscopic paraesophageal hernia repairs (PEH) repair risk substantial morbidity. The aim of this study was to analyze predictive factors for postoperative morbidity and mortality.

Methods: 354 laparoscopic PEH repairs were analyzed from the database of the Department of Visceral and Transplantation Surgery (SALTS). Age (>70 and ≥70 years) and risk (low: American Society of Anesthesiology (ASA) scores 1 + 2; high ASA 3 + 4) were defined and multivariate logistic regression was conducted.

Results: In patients ≥70 years postoperative morbidity (24.4% versus 10.1%) and mortality (2.4% versus 0%) was significantly higher compared to patients <70. In patients with gastropathy, this significant difference was again present (38.8% versus 10.5%) whereas in patients with fundoplication no difference between age groups occurred (11.9% versus 10.1%). Mortality did not differ. High risk patients had a significantly higher morbidity (26.0% versus 11.2%) but not mortality (2.1% versus 0.4%). The multivariate logistic regression identified the following variables as influencing postoperative morbidity: Age ≥70 years (OR 1.99); ASA 3 + 4 (OR 2.29); type of operation (gastropexy) (OR 2.36).

Conclusion: Age, ASA score and type of operation influence postoperative morbidity and mortality significantly. Morbidity is substantial in elderly patients and those with comorbidity, questioning the paradigm for surgery in all patients. If surgery is considered, repair with fundoplication should be preferred, independent of patient’s age.

Das Darmkrebs Screening mittels Kolonoskopie vermindert Mortalität und Auftreten späterer Kolonkarzinome massiv

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Hintergrund: Die Evidenz für die Effizienz des Screenings (S) mittels Kolonoskopie (K) ist v.a. indirekt. Die Inzidenz kolorektaler Karzinome (CRC) nach Polypektomie wurde einzig mit epidemiologischen Kohorten verglichen. Prospective auf der Durchschnittsbevölkerung basierende Daten fehlen.


Ergebnisse: Die Screeningperiode traten mS diskret mehr CRC auf. Die kumulative Inzidenz war nach 1 Jahr mS und oS ausgeglichen. Danach traten 217 CRC oS (62% Männer, 58% im Sigma) und 1 mS auf. 19,4% der CRC oS waren T1-2NoMo, 72% jener mS. Über 25% oS starben, einer mS (Infarkt). Landwirte liessen sich seltener scannen. Raucher und Arbeiter hatten gehäuft CRC, Kader leute seltener. 1% Verwandte mit CRC waren häufiger mS, der BMI war vergleichbar. Screeningpatienten lebten tendentiell diskret gesundheitsbewusster. In Uri mit 25% Leuten mit K zeigt sich ein Trend zur Abnahme der Ca.


Fulminant Liver Failure due to Sulfasalazine-induced DRESS Syndrome: Fatal Recurrence after Liver Transplantation

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Background: DRESS syndrome (Drug Rash with Eosinophilia and Systemic Symptoms) is a rare drug hypersensitivity reaction with a mortality of up to 10% precipitated by anticonvulsants, antibiotics and other drugs. Clinically, fever, eruptive skin rash, hypereosinophilia and organ involvement like hepatitis, myocarditis or interstitial nephritis may evolve.

Case Report: A 60-year-old man with polyarthritis had been treated with predinsone and sulfasalazine for 6 weeks. After hospitalization with fever, antibiotic treatment with Vancocin was started. He subsequently developed a generalized scaled exanthema and face oedema, hypereosinophilia 0.78G/l and elevated liver enzymes. After a rapid increase of the latter to AST 18,473U/l and ALT 6.745U/l, a liver biopsy was performed which showed hepatic necrosis and eosinophilic infiltration, compatible with DRESS syndrome. The patient deteriorated to fulminant liver failure and underwent super urgent liver transplantation. After recovering well initially, the patient developed generalized exanthema and elevated liver enzymes. Liver biopsy showed an acute graft rejection together with abundant eosinophilic infiltration.
eosiinophilic infiltrates. The patient was treated with high-dose methylprednisolon. After 24 hours, the patient presented with cardiac arrest and died despite immediate resuscitation. Post-mortem examination revealed a total necrosis of the liver transplant and histology confirmed recurrent DRESS syndrome.

Conclusions: DRESS syndrome with consecutive liver failure may recur following liver transplantation and can be fatal despite immediate immunosuppressive therapy.

Low systemic mannose-binding lectin (MBL) production associates with complicated Crohn's disease and experimental MBL deficiency leads to more severe pathogen-amplified DSS-colitis

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Background: Mannose-binding lectin (MBL) represents a first line of defense mechanism against yeasts and certain bacteria. Even though we have observed an association of MBL-deficiency with anti-Saccharomyces cerevisiae antibodies (ASCA) in Crohn's disease (CD), the role of MBL in the pathogenesis of CD is unclear. A possible correlation between distinct disease phenotypes as well as consequences of MBL deficiency in experimental colitis have not been addressed so far.

Methods: Serum concentrations of functional MBL were measured by ELISA in 164 CD patients, 32 patients with ulcercative colitis (UC) and 51 healthy controls (hc). CD patients were grouped according to the Montreal classification. MBL was classified deficient (<100 ng/ml), low (100-500 ng/ml) and normal-high (>500 ng/ml). MBL was further quantified in samples collected during endoscopy and from full thickness small bowel specimens. DSS administration was used to induce experimental colitis. Wild type and MBL deficient mice were immunized with yeast to assess experimental ASCA generation.

