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Percutaneous trans-hepatic cholangiography and drainage (PTCD) followed by a single balloon enteroscopy (SBE) assisted ERCP to treat a choledocholithiasis in a patient after Roux-en-Y surgery

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Background: Endoscopic access to the biliary system can be technically challenging in patients with surgically altered anatomy, such as a Roux-en-Y reconstruction. By using single (SBE) or double balloon enteroscopy (DBE) it is possible to perform an ERCP even in these patients thereby giving the potential to perform diagnostic or therapeutic intervention.

Methods: We present the case of an 80-year-old patient with cholangitis due to choledocholithiasis in a postoperative setting after Roux-en-Y surgery.

Results: SBE was used to gain access to the papilla under CO2 insufflation but unfortunately a selective cannulation of the duodenum. Recurrent cholangitis, inspite of PTCD, meant that an endoscopic stent removal. This proved difficult because the stent had migrated upwards into the CBD and couldn’t be seen anymore endoscopically, but nevertheless stent removal was successful. In addition to the stent removal another stone was extracted from the CBD. The patient had a good clinical course without any adverse events.

Conclusion: SBE- or DBE-ERCP is a safe and often successful procedure for treating biliary obstruction in patients post Roux-en-Y reconstruction. However it is sometimes necessary to first complete a PTCD and the balloon assisted ERCP still has several disadvantages (absence of side-viewing perspective; lack of an elevator; need of extra-long ERCP accessories).

Evaluation of the Controlled Attenuation Parameter (CAP)1 as a Non-Invasive Tool to Diagnose Liver Steatosis

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Background: Liver steatosis is a mostly benign and reversible condition. However, under certain conditions steatosis is associated with inflammation and liver fibrosis. Although liver biopsy with histology is the standard for assessment of hepatic steatosis, this technique is not readily available. Recognizing the increasing prevalence of steatosis (i.e., non-alcoholic fatty liver disease (NAFLD)) and the lack of specific laboratory findings, there is a need for non-invasive steatosis testing. In analogy to non-invasive fibrosis staging by vibration-controlled transient elastography (i.e., Fibroscan®) a novel ultrasonic attenuation control technique (CAP®) has been developed to detect and quantify steatosis.

Methods: We present the case of an 80-year-old patient with recurrent cholangitis due to choledocholithiasis in a postoperative setting after Roux-en-Y surgery.

Results: SBE was used to gain access to the papilla under CO2 insufflation but unfortunately a selective cannulation of the duodenum. Recurrent cholangitis, inspite of PTCD, meant that an endoscopic stent removal. This proved difficult because the stent had migrated upwards into the CBD and couldn’t be seen anymore endoscopically, but nevertheless stent removal was successful. In addition to the stent removal another stone was extracted from the CBD. The patient had a good clinical course without any adverse events.

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Toll-interacting protein Deficiency Protects Mice from Colitis-associated Cancer

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Background: Genetic deletion of the Toll-interacting protein (Tollip) -an IL-1R and TLR2/4 regulator- leads to increased acute and chronic colitis in mice. We sought to investigate whether increased susceptibility to inflammation could also favor inflammation-driven colorectal carcinogenesis.

Methods: Colitis-associated cancer (CAC) was induced in 18-20-week old littermates C57BL/6 mice by azoxymethane (AOM) i.p. injection and 3 cycles of 2.5% oral dextran sodium sulfate (DSS) treatment. Tumor development was assessed by colonoscopy.

Results: Tollip KO mice had significantly lower endoscopic tumor scores than WT littermates upon AOM-DSS exposure (8.3±7.78 vs 13.38±6.37, p>0.05). Likewise, tumor numbers (4.85±3.51 vs 7.06±2.99, p>0.05) and size (12.84%±13.64 vs 37.34%±20.53, p>0.05) were reduced. Immunohistological studies demonstrated reduced apoptotic index (79.2±75.07 vs 246.8±152.9, p>0.05) and a trend towards lower proliferation (20.86±8.53 vs 27.91±7.26, ns) in Tollip KO tumors when compared to wt controls.

Conclusions: Our data show that Tollip partially favors colonic oncogenesis despite being protective against colitis.

Maternal Microbiota-Derived Metabolites Shaping the Neonatal Immune System Are Transferred to the Offspring Ante- and Postnatally

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Introduction: Metabolic capacity and immune system development of the host are dependent on colonization with commensal microbiota. There is evidence that signals originating from commensals during early life or from maternal microbiota before birth are required to shape the neonatal immune system.

Methods: Our system of reversible colonization of germ-free (GF) mice with the auxotrophic E. colistrain, HA107, allows us to expose pregnant mice to microbiota without subsequently colonizing their offspring. We use this system to detect maternal microbiota-derived metabolites that are transferred to the offspring and to detect their influence on neonatal immunity.

Results: After colonization of pregnant GF mice with 13C-labeled HA107, microbiota-derived products were present in placenta, fetus and in maternal mice measured by liquid scintillation. Using 13C-labeled HA107 and mass spectrometry, we identified 13C-labeled products in the maternal milk and the offspring, indicating that maternal microbiota-derived products can reach the offspring. Exposing pregnant mice to HA107 increased the number of intestinal NKp46+ type 3 innate lymphoid cells (ILC3s) and F4/80+ CD11c+ mononuclear cells (MNCs) in the offspring and altered its sensitivity to LPS challenge.

Conclusion: Cross-fostering between reversibly colonized and GF mothers revealed that both ante- and postnatal transfer of maternal microbiota-derived metabolites are required to fully shape the neonatal immune system.

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Background
EUS-guided biliary drainage like choledochoduodenostomy, hepatocigastrostomy (HGS), antral stenting and rendezvous are alternative procedures in case of obstructive jaundice and altered anatomy or failed ERCP. Complications related to EUS-guided antral drainage (EUS-GAD) are described as substantial in up to 10% and combination of procedures is sometimes suggested to avoid adverse events.

Aims & Methods
To evaluate the efficiency and safety of EUS-GAD with transmucosal approach in case of technical success. We retrospectively reviewed patients who underwent EUS-GAD in a single, tertiary care center.

Results
20 patients were included (9/17M, mean age 68). Malignant stenosis in 19/20 (95%). Reasons for EUS-GAD was failed ERCP in 13/20 (65%), duodenal stenosis in 4/20 (20%), altered anatomy after surgery in 3/20 (15%). Intrahepatic bile duct puncture was done with a 19G EchoTip® Needle in 16/20 (80%), with an EchoTip® Access Needle in 7/20 (35%). A cystostoma 6fr was always used to create the hepatoantral tract, without puncture site closure. Sternosis dilatation was done in 15% and calibration with cystostoma 6fr in 45%. SEMS was transapillary in 95%. Drainage was completed in endoprostatic stage by HGS in 1/20 and by punctureaneous drainage of the right liver in 1/20. Overall clinical success was 17/20 (85%). 1/20 presented a persistent obstructive cholangitis treated by another SEMS via ERCP. 2/20 patients died of infectious complication with incomplete drainage in case of advanced cancerous disease. One of these 2 patients was treated by EUS-GAD and HGS in same time. None patients developed biloma or bile leakage.

Conclusion
EUS-GAD by transtapheptic way is clinical effective and safety. Closure of the gastric puncture site is not mandatory if drainage is efficient. Complementary method for biliary decompression should be combined in case of incomplete draining and not to prevent potential adverse events.

Clinical impact of routine anti-Tumour Necrosis Factor (anti-TNF) therapeutic drug monitoring (TDM) in the management of Inflammatory Bowel Disease (IBD) patients

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BACKGROUND. Few studies have focused on the utility of regular TDM in the management of IBD. Our primary objective was to evaluate routine use of TDM for 3 TNFα inhibitors and observe physician response.

METHOD. A retrospective study was conducted on all IBD patients, treated with TNFα-inhibitors, attending two IBD referral centres. TNFα-inhibitors trough levels and anti-drug antibody (ADA) were measured using Lisa Tracker Premium Kit. Patient demographics and clinical data were retrieved from medical records.

RESULTS. A total of 143 anti-TNFα and ADA assays were measured routinely in 79 IBD patients. 88% of patients were treated with infliximab, 8% adalimumab and 4% certolizumab pegol. The prevalence of ADA was 10%. A sub-therapeutic result was found in 40% of patients resulting in no change in dose (66%), an increase in dose (19%), or premature cessation of treatment (3%), a decrease in dose (2%) or an unrecorded response (3%). In response to ADA detection, 30% of clinicians increased the dose, 40% switched or stopped the agent and 20% did not change management.