Results: Low MBL levels were positively associated with complicated CD (P<0.001), while negatively associated with pure inflammatory disease (P<0.0001). MBL protein as well as mRNA was rarely detected in UC patients compared to wild type mice. Furthermore, MBL-deficient mice showed more severe DSS colitis especially when simultaneously challenged with an adhesive and invasive strain of E. coli, originally isolated from the ileum of a CD patient. The midgut of a 10-week-old fetus normally returns to the abdomen wall nor an obstruction of the duodenum existed. Furthermore, the appendix was removed. The postoperative course was uneventful.

Conclusions: The midgut of a 10-week-old fetus normally returns from the umbilicus to the abdominal cavity and undergoes counter-clockwise rotation about the superior mesenteric artery axis. Anomalies of intestinal rotation and fixation include nonrotation, incomplete rotation (malrotation grade I), reversed rotation (malrotation grade II) and anomalous fixation of the mesentery and often are associated with other anomalies such as duodenal stenosis, gastroscisis, omphalocele and situs inversus. When not operated in infancy adult patients with intestinal malrotation may present with acute or chronic obstructive symptoms. A Ladd procedure is recommended for incomplete rotation with obstruction of the duodenum by abnormal peritoneal bands. The appendix should be removed. Prompt recognition and surgical treatment usually lead to a successful outcome of this rare condition with excellent long-term results.

Intestinal malrotation – A rare cause of bowel obstruction in adults.

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Objective: Anomalies of intestinal rotation are very rare and may cause symptoms related to intestinal obstruction, peptic ulceration and malabsorption. 75% of patients develop intestinal obstruction in infancy.

Methods: We present the case of a 83 years old patient with a malrotation grade II as a rare cause of bowel obstruction and discuss the implications for diagnosis and therapy.

Results: A 83 years old patient was admitted due to crampy abdomen grade II as a rare cause of bowel obstruction and discuss the implications for diagnosis and therapy.

Conclusions: The midgut of a 10-week-old fetus normally returns to the abdomen wall nor an obstruction of the duodenum existed. Furthermore, the appendix was removed. The postoperative course was uneventful.

Conclusions: The midgut of a 10-week-old fetus normally returns from the umbilicus to the abdominal cavity and undergoes counter-clockwise rotation about the superior mesenteric artery axis. Anomalies of intestinal rotation and fixation include nonrotation, incomplete rotation (malrotation grade I), reversed rotation (malrotation grade II) and anomalous fixation of the mesentery and often are associated with other anomalies such as duodenal stenosis, gastroscisis, omphalocele and situs inversus. When not operated in infancy adult patients with intestinal malrotation may present with acute or chronic obstructive symptoms. A Ladd procedure is recommended for incomplete rotation with obstruction of the duodenum by abnormal peritoneal bands. The appendix should be removed. Prompt recognition and surgical treatment usually lead to a successful outcome of this rare condition with excellent long-term results.

Leptin-receptor deficiency protects from alcoholic and non-alcoholic liver fibrosis via lack of Cytochrome P450 2E1 induction in rats

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Background: Alcohol consumption may accelerate fibrosis development in coexisting non-alcoholic fatty liver disease. Apart from synergisms of fat- and alcohol-related pathophysiology, combined effects of both diseases on leptin-mediated fibrogenesis and cytochrome P450 2E1 (CYP2E1) induction are implicated. Our aim was to investigate the effect of chronic alcohol administration on liver fibrogenesis in obese, insulin-resistant rats.

Methods: Obese Zucker rats and their lean littermates (4 groups, n=10 each) were pair-fed a Lieber-De Carli alcoholic or control liquid diet for 12 weeks. Standard serum liver laboratory values were measured. Liver histology was assessed by Hematoxylin/Eosin, and fibro-
Abstracts Sup 41.qxp 3.9.2008 7:42 Uhr Seite 18

P26

A new method for Colorectal Cancer Screening: Capsule Endoscopy compared to Conventional Colonoscopy

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Background: Colorectal cancer (CRC) can be prevented by colorectal cancer screening. Microscope colonoscopy and sigmoidoscopy are the current methods for CRC screening. Since CRC screening cannot be ensured by only one screening method, a combination of different methods is recommended. Colonoscopy is the gold standard; it allows removal of colorectal neoplasms and polyps. Therefore, the aim of this study was to compare capsule endoscopy (CCE) with conventional colonoscopy (CC) in patients with colorectal polyps.

Method: A total of 59 patients were included at the University Hospital Basel (males 35, females 24; median age 59), the results were evaluable in 56 patients. The capsule endoscopy was complete in 36 subjects, and reached the colon in 21 patients but remained in the stomach in 1 case and in the small bowel in 2 cases. Of the 56 patients, 15 had significant findings; 10/27 (37%) of the relevant polyps were detected by CCE, compared to 24/27 (88.9%) on colonoscopy. (False positive findings on CCE for overall polyps were recorded in 11/41 (26.8%) cases, and in 3/15 (20%) cases with significant polyps. Overall sensitivity was 79%, specificity was 54%, positive predictive value was 63% and negative predictive value was 71%. Adjusted to significance of findings sensitivity was 33%, specificity was 95%, positive predictive value was 57% and negative predictive value was 93%. No adverse events were recorded.

Conclusion: Capsule endoscopy is a new alternative on the horizon for colorectal cancer screening, as suggested in previous pilot studies (3,4). The high negative predictive value supports its further role as a screening tool, however CCE were not able to detect all polyps found during colonoscopy. Whether CCE will be a valuable tool warrants controlled randomized testing.