CONCLUSION. This is the first study in Switzerland to evaluate utility of anti-TNF TDM. Routine TDM revealed subtherapeutic levels in 40% of cases and led to a change in clinical management in one third of cases. The approaches to subtherapeutic levels and presence of ADA varied between physicians. Further studies are required to develop consensus.

Outcomes and predictive factors of endoscopic management in case of relapse of high grade dysplasia or intramucosal carcinoma on Barrett’s esophagus after a successful initial endoscopic resection.


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(4) Division of Pathology, Paoli-Calmettes Institute, Marseille, France.

Background
The role of endotherapy in case of relapse of high-grade dysplasia and intramucosal carcinoma (IMC) on Barrett’s Esophagus (BE) after successful initial endoscopic resection is unknown.

Aims & Methods
To evaluate the efficiency of endotherapy in case of relapse of HGD/IMC on BE after successful initial ER. We performed a retrospective study in a single tertiary care center. Relapse was defined by histological presence of HGD/IMC, with at least 6 months from the end of initial ER.

Results
18 patients were included (19/17M, mean age 70). Initial mean Prague classification of BE was C3M4. Initial ER was done by EMR in 15/18 (89%), ESD in 2/18 (11%), with adjuvant radiofrequency (RF) in 5/18 (28%) or laser Argon in 1/18 (5%). Stenosis occurred in 17%, always treated endoscopically. Mean time between initial endotherapy and relapse was 18 months (range 6-33), 2/18 (11%) underwent immediate surgery and 16/18 (89%) an endotherapy before surgery for rel for EGD. 15/18 (89%) adjuvant RF in 3/18 (19%), with a technical and carcinological success in 11/16 (69%). In case of failed endotherapy, 2/3 underwent radiotherapy (RC) and 3/5 a salvage surgery. In case of successful endotherapy, 3/11 showed a secondary relapse after an average time of 20 months (range 13-34), 1/3 patients were treated by RC, 1/3 by salvage surgery and 1/3 by 6 sessions of ER without disease progression after 36 months. In total, endotherapy was efficient for treatment of relapse in 8/18 (44%) with a follow up of 28 months. 1/18 presented a metastasis progression and 3/18 died (1/3 of complications after surgery, 1/3 of a pancreatic cancer, 1/3 of an accidental disease).

Conclusion
Endotherapy could be a treatment for management of HGD or IMC on BE, but should be carefully used with strict follow up.
Portal hypertension in a Crohn’s patient with small intestinal bleeding treated by transjugular portosystemic shunt placement
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University Clinic for Visceral Surgery and Medicine, University of Bern

Introduction: Crohn’s disease patients treated with azathioprine can develop nodular regenerative hyperplasia (NRH), portal hypertension (PHT) and portal vein thrombosis. PHT and inflammatory mucosal lesions increase the risk for gastrointestinal bleedings.

Case description: A 56 year old patient with Crohn’s disease developed NRH under treatment with azathioprine. He was admitted with severe bleeding. Gastroscopy showed small esophageal varices without bleeding stigmata. Blood was detected in the terminal ileum. CT angiography revealed a partial portal vein thrombosis with extension to the superior mesenteric vein, thickening of the jejunal wall and splenomegaly. Because conservactive treatment was not sufficient to control bleeding, a TIPS procedure and aspiration of the thrombus was performed. The immunosuppressive medication was switched to infliximab to control the activity of Crohn’s disease. The blood panel including thrombocytopenia improved and bleeding stopped.

Discussion: PHT in a Crohn’s patient with NRH and partial obstruction of the mesenteric venous inflow to the liver can be efficiently treated by TIPS. In our case TIPS and systemic treatment with infliximab lead to the improvement of the blood panel and remission of the Crohn’s disease.

Identification of potent anti-proliferative agents against hepatic angiosarcoma
Christian Perez-Shibayama1,2, Mananne Kraus1, Christoph Driessen1
1Klinik für Gastroenterologie und Hepatologie, Kantonsspital St. Gallen, 9007 St. Gallen; 2Institut für Immunobiologie, Kantonsspital St. Gallen, 9007 St. Gallen

Background: Hepatic angiosarcoma (AS) is a rare and highly aggressive tumor. Conventional chemotherapy and first trials with anti-angiogenics showed only minor efficacy; new therapeutic approaches are therefore urgently needed. Our aim is to characterize potential new anti-tumor strategies against AS in vitro and in vivo by using our recently described murine angiosarcoma model (Rothweiler et al, 2015).

Methods: in vitro screening for effective pharmacological compounds was performed using MTS assays in isolated angiosarcoma cells. Identified anti-proliferative drugs were further assessed using in vitro capillary formation on Matrigel and by flow cytometry.

Results: Screening showed strong anti-proliferative effects by the proteasome inhibitor Carboplatin, the protease inhibitor Lopinavir and the pro-apoptotic compound Navitoclax. These compounds were active in nanomolar to micromolar ranges when evaluated as mono-therapeutic agents. Importantly, combination strategies using these compounds showed synergistic effects. Consistently, the tube formation capacity of AS cells on matrigel was strongly affected after treatment with these compounds. Flow cytometric analysis of the hepatic AS cell line after treatment revealed that the possible mechanism of cell death induced by the anti-tumor drugs was apoptosis.

Conclusions: We have identified three clinically available compounds with potent anti-proliferative effects against difficult to treat angiosarcoma. Combinatory treatments showed synergistic effects and are therefore promising candidates in AS treatment. In vivo models will complement and further support possible new strategies to treat hepatic angiosarcoma.

Survival after CRS/HIPEC for colorectal and appendicular peritoneal malignancy
Marcel Schneider, Dilumot Eshnumunin, René Vorlanthen, Philippe Garbod, Kuno Lehmann

Background: Cytoreductive Surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is a combined treatment for well-selected patients with peritoneal carcinomatosis (PC). Despite an increasing number of centers, survival data from Switzerland is scarce. Methods: Data of 130 patients with colorectal or appendicular carcinomatosis from two centers (Bellinzona n=17, 1998-2008) and Zurich (n=113, 2003-2014) were prospectively collected and analysed. Patients with malignant disease received standard perioperative chemotherapy. Patients with low-grade appendix tumors were directly operated. HIPEC was performed after radical cytoreduction (CC-score 0, no visible tumor). Follow-up included clinical exams, tumor markers and CT scans every six months. Results: Patients had carcinomatosis from appendix tumors in 63% (82/130), including low-grade (40/82) and high-grade (44/82) tumors, and colorectal cancer in 37% (48/130). Curative surgery was possible in 73% of operated patients. Major morbidity and mortality were 8.1% and 2%, and follow-up was 25 months. For colorectal PC, median overall survival (mOS) and disease free (DFS) survival were 34 and 12 months, and 3-year survival was 48%. For low-grade appendix tumors, OS and DFS were 100% and 87% at 3y. For high-grade appendix tumors, mOS was not reached, DFS was 28 months, 56% were disease free and 63% alive at 3 years. Signet ring differentiation was a highly negative prognostic factor on survival for colorectal and appendiceal tumors (p<0.01).

Conclusion: Disease free survival after curative CRS/HIPEC is excellent for appendix tumors, and well-selected patients with PC from colorectal cancer have a survival benefit. Patients with signet ring differentiation show worse outcomes.

A severe complication after laparoscopic low anterior rectum resection: a compartment syndrome of the upper extremity
R. Kraus, G. Curti, Department of Surgery, Kantonsspital Aarau

Introduction Laparoscopic surgical procedures decrease the tissue trauma compared to open surgery and result in less postoperative pain what have been shown in different studies. Despite proven advantages there are severe complications occurring during a laparoscopic procedure due to the positioning during surgery. We present a case of a compartment syndrome of the upper extremity after laparoscopic low anterior rectum resection.

Method A 57y old man underwent an incomplete endoscopic resection of a pT1 adenocarcinoma 8cm above the anal margin line therefore the patient underwent a laparoscopic low anterior rectum resection with a defunctioning loop ileostomy.