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J.B.P. and S.P. contributed equally to this study

P27

The Swiss Inflammatory Bowel Disease Cohort Study (SIBDCS): founding and first observations

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Background: After a pilot population-based cohort, established in the Canton de Vaud between July 03 and Dec 04, the project was expanded in 2006 to become national-wide. Besides studying risk factors associated with the disease, major aims of the study relate to appropriateness of therapy, health resource consumption and influence of new biological therapies and psychosocial aspects linked with exacerbation of the disease. A Biobank has been set up in order to study coupling effects of genetics on clinical observations. Methods: 6 major IBD centers at Swiss university-based tertiary hospitals recruit patients as well as physicians outside the centers. All adult or pediatric IBD patients, with permanent residence status or being treated regularly in Switzerland are eligible for enrolment, on condition that a radiological-, endoscopic- or surgery-confirmed diagnosis had been established at least 4 months prior to inclusion or after at least one recurrence of the symptoms. Patients are followed up once a year. Data are collected through physician and patient contact using questionnaires. Results: 81 physicians are participating since 1st Nov. 06 to patient recruitment, 75% from the 6 major centers, 11% from regional hospitals and 14% are private practitioners. 1039 patients were enrolled, 60% suffering from Crohn’s disease and 38% from ulcerative colitis. In 29 cases, the diagnosis was an indeterminate colitis. The proportion of females is 50.4%. Mean age of the cohort is 43 yrs (+/- 15), ranging from 16 to 89 yrs. 74% of the patients have already responded to the first questionnaire and 15% are on hold (time to sending <= 3 mths). Conclusion: The newly-established Swiss IBD cohort study was launched 15 months ago and offers a real challenge in acquiring data about epidemiology of IBD in Europe, as well as evaluating patient health care and costs linked to these diseases.

P28

Assessing dysphagia during esophageal manometry: how well do liquid and solid swallows reproduce patients’ symptoms?

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Background: Esophageal motility abnormalities are often reported in patients with dysphagia undergoing esophageal manometry. Explaining patients symptoms based on esophageal manometry findings is challenging. Correlations between esophageal symptoms and manometry findings are underreported. Our aim was to evaluate correlation between esophageal symptoms and high resolution manometry findings.

Methods: Patients presenting for esophageal manometry were asked to report severity and frequency of dysphagia during the last 2 weeks prior to testing (dysphagia score). Esophageal high resolution manometry (HRM) was performed using a 32-channel water-perfused system and included 10 water (10 ml each) and 10 solid (bread) swallows. During esophageal manometry patients were asked after each swallow if they experienced dysphagia or not.

Results:

Data from 61 manometries performed in 74 patients (43 F, 31 M, mean age 46.3; range 18-87 years) totalising 801 liquid and 782 solid swallows were included in the analysis. The per-swallow analysis for liquid swallows found manometric simultaneous and ineffective contractions more likely to be associated with symptoms (12/49; 24.5% and 21/125; 16.8% respectively) compared to manometric normal contractions (6/487; 3.8%). Similar results were noticed during solid swallows. The per-patient analysis found significant (p<0.01) but moderate correlations between dysphagia score and % swallows perceived during testing (r=0.399 liquid and r=0.409 solid swallows) and between dysphagia score and % manometric normal contractions during liquid swallows (r=-0.357). Correlation between % swallows perceived during testing and % manometric normal swallowing was significant (p<0.01) but poor (liquid swallows r=-0.368, solid swallows r=-0.268).

Conclusion: While manometric characteristics of esophageal contractions play a role in the perception of individual swallowing, the proportion of manometric abnormal contractions is not solely responsible for the intensity of dysphagic symptoms.

References:
Prophylactic drainage after laparoscopic appendectomy in complicated appendicitis: A case matched study

Background: Little evidence is currently available about the utility or danger of prophylactic drainage in open surgery, especially in complicated appendicitis. Due to the absence of data in laparoscopy, we investigated the impact of prophylactic drainage in laparoscopic appendectomy for complicated appendicitis.

Methods: 130 consecutive patients operated between November 2003 and December 2006 with laparoscopic appendectomy for complicated appendicitis (perforation or phlegmon) and prophylactic intrapertonal drainage were matched one by one to 130 patients operated with the same conditions but without drainage between January 2005 and June 2007, controlling for age, gender, ASA score and Body Mass Index. Primary end-point was surgical complications and secondary were operation duration, transit recovery time and length of stay.

Results: Patients without drain had significantly less overall complications (7.7% vs. 18.5%, p=0.01). Similarly for the secondary endpoints, patients without drain had lower operation duration (59.4 vs. 76.4 min, p<0.0001), transit recovery time (2.5 days vs. 3.5 days, p=0.0068) and length of stay (4.2 days vs. 7.3 days, p=0.001).

Conclusion: Prophylactic drainage after laparoscopy in complicated appendicitis has no benefit and does even increase postoperative complications, operation duration and hospital stay. A prospective randomized study would have been a better demonstration that drainages are useless and even harmful in complicated appendicitis, but due to a change in policy in our department a case matched retrospective study was preferred. The present study had a sufficient statistical power and is therefore the best available evidence up to now. We conclude that prophylactic drainage in complicated appendectomy is not to be recommended and may be omitted safely.

Ficolin-2 and Ficolin-3 in Crohn’s disease

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Background: Ficolins are complement activating soluble pattern recognition molecules, the epitope is N-acetyl-glucosamine which is found in the cell wall of bacteria and yeasts. Ficolin-2 (expressed by liver) and ficolin-3 (expressed by liver/lung) are found in serum/ plasma. The role of ficolins in Crohn’s Disease (CD) is largely unknown.

Aim: Evaluation of association between ficolin serum levels, and serum reactivity to mannans (ASCA) and distinct CD phenotypes.

Methods: Serum concentrations of ficolin-2, ficolin-3 and ASCA were measured in 182 CD patients. 67 patients with ulcerative colitis (UC) and 67 healthy controls (HC). CD patients were classified into the following phenotypes: non-stricturing, non-penetrating (B1), stricturing (B2), and penetrating (B3).

Results: Serum levels of ficolin-2 were significantly higher in CD (1693±876ng/mL) and UC (1480±943) compared to HC (1170±765) (P<0.001 and P=0.028). Serum levels of ficolin-3 in CD patients (22659±10606) were not different from HC (24265±9690), UC patients (P<0.0001 and P=0.028). Serum levels of ASCA in CD (in percent): 63; in UC: 4; and in HC: 0. Serological profiles: Positivity for ASCA in CD (in percent): 63; in UC: 4; and in HC: 0. ASCA titers were distributed into low, intermediate and high positive (exclusion). CD patients with intermediate/high ASCA titers had significantly lower ficolin-2 levels (P=0.044) compared to ASCA low positive and ASCA negative CD patients. CD patients with intermediate/high ASCA titers had significantly lower ficolin-3 levels (P=0.0093) compared to ASCA negative CD patients. We found no significant association between resistance of ficolin-2 and -3 and distinct CD phenotypes.

Conclusions: CD patients have significantly higher ficolin-2 levels compared to HC, possibly reflecting ficolin-2, but not ficolin-3, upregulation during inflammatory conditions. Association of high ASCA titers with low ficolin-2 and -3 levels may indicate reduced clearance of GlcNAc-carrying antigens such as yeast mannans. Ficolin-2 and ficolin-3 concentrations do not correlate with a distinct CD phenotype.
Longterm follow-up after multimodality treatment for locally advanced rectal cancer
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Longterm multimodality treatment of locally advanced rectal cancer patients has become a strategy to further improve the outcome of these patients. This report analyses the longterm follow up of patients concerning complications, response rate, local recurrence, disease stage (DFS) and overall survival (OS).

Methods: 149 neoadjuvant treated rectal cancer patients undergoing surgery at our institution from 9/95 to 12/07 were prospectively analysed. The median distance of the tumour to the dentate line was 4.5cm. Either 5-Fluorouracil or Capecitabine/Oxaliplatin concurrent with radiation (25x1,8Gy) was given. Surgery was performed within 4-8weeks after completion of neoadjuvant treatment.

Results: 117 (79%) patients got sphincter saving procedures. Histological complete responses (CR) was 13.5% (20 patients), 76 (51%) showed a partial response (PR), 32 (21.5%) were stable and 21 (14%) had progressive disease. Inhospital-mortality was zero. 89 (60%) patients had faecal incontinence (FI). CR survival rate was 16% (19/117). Presacral abscesses were observed in 20% (30/149). Reoperations were necessary in 19% (28/149). Median follow-up was 58 months. 7 patients got APR during follow up because of recurrence (2), faecal incontinence (5) or perforated diverticulitis (1). Therefore, longterm sphincter saving rate after 24 months is 73% (109/149). Patients with pathological CR (20) are all without any recurrent disease. Local/regional recurrence is 9% (14/149), deduced 1 to 9 months after primary surgery. Overall 5-year-survival is 70%.

Conclusion: Our results indicate a benefit of neoadjuvant treatment concerning CR and sphincter saving procedures. Pathological CR is a prognostic factor for a excellent longterm disease-free and overall survival. Severity of complications after longterm neoadjuvant radiochemotherapy in low rectal cancer should alert surgeons and oncologists. Further investigations should be done on more precise pretreatment and preoperative staging to prevent overtreatment. For patients with metastatic disease, Imatinib improves prognosis and amends a subgroup to secondary surgery.

Results: CD patients characteristics: 36% strictureting, 27% fistulizing, 37% inflammatory, Serological profiles: Positivity for pA4-Fla2/Fla-X/ASCAPanCA (in percent) in CD: 59/57/62/12; in UC: 6/6/4/51; in HC: 4/4/5/0, Antibodies to A4-Fla2, Fla-X, and ASCA were significantly associated with strictureting (P=0.006, P=0.023, P=0.0001), and fistulizing (P=0.029, P=0.01, P=0.016) phenotype, small bowel disease (P=0.002, P<0.0001, P<0.0001) and small bowel surgery (P=0.03, P=0.01, P<0.0001), P-ANCA associated significantly with inflammatory phenotype (P<0.0001). NC02 mutant alleles correlated with small bowel disease (P=0.025). Multiple antibody responses toward microbial antigens were associated with strictureting (P<0.0001) and fistulizing disease (P<0.002), and small bowel surgery (P<0.002).

Conclusions: ASCA and anti-flagelin antibodies are strongly associated with complicated CD phenotypes. CD patients with serum reactivity toward an increasing number of microbes have the highest frequency of strictures, perforations, and small bowel surgery. ASCA, anti-flagelin-antibodies and pANCA can help the clinician in risk assessment of CD patients.

Eosinophilic Esophagitis: Analysis of Food Impaction and Perforation in 251 Adult Patients
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Dilation in Eosinophilic Esophagitis: Safety, effectiveness and impact on mucosal inflammation
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Background: Topical corticosteroids are effective in Eosinophilic esophagitis (EE), but relapses occur early after cessation of therapy. In contrast, esophageal dilation often leads to long-lasting symptom improvement. Aim: To evaluate the effect of dilation on the underlying inflammation and to assess the efficacy and safety of the procedure.