Result The patient has been placed on a bean bag in lithotomy position with the right arm close to the body. The right arm has been padded and then the vacuum has been applied to the bean bag forming the bag safely around the body. During the procedure the patient has been steep head-down and tilted to the right side for 6 hours. Shortly after the extubation the patient complained of heavy pain in his right forearm and showed clinically a compartment syndrome. Immediately the hand surgeons opened the carpal tunnel and all the muscle compartments of the hand and forearm.

Conclusion This case illustrate the need of appropriate positioning and repositioning during surgery to prevent compartment syndrom not only of the lower extremity and to check the patient’s limb after surgery.

Identification of potent anti-proliferative agents against hepatic angiosarcoma
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**Evaluation of minimal hepatic encephalopathy using standard psychometric tests and computer assisted inhibitory control test (ICT) in patients with cirrhosis**

Laurent Spahr and Rachel Goldstein, Gastroenterology and Hepatology, Neurology, HUG

Minimal hepatic encephalopathy (MHE) is frequent (>50%) and presents as a spectrum of cognitive deficits in a cirrhotic patient with a normal neurological exam. Psychometric tests (PsyT) are used to detect MHE, but they are influenced by age and education and require professional expertise and training. The ICT, a computerized test for assessment of attention and response inhibition, has been reported as sensitive to diagnose MHE (Bajaj, GE 2008). **Methods:** We explored the performance of healthy subjects (n=23; age 43 years) and patients with cirrhosis (n=30; age 55 yrs.; MF: 20/10; alcoholic cirrhosis 77%; Child A/B/C: 5/19/6; lactulose therapy: 11/30) on a battery of PsyT (Trail-A, Trail-B, Digit Symbol Test, DST) and the computerized ICT administered to detect MHE. **Results:** values are given as Z-scores (raw score ; time ; correct lure response). The ICT could be completed by all patients. Patients with cirrhosis were significantly impaired with regard to PsyT and ICT performance compared to controls. Twenty one patients (70%) had abnormal values on at least 2 tests of the PsyT battery, meeting the accepted criteria for MHE diagnosis (EASL criteria: >100% of normal). **Conclusion:** In this small group of patients with cirrhosis, both psychometric tests and the ICT allow to diagnose MHE. The use of ICT by non specialists could increase the testing rate for MHE. (Supported by FLAGS in Geneva)

**Familial Eosinophilic Esophagitis (EoE) Uncovers a New EoE-like Syndrome without Tissue Eosinophilia**

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**Background:** Eosinophilic esophagitis (EoE) is a chronic-inflammatory, genetically-impacted disease with rapidly increasing incidence, defined clinically by symptoms of esophageal dysfunction and pathologically by an eosinophil-predominant infiltration. We identified in four EoE-families five members presenting with EoE-like symptoms and eosinophilic infiltration, without symptoms and without tissue eosinophilia. We aimed to investigate this eosinophil-predominant infiltration. We identified in four EoE-families five members presenting with EoE-like symptoms and eosinophilic infiltration. **Methods:** We explore the performance of healthy subjects (n=23; age 43 years) and patients with cirrhosis (n=30; age 55 yrs.; MF: 20/10; alcoholic cirrhosis 77%; Child A/B/C: 5/19/6; lactulose therapy: 11/30) on a battery of PsyT (Trail-A, Trail-B, Digit Symbol Test, DST) and the computerized ICT administered to detect MHE. **Results:** values are given as Z-scores (raw score ; time ; correct lure response).

<table>
<thead>
<tr>
<th>Test</th>
<th>Controls</th>
<th>Cirrhosis</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trail-test A</td>
<td>0.21 ± 0.7</td>
<td>-3.14 ± 4.4</td>
<td>&lt;0.0001</td>
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<tr>
<td>Trail-test B</td>
<td>-0.47 ± 1.1</td>
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<td>DST</td>
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<td>ICT (correct lure response)</td>
<td>0.51 ± 0.5</td>
<td>-0.39 ± 1.1</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

The frequency of first generation offspring of EoE-like syndrome patients affected by EoE or EoE-like syndrome was 40%. Immunohistochemistry confirmed definitely a lack of eosinophils in esophageal tissue of patients with EoE-like syndrome, but revealed a considerable T cell infiltration comparable with EoE. In contrast to EoE, eotaxin-3 mRNA was not, and eotaxin-3 protein markedly less elevated in EoE-like syndrome. The mRNA expression of selected EoE-genes was disregulated in EoE-like syndrome, either at the level of EoE or at a level in-between EoE and normal epithelium. **Conclusions:** These five members of EoE-families suffering from "EoE without eosinophilia" do formally not fulfill the diagnostic criteria of EoE. However, clinical manifestation, the bequest of EoE to their offspring, immunohistochemistry and gene-expression pattern suggest a uniform underlying pathogenesis. Conventional EoE with the predominant eosinophilia is therefore likely only one phenotype of a broader "inflammatory dysphagia syndrome". The role of the eosinophils, the definition of EoE and its diagnostic criteria must be reconsidered.

**Clinical Long-term Outcome of Patients Treated With Endoscopic Rendez-vous Dilatation of Complete Obstructions in the Proximal Oesophagus**

Michael C. Stutz1, Reto Bertolami1, Paul Martin Putora2, Franziska Albrecht1, Martina A. Brogle-Däppen1, Sandro J. Stöckli1, Christa Meyenberger1.

**Background:** Endoscopic Rendez-vous and Balloon-Assisted Dilatation is commonly used to treat proximal oesophageal strictures. However, long-term results are limited and heterogeneous. We report our experience with balloon-assisted and rendez-vous dilatation of complete proximal oesophageal strictures over a 10-year period. **Methods:** 119 patients (mean age 61 years, 87 males) were treated with balloon-assisted and rendez-vous dilatation. Technical success was achieved in 98 of 119 patients (81%). Clinical success was achieved in 83 of 98 patients (85%). **Results:** 11 patients (9.9%) experienced complications, 8 of which were severe (7.5%). **Conclusions:** Balloon-assisted and rendez-vous dilatation is an effective and safe technique for the treatment of complete proximal oesophageal strictures. Long-term results are promising, and the technique should be considered as a first-line treatment option.

**An unusual cause of an obscure gastrointestinal bleeding in the small bowel - sometimes capsule endoscopy only shows "the tip of the iceberg"**

Andreas Stulz1, Walter Arnold2, Patrick Aepli1

1 Division of Gastroenterology and Hepatology, Department of Medicine, Luzerner Kantonsspital, Lucerne
2 Department of Pathology, Luzerner Kantonsspital, Lucerne

**Background:** Obscure gastrointestinal bleeding (OGBB) is defined as recurrent or persistent bleeding or the presence of iron deficiency anaemia after evaluation with negative gastroscopy and colonoscopy. OGBB accounts for 5% of GI bleeding and presents a diagnostic challenge. Capsule endoscopy and balloon assisted enteroscopy remain the cornerstone of investigation in OGBB given their high diagnostic yield. **Methods:** We present the case of an 86-year-old patient with a 1-year-history of severe iron deficiency anaemia in spite of repeated blood transfusions and iron therapy. Over the past 16 years the patient had been treated for several malignancies (colorectal, prostate, melanoma).

**Results:** Gastroscopy (incl. duodenal biopsies) and colonoscopy were normal, in particular no bleeding source was seen. We then performed a capsule endoscopy which showed a few small polypoid lesions and a minimal amount of blood in the proximal jejunum. In response to these findings, an antegrade (single balloon) enteroscopy was performed where several ulcers up to 3 cm in size with noticeable black colouration were found in the first 1.5 metres of the small bowel. Extensive biopsies were taken. The final histological results confirmed our suspicion that these lesions were metastasis from a melanoma.

**Conclusion:** Sometimes the findings in a capsule endoscopy are minimal because they show only the "tip of the iceberg". As a result every relevant lesion in a capsule endoscopy should be followed by an enteroscopy which allows detection, biopsy and treatment.

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**Conclusion:** Sometimes the findings in a capsule endoscopy are minimal because they show only the "tip of the iceberg". As a result every relevant lesion in a capsule endoscopy should be followed by an enteroscopy which allows detection, biopsy and treatment.
Short-term Outcomes of Transanal Total Mesorectal Excision for Low Rectal Cancer


Background: Transanal total mesorectal excision (taTME) is an alternative to conventional mesorectal excision owing to its ability to achieve clear distal and circumferential resection margin in low cancers.