Methods: Retrospective analysis of the Swiss and Chicago EE Database. Inclusion: EE patients undergoing 1) Baseline EGD with esophageal biopsies; 2) Subsequent dilation for dysphagia; and 3) Follow-up EGD with repeated biopsies. Any therapy with anti- eosinophilic medication had to be discontinued at least 12 weeks prior to dilation and until after the post-dilation EGD. Dysphagia was graded using a validated score (0-4). Eosinophilic peak infiltration was graded semi-quantitatively (0-3).

Results: We identified 46 patients (38m/8f), mean age at symptom onset 28±15years, mean duration of symptoms prior to dilation was 13±10years. Mean duration between completed dilation therapy and re-appearance of symptoms was 24±23months. Mean dysphagia score before dilation was 1.9±0.4 compared to 1.0±0.6 after dilation (P=0.0001). A mean of 2.3±2.7 dilation endoscopies were performed until dilation therapy was considered effective. No major complications (esophageal perforation or major bleeding) occurred. The grade of eosinophilic peak infiltration before dilation was 2.1±0.8 compared to 2.0±0.4 in the post-dilation EGD (P=0.76).

Conclusions: 1) In EE, esophageal dilation can be safely performed and is effective in providing long-lasting symptom relief and a significant reduction of the dysphagia score. 2) Underlying eosinophilic inflammation is not influenced by the dilation. 3) Esophageal remodelin likely contributes to the swallowing disturbances in EE.
**Abstracts Sup 41.qxp 3.9.2008 7:42 Uhr Seite 21**

**Results:** During an 18-year period, 87 of the 251 EE-patients (34.7%) experienced a total of 134 long-lasting food impactions requiring endoscopic food impaction. Food impaction occurred exclusively in untreated patients. The impacted bolus was removed 124 times by flexible (62.5%) and 10 times (7.5%) by rigid endoscopy. The rate of transmural perforation was significantly higher (p<0.001) in rigid 2/10 (20%) compared with flexible 0/124 (0%) procedures. Furthermore, one (0.4%) spontaneous esophageal rupture (Boerhaave’s syndrome) was observed after severe esophageal perforation and should be avoided. Whether food impaction and esophageal wall remodeling can be prevented with consequent anti-inflammatory medication is still undetermined. All Boerhaave syndrome cases should be evaluated for underlying eosinophilic esophagitis.

**Low Mannan Binding Lectin serum levels are associated with complicated Crohn’s Disease phenotypes and reactivity to oligomannan (ASCA)**

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**Background:** Mannan-binding lectin (MBL) acts as a recognition molecule directed against oligomannan which is part of the cell wall of yeasts and different bacteria. We have previously shown an association between MBL deficiency and ASCA positivity. Aim: to evaluate if MBL deficiency is associated with complicated CD phenotypes in the Swiss IBD cohort.

**Methods:** Serum concentrations of MBL and ASCA were measured (ELISA) in 427 CD patients, 70 with ulcerative colitis (UC) and 76 healthy controls (HC). CD patients were classified according to the Vienna criteria into inflammatory (43%), strictureing (26%), and penetrating (31%) phenotypes. MBL was classified as low (<500 ng/mL) and normal (500-4000ng/mL).

**Results:** Mean MBL in UC patients (1697±1421ng/mL) was not different from HC patients with stenosis and/or fistula (1539±1426ng/mL) compared to inflammatory phenotypes (1909±1392ng/mL) and normal (1909±1392ng/mL) patients. Lower MBL was observed in CD patients (1853±1353) compared to UC-like CD patients (P<0.0001). Mean MBL was lower in ASCA-positive CD patients (P=0.0001), UC patients (P<0.0001) and controls (P<0.0001). Mean MBL was lower in ASCA-positive CD patients (1575±1465ng/mL) compared to ASCA-negative CD patients (1909±1392ng/mL) (P=0.0001). ASCA-positive CD patients (56%) in CD, UC=8, 6 with indeterminate colitis (IC). The indication for IFX was a steroid dependent or refractory course of disease in 32%, fistulae in 40%, intolerance or ineffectiveness of immune suppressive treatment in 28% of patients. A total of 186 infusions of IFX were given. All 52 patients but 4 were on an IFX maintenance therapy. IFX was stopped in 13 patients due to a stable remission, 65% of patients responded well to IFX according to the opinion of the treating physician. An improvement was described in 31 %, and 2 patients did not respond to IFX. The average CRP was 23.3mg/L before and 7.1mg/L after under IFX treatment (p<0.0001). The mean CDAI decreased 60 points in CD patients (p<0.0001). The average weight increased after IFX: 2.3kg in CD, 2.1kg in UC, 4.3kg in IC. 21 CD patients were suffering from fistulae, 12 (57%) had a complete closure of fistula. A partial response to IFX was seen in 6, no response in 3 CD patients with fistula. Only 2.6% of CD patients had a 100% ability to work before but 48.5% of patients after IFX treatment UC=25% before, 87% after IFX (p<0.0001). Conclusions: In the Bern IBD cohort we observed a good clinical response to IFX regarding disease activity and fistulae closure. The ability to work was significantly increased what may balance the relatively high treatment costs.

**Clinical efficacy of infliximab and its effect on ability to work in a Bern IBD cohort**

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**Background:** Anti-TNF-Alpha-antibodies such as infliximab (IFX) (Remicade®) are used as second and third-line therapy in active Crohn’s Disease (CD) and ulcerative colitis (UC). The aim of this study was to investigate the clinical efficacy and economical consequences of an IFX therapy.

**Methods:** The IBD data bank of Bern was screened for patients treated with IFX in 2006. Data about disease activity (CRP, CDAI, weight change), doctors diagnosis (active or remission) and reactivity ability to work before and after IFX treatment were extracted.

**Results:** 52 patients with IBD were treated with IFX in 2006 (CD=38, UC=8, 6 with indeterminate colitis (IC)). The indication for IFX was a steroid dependent or refractory course of disease in 32%, fistulae in 40%, intolerance or ineffectiveness of immune suppressive treatment in 28% of patients. A total of 186 infusions of IFX were given. All 52 patients but 4 were on an IFX maintenance therapy. IFX was stopped in 13 patients due to a stable remission, 65% of patients responded well to IFX according to the opinion of the treating physician. An improvement was described in 31 %, and 2 patients did not respond to IFX. The average CRP was 23.3mg/L before and 7.1mg/L after under IFX treatment (p<0.0001). The mean CDAI decreased 60 points in CD patients (p<0.0001). The average weight increased after IFX: 2.3kg in CD, 2.1kg in UC, 4.3kg in IC. 21 CD patients were suffering from fistulae, 12 (57%) had a complete closure of fistula. A partial response to IFX was seen in 6, no response in 3 CD patients with fistula. Only 2.6% of CD patients had a 100% ability to work before but 48.5% of patients after IFX treatment UC=25% before, 87% after IFX (p<0.0001). Conclusions: In the Bern IBD cohort we observed a good clinical response to IFX regarding disease activity and fistulae closure. The ability to work was significantly increased what may balance the relatively high treatment costs.

**Simultaneous Interdisciplinary Approach to FGID – Results of a Pilot Study**

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**Background:** Since July 2007, we run an university outpatient clinic with a simultaneous interdisciplinary approach to functional gastrointestinal disorders (FGID). This study intended to analyze characteristics of patients admitted to our outpatient clinic. The interdisciplinary clinic for functional abdominal disorders (IBSP) from July 2007 until January 2008.

**Methods:** Patients have been referred to the ISBP on a nationwide scale by tertiary care outpatient clinics, general practitioners or spontaneously by patients. In every second patient on OMT in ZH, the necessary tests were not performed to determine whether antiviral treatment should be offered. Measures to improve adequate testing for HCV are necessary.

**Results:** 63 physicians or institutions (18% of OMT providers in ZH) participated in this study. They care for 1575 patients, which represents 43% of all patients on OMT in ZH. 279 randomly selected patient’s charts were analyzed. In 197 (70.6%) cases HCV antibodies were tested; among them 113 (57.4%) were positive and 84 (42.6%) were negative. In 82 (29.4%) charts no HCV antibody testing was found and in 67 (24.0%) not even liver enzymes were determined. 88 of the 113 HCV infected patients were positive for HCV-RNA-PCR, none were negative; in 25 cases no PCR-results were found. Genotype 1 or 2 were identified in 29 (33%) cases, genotype 2 or 3 in 12 (13.6%) respectively; in 47 patient charts (53.4%) we did not find any genotype results. 15 patient charts (17%) reflect a positive HCV test for HCV and ribavirine. 67 (24.0%) patients received less than minimal diagnostics even according to earlier guidelines. Also among HCV antibody positive patients, we found 72 (25.8%) patients who are not informed on chronicity of the infection (25) or about genotype (47).

**Conclusions:** In every second patient on OMT in ZH, the necessary tests were not performed to determine whether antiviral treatment should be offered. Measures to improve adequate testing for HCV are necessary.
categorized based on the diagnosis of the referring physician, reason for referral and prior examinations. ROME III criteria, ROME-FGID questionnaires, validated symptom questionnaires for vegetative disorders and standardized procedures for the exclusion of somatic disorders were applied.

Results: 20 patients were seen. In 8/13 patients (61%) admitted on the assumption of FGID, diagnosis had to be changed from FGID to functional disorders with abdominal symptoms (FDAS): Depression (n=5); PTSD (n=3); and anorexia nervosa (n=2). Of 9 patients externally diagnosed for IBS, only 4 met the ROME III criteria.

Conclusion: Patients are most often sent to the IBSP without adequate examination and classification. Due to the simultaneous interdisciplinary point of view, patients could be diagnosed earlier. Even Glasscocked specialties tend to neglect proper use of ROME III criteria.

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**Diagnostic performance of liver fibrosis in hepatitis C using transient elastography: the Geneva experience**

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**Background:** Transient elastography (Fibroscan, FS) is a non-invasive method to evaluate fibrosis in liver diseases. FS has been validated in hepatitis C, although cut-off values for significant fibrosis may vary among studies. FS values are considered valid provided that measurements are made according to the recommended standards (interquartile range IQR < 30%, success rate > 80%). The aim of the study was to investigate the diagnostic performance of FS in the evaluation of liver fibrosis in patients with chronic hepatitis C in our centre.

**Patients and Methods:** From October 2006 to March 2008, all patients with chronic hepatitis C who completed a diagnostic work-up in our hospital, using a FS (with values accepted as valid) and a liver biopsy (performed within <6 months of FS measurement) were included. The KUBAVIR liver fibrosis stage was determined on the liver biopsy by a single histopathologist (LRB) blinded to the patient's FS values. Efficiency of FS and optimal cut-off values for significant fibrosis stage assessment were determined by a receiver operating characteristics (ROC) curve analysis.

**Results:** The study population consisted in 98 patients (mean age 43 yrs, M/F: 60/38). FS values ranged from 5 to 45 kPa, with a mean IQR of 8%. The distribution of fibrosis stages (F0/1/2/3/4) among patients was as follows (in %): 24.5/27.8/9.2/10.2/29.6. The median FS value according to METAVIR stage 0/1/2/3/4 fibrosis were 4.69/6.2/8.35/9.8/14.5 kPa, respectively. FS values were well correlated with fibrosis stages (Spearmann rank correlation r = 0.675, p<0.0001). The areas under ROC curves were 0.86 for F0-1 versus F2-3-4, and 0.87 for F0-1 versus F3-4.