Methods: Consecutive patients were included in a prospective cohort study. Perioperative and functional outcomes were measured along regular clinic visits and with validated questionnaires. Results: were reported as median and interquartile range (IQR).

Results: 28 patients with a low rectal cancer (6.5cm to anal verge, IQR 6-8) underwent a taTME between Feb 2013 and Jan 2015. Age and body mass index were 65.5 years (IQR 60-76) and 25.5kg/m² (IQR 24.6-30.7). 17 patients had neoadjuvant radiochemotherapy. Median surgery time was 356.5 minutes (IQR 326.2-420.7), including an ileostomy. Median length of stay was 13.5 days (IQR 10.2-15.5). Mortality was 0 and 30-day morbidity totaled 40% minor and 18% major complications (Dindo-Clavien I-II, resp. III-IV). Dissection of the mesorectum was good (Quirke 3) and all distal and circumferential margins were clear. Median T stage was 3 (IQR 2-4). 3 patients had lymphnode metastases for a median number of retrieved nodes of 22 (IQR 14-34). Functional outcomes were assessed in 10 patients (10-month follow-up), of those 6 were stoma-free. Quality of life was good with a QLQ-C30 score of 70.8 (IQR 66.7-75), as was the urinary function (ICS voiding 7, IQR 6.3-10, incontinence 7.5, IQR 6-8). Sexual function in males (IIEF-5 score 2.5, IQR 2-7.5) and females alike (FSFI 6, IQR 3-6) was limited. Anal continence score was acceptable (FISI 17, IQR 2-28), as was the bowel emptying score (17, IQR 15.5, 17.5).

Conclusion: Transanal total mesorectal excision appears as an oncologic and functionally suitable procedure for distal rectum cancer.

Percutaneous Tibial Nerve Stimulation (PTNS): a successfull treatment for patients with anal incontinence (urgency), leading to a sustained response and modulating anal sphincter pressure and rectal perception

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Background: To assess the long-term clinical response, anorectal motor and sensory function in incontinent patients treated by PTNS

Methods: Retrospective analysis of prospective gathered data of 100 patients with anal urge incontinence treated with PTNS. Patients had 21 treatment sessions within 6 months. St. Marks Incontinence-score and Visual Analogue Scale (VAS)-score were collected at baseline, after 3, 8, 10 and 20 months. All patients had a high resolution manometry at baseline and after 12 weeks.

Results: A successful clinical response (≥50% reduction of the St. Marks, resp. VAS-score) was reached at end of treatment (8 months) in 74% resp. 82.2% and at one year after end of treatment (20 months) in 71.1%, resp. 80.6% of the patients (p>0.001). The sphincter squeeze pressure significantly improved from 126.5mmHg at baseline to 137.6 mmHg (p<0.001) at 12 weeks. The constant perception for urge changed from 101.4ml to 120ml (p>0.002), the maximal tolerable volume from 155.5ml to 183.7ml (p<0.001) after 12 weeks PTNS treatment. A significant, although weak correlation between clinical response and improvement of rectal sensory function was observed (p<0.04, Spearman coefficient=0.25).

Conclusions: PTNS is a minimal invasive treatment, with negligable side effects and a response rate of 80%. The therapeutic effect sustains at least one year after end of treatment. The treatment leads to a significant improvement of the sphincter squeeze pressure as well as the rectal perception.

Successful stenting of a stenosis in the hepatic venous outflow tract in a patient with secondary Budd-Chiari syndrome and refractory asces

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Background: Transjugular intrahepatic portosystemic shunt (TIPS) is often the treatment of choice in patients with portal hypertension and refractory ascites due to chronic liver failure. Whether transjugular stent insertion in the hepatic venous outflow tract is effective in patients with portal hypertension and refractory ascites due to posthepatic obstruction is less clear.

Methods: We present the case of a 44 year-old patient with portal hypertension and refractory ascites due to a membranous stenosis at the level of the hepatic venous outflow tract, resulting in a secondary Budd-Chiari-syndrome with a singular remaining left hepatic vein, atrophic right liver lobe and hypertrophic left liver lobe. We don’t know whether the right lobe was congenitally agenetic or underwent secondary atrophy due to visible liver vein obstruction.

Results: Transjugular percutaneous transluminal angioplasty (PTA) of the web-like, membranous stenosis between the singular remaining left hepatic vein and the inferior vena cava followed by stent insertion (18 x 40 mm) resulted in immediate reduction of the pressure gradient from initially 22 mmHg to 0 mmHg after the intervention. Stent insertion led to complete and rapid resolution of ascites.

Conclusion: Transjugular stent insertion between the hepatic outflow tract and the inferior vena cava can be a safe and effective treatment in patients with portal hypertension with refractory ascites due to posthepatic stenosis.

Two similar cases of elderly women with moderate abdominal pain and pneumoperitoneum of unknown origin:

A surgeon’s successful conservative management

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Background: Patients presenting with abdominal pain and pneumoperitoneum in radiological examination usually require emergency explorative laparoscopy or laparotomy. Mostly pneumoperitoneum associates with gastrointestinal perforation. There are very few cases where surgery can be prevented in patients with a combination of pneumoperitoneum and abdominal pain. People could benefit from a non-surgical treatment.

Methods: We present a successful conservative management of an 89 and 87-year-old female patient with moderate abdominal pain and free abdominal gas of unknown origin.

Results: Two elderly women presented with moderate abdominal pain in our emergency room in a short period of time. There was no medical intervention in the recent past history. Physical examination revealed mild tenderness in the upper respectively lower abdomen, but no clinical sign of peritonitis. Cardiopulmonary examination remained unremarkable. Blood studies showed no abnormalities, in particular inflammation parameter were within normal limits. Finally an obtained computed tomography (CT) showed free abdominal gas of unknown origin in both cases. We performed a conservative management with nil per os, total parenteral nutrition and prophylactic antibiotics. After 2 weeks both patients were discharged home.

Conclusion: Conservative management should be taken into account in patients with moderate abdominal pain and pneumoperitoneum of unknown origin in absence of clinical signs of peritonitis.
Non-CO2-insufflation and acute abdominal compartment syndrome in advanced obstructive tumor of the gastro-esophageal junction with severe bleeding. 1Reiiner Wiest, 2Jan Niess, 2Hans-Ulrich Rothen, 2Tobias Merz, 2Jukka Takkala; 3Thomas Malinka, 3Christian Seiler; 1Department of Visceral Surgery and Medicine (Inselspital); 1Department of Intensive Care Medicine, (Inselspital), Freiburg-strasse, 3010 Bern; 2equal contribution

Case: A 38 y old man suffering from advanced adenocarcinoma of the gastro-esophageal junction under palliative therapy was admitted with sever upper gastrointestinal bleeding. Emergency endoscopy utilizing room air was performed showing an highly obstructive tumor with active bleeding. The tumor could hardly but finally, successfully be passed and bleeding was stopped successfully by adrenalin injections and clipping. Immediately after endoscopy the patient showed clinical signs of an acute, severe abdominal compartment syndrome. CT imaging revealed a completely compressed abdominal aorta induced by massively distended and pressurized intestine. Even before emergency laparotomy could be performed the patient presented with pulsless electrical activity and died. Conclusion: CO2 is recommended to be used in emergency endoscopies – at least in cases with obstructing tumors. Pressure sensing devices should be developed and utilized improving safety of endoscopic procedures.

ORALS

G1

Measurement of functional blockade of TNF-alpha by anti-TNF agents is a stronger predictor than trough levels and anti-drug antibodies: 3-year prospective clinical data.

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Background: In case of loss of response (LOR) to anti-TNF agents in inflammatory bowel disease (BD) patients, interventions, such as dose increase and shorten the interval, lead only to a transient improvement and a majority of patients will eventually lose response. A functional in vitro test (CD62L shedding) measuring TNF functional blockade should help us identify those specific situations.

Method: An in vitro test was used to predict the response to the drug, the shedding of the L-selectin (CD66L) quantified by flow cytometry on the surface of monocytes before and after the anti-TNF agent administration. In a subgroup of patients trough level of the drug (TL) and antibodies against the drug (ADA) have been performed in order to compare both tests. The treatment strategy during the 2 years of the study was blinded to the results of the CD66L shedding. TL and ADA and followed clinical-based interventions switch by BD specialists.