**Conclusions:** In our local experience, the use of FS for the detection of significant fibrosis in patients with chronic hepatitis C appears reliable and compares favourably with published data (Ziol, Hepatology 2005; Castera Gastroenterology 2005).

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**Severe hepatotoxicity after ingestion of Herbalife® nutritional supplements contaminated with Bacillus subtilis**

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**Background:** Recently, severe hepatotoxicity after the ingestion of Herbalife® preparations was reported, but hepatotoxic mechanisms remained unclear.

**Patients and Methods:** Two patients presented with cholestatic and severe cytolytic hepatitis. In a male patient, subacute liver failure developed with coagulopathy, whereas a female patient developed severe pruritus. Viral, metabolic, autoimmune, neoplastic, toxic and vascular liver diseases were ruled out. Both patients reported long-term intake of Herbalife® products. Patients were tested for immunoregulatory sensitization and Herbalife® products screened for contamination with drugs, pesticides, heavy metals, and contaminants.

**Results:** For microbiological analysis, Herbalife® samples were processed by standard and molecular procedures.

**Conclusions:** Histology showed cholestatic and mixed hepatitis with cirrhosis in the male patient, and biliary fibrosis with ductopenia in the female patient. Toxic contamination was ruled out, and hypersensitivity testing testing towards ingested substances of patients with active samples of Herbalife® products from each patient showed growth of gram-positive rods after 48h of culture. Bacteria were identified as Bacillus subtilus by sequencing the 16S rRNA gene and analysis of cellular patterns of responsiveness: One patient achieved a marked response and to reduce markedly the resulting symptoms. In contrast to the overall-analysis of this first translational study analyzing the efficacy of a TNF-α blocker, Infliximab, a monoclonal Antibody to TNF-α, for severe Eosinophilic Esophagitis in Adults: A prospective, translational Pilot-Study

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**Background:** Eosinophilic esophagitis (EE) is a clinicopathological defined condition characterized by PPI-refractory esophagus-related symptoms in combination with a dense esophageal eosinophilia. The pro-inflammatory cytokine TNF-α is up regulated and highly expressed in the squamous epithelial EE. TNF-α is therefore a promising therapeutic target. Infliximab, a chimeric monoclonal IgG1 antibody, is a potent inhibitor of the soluble and the membrane-bound form of TNF-α. The purpose of this study was to evaluate the efficacy and the tolerability of infliximab in adults with severe EE unresponsive to conventional therapy.

**Methods:** Three male adult patients (mean age 38 yr) with active EE (>20 eos/hpf and dysphagia), unresponsive to, or dependent on corticosteroids, received after a 4 week run-in period, infliximab, 5 mg/kg bodyweight, by intravenous infusion at week 4 and 6. Pre-and post-treatment disease activity was assessed clinically, endoscopically, histologically, and via biomarkers in the blood (ECP, TNF-α and tissuetype (ECP, TNF-α) expression, eosin(3)-Symptoms were recorded with a diary.

**Results:** All three patients had at baseline highly active EE with a dense eosinophilic infiltration of the esophagus (peak values 209, 311 and 79 eos/hpf) and with severe dysphagia. Treatment with infliximab did neither reduce significantly eosinophilic tissue infiltration (mean value pre-treatment 101 eos/hpf, post-treatment 121 eos/hpf) nor symptoms (symptom-score pre-treatment 8.6, post-treatment 7.6). A mild decrease of the TNF-α expression in the tissue was observed in two patients. Infliximab was well tolerated and no relevant adverse events occurred.

**Conclusions:** The overall-analysis of this first translational study analyzing the efficacy of a TNF-α blocker in adult patients with severe, refractory EE, unresponsive to conventional treatment or dependent on corticosteroids, shows that infliximab in a standard induction dosage-schedule is not able to induce a resolution of the eosinophilic tissue infiltration and to reduce markedly the resulting symptoms. In contrast to the general evaluation, the per-patient analysis reveals three different patterns of responsiveness: One patient achieved a marked response with a 30 percent reduction of his baseline eosinophil load resulting in a mild decrease of his symptoms; one patient experienced histologically a pronounced flare-up with an increase of his baseline eosinophil load of more than 150% leading to a mild increase of his symptoms; and the third patient was almost refractory and did not show any relevant changings. The value of the study is limited by its design as an open-label, non-randomized pilot trial with a small patient number. Further studies, working with alternative infliximab application modes and dosages are therefore needed to develop therapeutic options for the minority of patients with severe, refractory EE.
Hepatitis C infections in Opioid-dependent Patients (HepCOP): What determines the state of care in the canton of Zurich?

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Background: A representative survey in patients on opioid maintenance treatment (OMT) in the canton of Zurich (ZH) revealed that required tests to determine whether antiviral treatment should be offered were not done regularly. Treatment against chronic hepatitis C (CHC) was highly rare. The objective of this study was to identify patients’, physicians’ and institutional characteristics associated with an appropriate diagnostic work-up of these patients.

Methods: The survey included a representative sample of all patients on OMT in ZH. We developed a questionnaire to collect information from patients’ charts (demographic data, laboratory tests, antiviral treatment) and used a validated questionnaire to gather information on physicians’ attitudes. Multiple regression analysis was applied. A bootstrap-stepwise selection method was used in order to identify the most important factors influencing adequate diagnostic work-up.

Results: 63 physicians or institutions (18% of OMT providers in ZH) participated in this study. They care for 1575 patients, which represent 43% of all patients on OMT in ZH. 279 patients’ charts were analyzed. 67 patients had an inadequate diagnostic work-up. Physicians without own laboratory facilities (OR=4.17, p<0.01), referring their clients for primary somatic care (OR=2.19, p<0.01), and physicians with an abstinence oriented attitude (OR=1.42, p<0.01) or refusing illicit heroin consumers (OR=1.55, p<0.01) were more likely to work with patients inadequately. Patient characteristics (job, housing, alcohol consumption) had only a small impact on adequate testing.

Conclusions: For adequate diagnostic work-up attitudes of physicians with an abstinence oriented attitude (OR=1.42, p<0.01) or physicians without own laboratory facilities (OR=4.17, p<0.01) are of higher importance than individual characteristics of the patients. Measures to improve adequate testing for CHC and the rate of CHC treatment are necessary.

Air Suctioning During Colon Biopsy Acquisition Reduces Bacterial Contamination

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Background and Aim: Contamination of endoscopy suites with bacteria during procedures is of concern. It has been advocated that air suctioning while removing biopsy forceps could help to reduce bacterial bioaerosols. The aim of the present study was to evaluate the efficacy of air suctioning during removal of biopsy forceps.

Methods: During colonoscopy endoscopists were asked to remove the biopsy forceps with and without suction after having touched the sigmoid mucosa. Fifty liters of air were collected continuously for 30 seconds at 30 cm distance from the colonoscopy suction channel. Aerobic bacteria were collected by an impactor air-sampler (MAS-100). Standard blood agar plates were cultured in aerobiosis at 37°C overnight.

Results: Measurements were performed during 50 consecutive colonoscopies. At the beginning and at the end of the colonoscopy program the bioaerosol burden were 4.2 ± 1.8 cfu/cm² and 15.6 ± 2.5 cfu/cm² respectively. Applying suction during removal of the biopsy forceps reduced the bioaerosol burden from 29.4 ± 4.6 cfu/cm² to 15.1 ± 2.7 cfu/cm² (p<0.001). The analysis of the colonies on the CNA blood agar identified predominantly enterococci.

Conclusion: The present study indicates that the bioaerosol burden during handling of biopsy specimens is not neglectable and can be reduced by the simple habit of applying suction when removing biopsy forceps. This practice might be an important infection-control measure during gastrointestinal endoscopies.

Colonoscopic withdrawal times in a Swiss tertiary center

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Background and Aim: Current literature and expert opinion suggest 6 minutes as the minimum adequate mean withdrawal time for screening colonoscopy. A recent major study concluded that colonoscopists find more polyps when the examinations take longer. The aim of the present ongoing study was to record the colonoscopic withdrawal time in endoscopists, who did not know, that they were being monitored. Secondary endpoints were whether gastroenterologists change their withdrawal time habit when they are aware that they are being watched and whether they can estimate subjectively their withdrawal times.

Methods: In the first part of the study, seven experienced gastroenterologists performed 350 colonoscopies during a nine-month period. Colon retraction times were measured without the gastroenterologist’s knowledge. In the second part of this study, withdrawal times were measured with the knowledge of the performing gastroenterologist and subjective withdrawal times were recorded.

Results: There were large differences among gastroenterologists in colon withdrawal times from the cecum to the anus. Without the knowledge of the gastroenterologist, the mean withdrawal time without intervention was 4.6 ± 1.6 minutes (range 1.1-13 minutes) and with intervention 7.0 ± 3.9 minutes (range 4-25 minutes). In endoscopists being aware of monitoring their withdrawal time without intervention rose to 7.9 ± 2.6 minutes and with intervention to 9.9 ± 4.2 minutes (p<0.05). The subjective time feeling was mostly lower than the effective time (without intervention 6.2 ± 1.7 minutes).

Conclusions: In this large tertiary referral hospital-based study, we observed that an announced and monitored measurement of colon withdrawal time leads to an increase of the time spent on retraction from cecum to anus. Whether this leads to a higher detection rate of adenomas needs to be studied in future studies.

Anemia in inflammatory bowel disease. Differences between private practice and University Hospital: a prospective study

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Background and Aim: Anemia is a common complication of inflammatory bowel disease (IBD) in both Crohn’s disease (CD) and ulcerative colitis (UC). Studies on anemia in patients with IBD are usually conducted in tertiary referral centers. Unfortunately, data from private clinical practice is missing. The aim of the present ongoing study was to investigate the occurrence and severity of anemia in IBD patients from two University Hospitals (Zurich and Basel), in patients from two private practices (Ofteff and Liestal) and to compare these results to healthy blood donor candidates.

Methods: Data (such as age, gender, hemoglobin level, disease severity) was acquired prospectively from patients included in the Swiss IBD Cohort Study. The control population consisted of healthy first-time blood donor candidates at the blood transfusion center, Swiss Red Cross, Basel between 2004 to 2008.

Results: 124 patients from University Hospitals (66 CD and 58 UC) and 43 patients from private practices (29 CD and 14 UC) were included and compared to a control population (6074 blood donor candidates). In women, hemoglobin levels from University Hospitals were significantly lower (131 g/L in CD, 126 g/L in UC) than in private practice and control group (136 g/L in CD, 141 g/L in UC, 139 g/L control group; p< 0.01). Similar in men, hemoglobin concentrations from University Hospitals were lower (139 g/L in CD, 157 g/L in UC) than in private practice and control group (148 g/L in CD, 152 g/L in UC, 154 g/L in control group; p<0.05). Less severe IBD-activity and more UC-proctitis manifestations were reported in the private practice patients.

Conclusions: Frequency of anemia in IBD patients is overestimated in the literature due to the center bias of studies mainly performed at tertiary referral centers.