Results: From June 2012 to May 2015, 33 BD treated with anti-TNF agents at Bern University Hospital were followed prospectively (clinicians blinded) to correlated clinical results: In a mean follow up of 25 months (range 7-41; 77 patient-years follow up), 25 medico-survival events occurred (3 adverse events (AE), 1 CMI colitis, 16 flares treated with medication, 3 intestinal resections and 2 operations of fistula) in 9 in R and 16 in NR, which means 14% vs. 60% (p<.001) of the patient-year follow up. The mean calprotectin during follow up (about 1 measurement per patient available) was 119 (±159 SD) for R and 310 (± 226 SD) for NR. ADA and TL measurement could be performed in 15 patients (45%); 9 R and 6 NR. Only 2 patients developed ADA (one in each group). There was no significant difference in trough levels between R and NR (2.8 vs. 4.9, p=0.4) and 62% had a therapeutic level (>1.5). Patients stable without need for intervention were 16/21 (84%); 1 AE in R vs. 19 (2 AE) in NR (p<0.001). In the NR group all the dose optimization failed, whereas in the responders group, interventions that would have been suggested on the basis of TL and ADA have not been performed (clinicians blinded), but were finally not required, based on the favorable clinical outcome.

Conclusions: Testing the in vitro functional blockade of TNF alpha (CD66L shedding) in anti-TNF treated BD patients seem to be a better long term predictor than trough levels and antibodies against the drug measurements. This could minimize interventions and therefore reduce costs and risk of adverse events.

G2

Systematic immunohistochemical screening for Lynch syndrome in colorectal cancer: a single-center experience of 488 patients

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Objective: Mutations in DNA mismatch repair (MMR) genes cause autosomal dominantly Lynch syndrome (LS), characterized by early development of colorectal cancer (CRC) and other cancers. LS patients benefit from intensive cancer surveillance. We aimed to assess detection rate of LS at our institution after introduction a systematic immunohistochemical (IHC) screening of CRCs in 2011.

Methods: Following EGAPP recommendations, starting in June 11, all CRCs were prospectively tested by IHC for the presence of MMR proteins MLH1, PMS2, MSH2 and MSH6. In case of loss of MLH1, BRAF mutation V600E was assessed by molecular testing/IHC. Follow-up and genetic counseling was evaluated in patients suspected being LS carriers (i.e. tumors showing loss of MLH1 combined with absence of BRAF V600E loss of PMS2, MSH2 or MSH6).

Results: Loss of MMR expression was found in 71 (14.5%) of 488 patients (76 ± 13 year) who underwent CRC surgery from June 11 to May 15. 27 (5.5%) patients were classified as potential LS carriers (68 ± 14 years). Sporadic MMR deficiency patients had a mean age of 78 ± 16 years. In 27 potential LS carriers, genetic counselling and germline testing was recommended, which revealed in 60% a positive result for LS, corresponding to a LS rate of 3.2% out of all our CRC patients.

Conclusions: All CRC should be tested by IHC. Tumorboard protocols should systematically evaluate IHC status; suspected LS patients need genetic counselling and testing.

Background: Gastrectestinal eosinophils are a major innate cell type in the lamina propria. In many inflammatory disorders eosinophils have been demonstrated to accumulate and are linked to fibrotic remodeling of the tissue. Since the intestinal microbiota has a strong impact on the immune status of the intestine (in health, active disease and remission), we asked how microbial colonisation influences the life cycle of eosinophils, their turnover and functional properties in the small intestine.

Methods: We employed germ-free mice and deliberately colonized them with a complex microbiota. We used quantitative real-time PCR and RNA sequencing to assess transcriptome activity; electron microscopy to perform ultrastructural analysis in the tissue; cell cycle analyzing dyes (BrDU and DAPI) to analyse the life cycle turn over of eosinophils. Finally, we have re-derived the eosinophil-deficient mouse strain dbiGATA1+ to investigate microbial responses in the absence of eosinophils.

Results: We show that eosinophil proliferation is stimulated in the bone marrow following bacterial colonisation that brings along a transient eosinophilia in the blood. Under steady state conditions, eosinophils show higher intestinal turn over in the presence of microbes that reflects a more activated phenotype and alterations in gene transcription.

Conclusions: Microbial colonisation feeds into the eosinophil life cycle and causes functional alterations that may turn out to be relevant in inflammatory conditions of the intestine.

The impact of the intestinal microbiota on eosinophils

Yasmin Löhrmann, Kathy McCoy

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Background:

Microbial colonisation feeds into the eosinophil life cycle and causes functional alterations that may turn out to be relevant in inflammatory conditions of the intestine.
Acute Herpes simplex viral Esophagitis occurring in immuno-competent Individuals with Eosinophilic Esophagitis

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Background Herpes simplex esophagitis (HSE) is an acute, severe virus infection of the esophagus rarely occurring in immuno-competent individuals. Eosinophilic Esophagitis (EoE) is an immune-mediated esophageal disorder which is also rare.

Description of Cases We recently observed 5 severe HSE cases (mean age 29 years), all affecting patients having a diagnosis of EoE. The coincidence of these two rare conditions raises the question of a causal relationship. Because 6 of the 5 patients had active, untreated EoE at the time of infection, a side effect of swallowed topical corticosteroids, the first line medical treatment of EoE, is likely not the explanation.

Conclusion The striking accumulation of HSE and EoE is suspicious that active, untreated EoE might predisposes to esophageal herpes simplex infection.

Figure 1a-c: Endoscopy (1a), histology (1b) and immuno-histochemical staining (1c) in one of the EoE patients during HSE.

Figure 2a-b: Endoscopy during HSE (2a) und follow up EGD (2b) in one patient who was diagnosed with EoE after an episode of acute HSE.

Short and long term mortality after percutaneous endoscopic gastrostomy (PEG) tube placement. Laurent Borchaty, Emiliano Giosta, Nicolas Goessens, Jean Louis Frossard.

Gastroenterology and Hepatology Service, Geneva University Hospital Geneva, Switzerland. Background: Patient with too short life expectancy should not receive PEG tube. Furthermore, it is well known some evolving disease do not benefit from PEG tube placement, e.g patient with dementia. We aim to study the short and long term mortality after PEG tube placement at the gastroenterology unit of the university hospital of Geneva between 2011 and 2012. Methods: All patients that had a PEG procedure between January 2011 and December 2012 were included. Age, sex, indication for PEG tube placement, judgment capacity, type of sedation, ASA score, endoscopist experience, antiaggregant treatment, biological value and cause of death were analysed. Short term and long term mortality were defined as death occurring within or after 30 days following PEG procedure respectively. Results: 90 patients had a PEG tube placement and 10 died within 30 days (11%). On univariate analysis, age, indication, higher ASA score, use of antiaggregant treatment and higher creatinine level were significantly associated with 30 days mortality. On multivariate analysis, age (p<0.03), use of antiaggregant treatment (p=0.08) and higher creatinine level (p=0.03) were associated with 30 days mortality. Finally 36 death (40%) were observed. The mean survival time was 250 days (4-990) whereas the median of survival was 497 days. Progression of neurological condition and pulmonary sepsis were the main causes of death. Conclusions: As previously described in the literature, age, renal function and use of antiaggregant are associated with 30 days mortality. Even with a lack of power due to the small number of event, we can observe that patient with neurologic problems are most at risk of death within 30 days.

Escalating Incidence of Eosinophilic Esophagitis in Canton of Vaud, Switzerland, 1993 to 2013: a population-based study

Bénédicte Giriens1, Ekaterina Safoneeva2, Marcel Zawahlen2, Alex Straumann3, Alain Schoepfer1. 1CHUV, Lausanne, 2ISPM University of Bern, 3Swiss EoE Center Olten.

Background: Eosinophilic esophagitis (EoE) is a chronic, inflammatory disease of the esophagus with a rapidly increasing incidence. However, population-based epidemiologic data on EoE are rare and limited to regions with less than 200,000 inhabitants. We evaluated the incidence and prevalence of EoE over time in Canton of Vaud, Switzerland. Methods: Canton of Vaud lies in the French-speaking, Western part of Switzerland. As of 12/2013, it had a population of 743,317 inhabitants. We contacted all Pathology institutes (n=6) in this canton in order to identify patients that have been diagnosed with esophageal eosinophilia between 1993 and 2013. We then performed a chart review in all adult and pediatric gastroenterology practices in order to identify EoE patients and to assess their clinical, endoscopic, and histologic characteristics.

Results: Out of 263 patients with esophageal eosinophilia, a total of 179 fulfilled the diagnostic criteria for EoE. Median diagnostic delay was 4 (IQR 1-9) years. No patient was diagnosed with EoE prior to 2003. Incidence of EoE increased from 0.16/100,000 inhabitants in 2004 to 6.3/100,000 inhabitants in 2013 (p<0.001). The cumulative EoE prevalence in 2013 was 24.1/100,000. The incidence in males was 2.8 times higher (95%-CI 2.01-3.88, p<0.001) when compared to that in females. The annual EoE incidence was 10.6 times higher (95%-CI 7.51-14.87, p<0.001) in the period from 2010–2013 when compared to that in the period from 1993–2009.

Conclusions: The incidence and cumulative prevalence of EoE in Canton of Vaud, Switzerland, has rapidly increased in the past ten years.
Eosinophilic Esophagitis: Diagnostic Accuracy of Symptoms in predicting Endoscopic and Histologic Remission
Ekaterina Safonoeva1, Michael Čošlovský1, Claudia Kuehn1, Marcel Zwahlen1, Sven Trelle1, Nadine Haas3, Alex Straumann2, Alain Schoepfer3; International EEsAI study group. 1ISPM University of Bern, 2Swiss EoE Center Olten, 3CHUV, Lausanne

Background: We aimed to evaluate the controversially discussed relationship between clinical severity, and endoscopic and histologic activity in adult patients with eosinophilic esophagitis (EoE).

Methods: Patients completed the validated EEsAI Patient Reported Outcomes (PRO) instrument (range 0-100 points) and then underwent endoscopy with esophageal biopsy sampling. Endoscopic remission was defined as follows: 1) absence of white exudates; 2) absence of moderate and severe rings; 3) absence of strictures; 4) furrows and edema could be present but not in combination. Histologic remission was defined as <20 eosinophils/mm2. ROC curves were calculated to determine the best EEsAI PRO cutoff values to predict remission.

Results: A total of 269 EoE patients was recruited (67% males), of these 111 (41.3%) had a PRO score <20 points, 79 (29.7%) were in endoscopic and 75 (27.9%) were in histologic remission. The AUC was 0.6719, 0.6007, and 0.6797, to predict endoscopic, histologic, and combined endoscopic and histologic remission, respectively. The best overall accuracy to predict endoscopic, histologic, and combined endoscopic and histologic remission was found for an EEsAI PRO score of 21 points (accuracy 65.2%), 21 points (accuracy 62.1%), and 15 points (accuracy 67.7%), respectively.

Conclusions: The EEsAI PRO has a sufficient accuracy in predicting endoscopic and histologic remission. In addition to assessing PRO measures, assessment of endoscopic and histologic alterations remains to be an important element in the judgment of overall disease activity.

Eosinophilic Esophagitis: relationship of quality of life with clinical, endoscopic, and histologic activity
Ekaterina Safonoeva1, Michael Čošlovský1, Claudia Kuehn1, Marcel Zwahlen1, Nadine Haas3, Alex Straumann2, Alain Schoepfer3; International EEsAI study group. 1ISPM University of Bern, 2Swiss EoE Center Olten, 3CHUV, Lausanne

Background: Knowledge about determinants of quality of life in eosinophilic esophagitis (EoE) patients helps to identify patients at risk of experiencing poor QoL and to tailor therapeutic interventions accordingly. We evaluated the impact of symptom severity, endoscopic and histologic activity on EoE-specific QoL in eosinophilic esophagitis (EoE) patients helps to identify patients at risk of experiencing poor QoL and to tailor therapeutic interventions accordingly. We evaluated the impact of symptom severity, endoscopic and histologic activity on EoE-specific QoL in adult EoE patients.

Methods: Ninety-eight adult EoE patients were prospectively included (64% male, median age 39 years). Patients completed two validated instruments to assess EoE-specific QoL (EoE-QoL-A) and symptom severity (adult EoE activity index patient-reported outcome) and then underwent EGD with biopsy sampling. Physicians reported standardized information on EoE-associated endoscopic and histologic alterations. The Spearman’s rank correlation coefficient was calculated to determine the relationship between QoL and symptom severity. Linear regression and analysis of variance was used to quantify the extent to which variations in severity of EoE symptoms, endoscopic and histologic findings explain variations in QoL.

Results: QoL strongly correlated with symptom severity (r=0.610, P<0.001). While the variation in severity of symptoms, endoscopic and histologic findings alone explained 38%, 35%, and 22% of the variability in EoE-related QoL, respectively, these together explained 60% of variation. Symptom severity explained 70% of the variation in each of the five QoL subscale scores.

Conclusions: EoE symptom severity and biologic disease activity determine QoL in adult EoE patients. Therefore, reduction of both EoE symptoms as well as biologic disease activity is essential for improvement of QoL in adult EoE patients.
Background: chronic immune mediated diseases (IMID) are characterized by recurring episodes of inflammation. The underlying mechanisms involve an inappropriate immune response to environmental triggers. Macrophages are a key player in the development of chronic inflammation. In the gut, they can sense extrinsic microbes and pathogen-derived molecules through pattern recognition receptors. In this study, we have investigated the repertoire of IgE in GF mice using a high throughput sequencing approach.

Methods: RNA was isolated from the mesenteric lymph nodes except for IgE. The high efficiency and high performance of an oligo dT primer (Invitrogen) was used for cDNA synthesis. The PCR product was gel purified for 650-800bp length. After the addition of barcodes, samples were sequenced on the Illumina MiSeq platform with 300bp paired end reads. Data analysis was executed with IMGT Hi V-Quest or IgBlast. Graphical output was created with IgGalaxy, Excel and R.

Results: Bone marrow-derived macrophages expressed significantly more IL-18 than dendritic cells. IL-19 expression was upregulated after stimulation with Toll-like receptor ligands. The addition of IL-18 to macrophages stimulated with LPS decreased secretion of the proinflammatory cytokine IL-6. IL-19 expression was only found in mesenteric lymph nodes, but not in other organs tested. IL-19 is produced by phagocytes isolated from the large intestine of mice with colitis. IL-20R was expressed in all investigated organs with the highest expression in the skin. IL-20RA was expressed in the epidermis, the stomach and the proximal colon. IL-20RA and IL-20R expression depend on the hygiene status because highest expression was observed in germ-free animals.

Conclusions: Macrophage derived IL-19 might act on mucosal sites where the type I IL-20 receptor is expressed.

The Cytokine IL-19 is Expressed by Macrophages
Anna Steinitz, Andrew Macpherson and Jan Niess
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Background: Macrophages are rather an undefined cell population in the gut. We hypothesized that myeloid cells in the gut can be identified the expression of IL-19, a member of the IL-20 cytokine family.

Methods: To identify the source of IL-19, a reporter mouse line was constructed in which the IL-19 promoter drives the expression of the red fluorescent protein tdTomato. Expression levels of IL-19 and of the type I IL-20 receptor (formed by the IL-20 receptor alpha (IL-20RA) and beta (IL-20RB) subunits) were determined in mice with different hygiene statuses.

Results: Bone marrow-derived macrophages expressed significantly more IL-19 than dendritic cells. IL-19 expression was upregulated after stimulation with Toll-like receptor ligands. The addition of IL-18 to macrophages stimulated with LPS decreased secretion of the proinflammatory cytokine IL-6. IL-19 expression was only found in mesenteric lymph nodes, but not in other organs tested. IL-19 is produced by phagocytes isolated from the large intestine of mice with colitis. IL-20R was expressed in all investigated organs with the highest expression in the skin. IL-20RA was expressed in the epidermis, the stomach and the proximal colon. IL-20RA and IL-20R expression depend on the hygiene status because highest expression was observed in germ-free animals.

Conclusions: Macrophage derived IL-19 might act on mucosal sites where the type I IL-20 receptor is expressed.
Maternal microbiota educates the immune system of the offspring through natural antibodies

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Background: Mammalian embryonic immune system development occurs in the absence of live bacterial exposure, although it is possible that the developing fetus may be exposed to microbial products from the maternal microbiota. However, the potential impact of the maternal microbiota on immune development and health of the offspring is not clearly understood.

Methods: Germ-free (GF) mice were transiently colonised with bacteria during the pregnancy by oral gavage with an auxothrophic Escherichia coli strain HA107. Innate immune cells of the offspring were analysed by FACS at different time points.

Results: We have found that the offspring from mothers exposed to intestinal microbes only during pregnancy showed an increased intestinal NKG2D+Rorc+ innate lymphoid cells and F4/80+CD11c+ mononuclear cells. Moreover, the expression of genes involved in microbial adaptation was impaired by maternal microbiota. The mothers from microbial-treated mothers were protected against microbiota challenge preventing bacterial translocation to mesenteric lymph nodes and modulating gene expression. In the absence of natural antibodies and B cells, maternal microbiota failed to shape the innate immune system in the offspring resulting in increased bacterial translocation following challenge. Furthermore, maternal antibodies required loading with maternal bacterial products to control the development and the efficiency of the innate immune system of the offspring.

Conclusions: Our results reveal the tremendous role played by maternal microbiota and natural antibodies in setting the baseline of the innate immune system in the offspring.

Infliximab treatment outcome in steroid-dependent/refractory Crohn’s Disease patients: a single center report

T. Kaymak, F. Morici, C. Beglinger, P. Huz

Background: The anti-TNF antibody Infliximab (IFX) is an efficient therapy in patients with Crohn’s Disease (CD) who have a steroid-dependent, steroid-refractory or a complicated (e.g. fistula) disease course. Many patients receive a long-term treatment. Recommendations with respect to discontinuation of the IFX therapy are not well established. As IFX is an expensive therapy with potential side effects the outcome of stopping an IFX is an important question. The aim of the current study was 1) to analyze long-term treatment outcome in CD patients and 2) to evaluate withdrawal of IFX in CD patients in remission.

Methods: In a single center retrospective analysis we report the outcome of CD patients treated with IFX between 2008 and 2015 (m=109) at the University Clinic of Basel. The indication for IFX treatment was steroid-dependent, steroid-refractory or a complicated (e.g. fistula) disease course. Every patient was initially treated with a regular induction scheme (IFX 5mg/kg body weight at 0, 2, 6 weeks). Clinical remission was defined as CDAI<150, no steroid use and absence of clinical symptoms. "Discontinuation of treatment" was defined as a permanent stop of IFX therapy after 2 years of clinical remission with a bland endoscopic and histological examination before stopping the treatment.

Results: After the induction treatment with IFX 41/109 (37.6%) patients achieved remission. Of these patients, 13/41 (31.7%) were on long-term remission and discontinued from IFX due to a steroid dependent, steroid-refractory or a complicated disease course. Many patients received a long-term treatment. IFX therapy due to a steroid dependent, steroid-refractory or a complicated disease course can be discontinued from IFX treatment.

Conclusion: Our single center analysis demonstrates that only a minority of patients started on IFX therapy due to a steroid dependent, steroid-refractory or a complicated disease course can be discontinued from IFX treatment. Withdrawal of IFX therapy led to a relapse in 73.3% of our patients in remission with good response to re-induction of IFX.

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Conclusions: Our results reveal the tremendous role played by maternal microbiota and natural antibodies in setting the baseline of the innate immune system in the offspring.

Buried Bumper Syndrome: a case-series of a new technique for the endoscopic management of an old complication

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Background: Buried bumper syndrome (BBS) is rare complication of percutaneous endoscopic gastrostomy (PEG) and percutaneous endoscopic jejunostomy (PEJ) due to excessive external traction that leads to erosion of the internal bumper with its inclusion into the visceral and paraluminal walls. Since it was first described in 1988 by Shlaiman et al. several different techniques for endoscopic treatment have been proposed. Among the most commonly used we can include the needle-knife incision of the gastric wall, the push-and-pull “T” technique, the extraction using the tapered tip of a new PEG tube and the dilation of the opening using an external placed balloon catheter. Methods: From July 2013 to May 2015 four cases of BBS were diagnosed in our tertiary center. Three of the cases were complications of a PEG and one a complication of a PEJ. All these cases were treated with the following technique: we cut the external end of the tube at 10 cm from the abdominal wall and insert a 0.25-inch VisiGlide® guide wire through the feeding tube lumen into the stomach. The guide wire is recuperated with a 13mm snare. We then advance a Hurricane™RX Biliary Ballon Dilation Catheter with 6mm of outside diameter and 4cm in length into the lumen of the stomach. A new balloon-type feeding tube is then inserted. Results: The average time to diagnosis of BBS after the PEG or PEJ procedure was 21.5 months. All of the cases were successfully treated and immediate placement of a new balloon-type feeding tube trough the same PEG/PEJ was performed with no complications. All the PEG/PEJ are still functional and in use. Conclusions: Our technique as shown to the effective and safe and can be added to the arsenal of endoscopic procedures available to treat BBS of PEG and PEJ.

Mucosal consequences of systemic antimicrobial CD4+ T cell reactivity

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Background: Healthy host-microbial mutualism relies on compartmentalization and proper regulation of systemic and mucosal immune responses. Despite this, the systemic immune system is frequently exposed to some levels bacterialaeas, which can trigger systemic antimicrobial immune reactivity including CD4+ T cells. This can occur for example when immune compartmentalization is compromised, in the presence of deficient innate immunity, or use of nonsteroidal anti-inflammatory drugs (NSAID). Importantly, systemic hyper reactive CD4+ T cells might be involved in the pathogenicity of inflammatory bowel diseases (IBD).

Methods: We generated a genetically modified Escherichia coli strain expressing a defined T helper epitope to study antigen-specific antimicrobial CD4+ T cells.

Results: We found that the bacterial load threshold required for the induction of systemic antimicrobial CD4+ T cell proliferation was very high and not easily reached under physiological conditions. However, when intestinal barrier function was compromised by induced damage to the intestinal epithelium, the presence of systemic anti-microbial CD4+ T cells resulted in dramatically increased levels of bacterial translocation.

Conclusions: Systemic antimicrobial CD4+ T cell reactivity might impact adversely on the mucosa under conditions of reduced barrier function.

Infliximab treatment outcome in steroid-dependent/refractory Crohn’s Disease patients: a single center report

T. Kaymak, F. Morici, C. Beglinger, P. Huz

Background: Mammalian embryonic immune system development occurs in the absence of live bacterial exposure, although it is possible that the developing fetus may be exposed to microbial products from the maternal microbiota. However, the potential impact of the maternal microbiota on immune development and health of the offspring is not clearly understood.

Methods: Germ-free (GF) mice were transiently colonised with bacteria during the pregnancy by oral gavage with an auxothrophic Escherichia coli strain HA107. Innate immune cells of the offspring were analysed by FACS at different time points.

Results: We have found that the offspring from mothers exposed to intestinal microbes only during pregnancy showed an increased intestinal NKG2D+Rorc+ innate lymphoid cells and F4/80+CD11c+ mononuclear cells. Moreover, the expression of genes involved in microbial adaptation was impaired by maternal microbiota. The mothers from microbial-treated mothers were protected against microbiota challenge preventing bacterial translocation to mesenteric lymph nodes and modulating gene expression. In the absence of natural antibodies and B cells, maternal microbiota failed to shape the innate immune system in the offspring resulting in increased bacterial translocation following challenge. Furthermore, maternal antibodies required loading with maternal bacterial products to control the development and the efficiency of the innate immune system of the offspring.

Conclusions: Our results reveal the tremendous role played by maternal microbiota and natural antibodies in setting the baseline of the innate immune system in the offspring.
IL-22-induced antimicrobial peptides are key determinants of vaccine-induced protection against Helicobacter in mice

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BACKGROUND: Despite the proven ability of immunization to reduce Helicobacter infection in mice, the precise mechanism of protection has remained elusive. In this study, we evaluated the role of IL-22 in vaccine-induced reduction of Helicobacter infection.

METHODS: Vaccine-induced reduction of Helicobacter infection was compared in vaccinated mice with or without functional IL-22.

RESULTS: Gastric IL-22 levels were increased in mice immunized and challenged with H. felis, as compared to controls (18±11 and 8±8 ng/ml for IL-22 protein, p<0.05, respectively). FACS showed that a peak of CD4+IL-22+ T cells infiltrating the gastric mucosa occurred in immunized mice in contrast to control mice (2.06±0.60% and 0.79±0.26%, p<0.01, respectively). Injection of anti-IL-22 to immunized mice significantly prevented the reduction of Helicobacter infection (2 out of 9 mice (anti-IL-22) versus 8 out of 9 (control) mice reduced Helicobacter infection p<0.001). Finally, AMPs extracted from stomachs of vaccinated mice or mice injected with IL-22Fc, but not from the stomachs of non-immunized or immunized mice injected with anti-IL-22 efficiently killed Helicobacter in vitro.

CONCLUSION: These results demonstrate that IL-22 plays a critical role in vaccine-induced reduction of Helicobacter infection, by promoting the expression of AMPs capable of killing Helicobacter.

Success and complications of an intraductal fully covered metal stent to treat anastomotic biliary strictures (ABS) after orthotopic liver transplantation (OLT)

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Background: Metal stents for benign biliary strictures are gaining acceptance with many published series. Traditional metal stent designs seem to have poor durability in ABS after OLT. Novel intra-ductal stents show promise in these strictures.

Methods: A retrospective multi-centre Australian study of ABS after OLT treated with a novel intraductal stent. Records from 3 liver transplant centre databases were reviewed.

Results: Totally 36 removable fully covered self expanding metal stents (RCSEMS) were inserted in 31 cases to treat an ABS after OLT. The mean age of the patients was 56 years. Treatment with the RCSEMS was performed with an average treatment time of 3.8 months. Stricture resolution was achieved in 93.5 %. All attempted stents removals were successful without any difficulty. Follow-up showed 7 cases of ABS recurrence (24.1 %) and all were treated successfully with repeat ERCP and stenting (some metal and some plastic). The mean time of ABS presentation after OLT was 20.3 months. Complications were reported in 6.5 % (one patient had mild cholangitis on stent removal, one patient required re-stenting because of cholangitis at a secondary stricture). Finally it was pleasing, that no cases of stent migration were seen.

Conclusion: These novel intraductal fully covered metal stents have a high clinical success and low complication rate, in particular there were no cases of stent migration. As a result this stent type is preferred to traditional metal stents for treating ABS after OLT.

Microbiota-mediated fine-tuning of the threshold of intestinal inflammamma activation in host-microbial mutualism.

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Background: The inflammasome is a complex of proteins that controls the activity of caspase-1, pro-IL-1beta and pro-IL-18. It acts in inflammatory processes and in pyropoptosis. The lower intestine is densely populated by a community of commensal bacteria that, under healthy conditions, are beneficial to the host. Some evidence suggests that the gut microbiota influences regulation of the inflammasomes. Components of inflammasomes have been shown to have a protective function against development on experimental colitis, dependent on IL-18 production. However the precise mechanisms and the role of the inflammasome in maintaining a healthy host-microbial mutualism in the absence of pathogens remains unknown.

Methods: To address this question, we have performed in vivo experiments colonising germ-free (GF) mice with limited and diverse but undefined commensal bacteria to investigate how the inflammasome components, particular within intestinal epithelial cells (IECs), are regulated under different hygiene conditions.

Results: We have established that gene expression of the inflammasome components NLRC4, NLRP3, NLRP6, NLRP12, caspase-1, ASC and IL-18 do not differ between GF and colonised conditions under steady-state, even when colonised with a highly diverse intestinal microbiota. Under steady state, we observed high expression of NLRs and IL-18 in the gut, even in absence of microbiota. As expected, induction of IL-18 was observed following infection with the pathogen Citrobacter rodentium. In contrast, IL-18 was induced transiently upon colonisation of germ-free mice. We are now investigating the dynamics of microbial colonisation at early time points to determine whether this early induction of IL-18 is required for homeostasis.

Conclusion: Our data suggest that in contrast to pathogenic bacteria commensal bacteria do not dramatically induce expression or activation of the inflammasome in IEC. Nevertheless, modulation of IL-18 may occur during the first phase of colonisation. We are now investigating the impact of steady-state expression of the inflammasome under different hygiene conditions using mice that are deficient for protein members or products of the inflammasome complex, such as ASC and IL-18 gene-deficient mice.

A rare case of a pigmented neuroendocrine tumour of the stomach in the setting of autoimmune gastritis

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Background: Neuroendocrine tumours of the gastrointestinal tract (GI-NETs) account for 2% of all GI-Tract neoplasms. Individual GI-NETs may exhibit widely different clinical courses, reflecting their underlying heterogeneity at the genetic, molecular and cellular level that influences their biological behaviour.

Results: We report an extremely rare case of a "black" pigmented gastric tumour of 3mm in size found in a 68 year-old male patient with newly diagnosed chronic atrophic gastritis and known chronic alcohol abuse. Histologic examination revealed a NET with trabecular growth and monomorphic cells which showed immunopositivity for pancytokeratin, chromogranin and synaptophysin and were negative for S100, Melan A and HMB45. The MIB1 Index was <2%, compatible with a NET G1. Perl’s stain was negative, while electron microscopy revealed melanosome in the pigmented tumour cells compatible with presence of melanin pigment.

Conclusion: To our knowledge, this is the first reported case of pigmented gastric NET. Pigmented NETs may represent a diagnostic challenge due to their endoscopic similarity to melanoma. Since epidemiological data show an increasing incidence of gastrointestinal neuroendocrine tumours, endoscopists may be faced with pigmented NETs more frequently in the future.
Alcohol Consumption and Impact on Gastrointestinal Symptoms among Swiss IBD Patients

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Introduction
Little is known about alcohol drinking behavior and its influence on gastrointestinal symptoms among patients with inflammatory bowel disease (IBD).

Aims & Methods
A questionnaire was sent to patients randomly selected from 3 different groups according to reported frequency of alcohol consumption at enrolment to the Swiss IBD cohort. It was designed to assess the average alcohol intake per day, type of drinking, number of days drinking per week, influence of alcohol on gastrointestinal symptoms and smoking. Other data on demographics and disease characteristics were gathered from the most recent follow up visit.

Results
383 of 537 (72%) questionnaires were answered. The rate of abstainers was similar to the Swiss population (12%). Among drinkers, 52% drank up to 1x weekly, 25% on 2-3 and 19% on 4-7 days per week. The amount of alcohol per occasion was 0-20g in 70%, 20-40g in 24% and 40-60g in 5% and similar for both diseases. After being diagnosed with IBD, 61% did not change, 29% reduced, 6% quit or 4% increased alcohol consumption. In both, CD and UC, 30% of patients reported worsening of diarrhea, 15% worsening of abdominal pain and bloating after drinking alcohol. The type of preferred beverage did not significantly influence gastrointestinal symptoms.

Conclusion
Drinking behavior in Swiss IBD patients is similar to the general population. A third of patients reduced or quit drinking after being diagnosed with IBD. Worsening of diarrhea, abdominal pain and bloating after drinking alcohol was reported in 15-30% by both UC and CD patients, independently of the preferred drinks.

Predictors of success for double balloon assisted endoscopic retrograde cholangiopancreatography (DBE-ERCP) in patients with Roux-en-Y anastomosis

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Background: Performing ERCP in patients with Roux-en-Y anastomosis (REYA) is a major challenge to endoscopists since the biliary anastomosis is not reachable with a standard duodenoscope. The use of DBE-ERCP has been shown to permit endoscopic intervention in this setting.

Methods: We retrospectively studied all patients with REYA who had a DBE-ERCP between 2009 and 2015 at our liver transplant centre.

Results: In totally 47 patients we performed 76 DBE-ERCPs. Patients had REYA for different indications (mostly orthotopic liver transplantation, OLT). DBE-ERCP was mainly performed for biliary obstruction (often with concomitant cholangitis). Overall, DBE-ERCP was technically successful in 65.8%. The success rate was 84.0% in patients with REYA from non-transplant surgery performed in adulthood, 57.8% in patients post OLT and only 20.0% in biliary atresia patients. Therapeutic interventions (e.g. biliary stenting, stent removal, dilatation) were successful in 72.1%. Complications occurred in only 2 cases, both developed cholangitis which resolved with conservative management.

Conclusion: The initial indication for REYA appears to be predictive for successfull DBE-ERCP. The procedure is most successful in patients after non-transplant adult surgery (previous bile duct injury, gastrectomy, pancreatoduodenectomy), intermediate successful in patients post OLT and least successful in patients with biliary atresia. Patients predicted to have low success rates should be initially referred for alternative procedures (PTCD or EUS-guided biliary access).

Swiss Snapshot Diverticulitis Trial: Current Practice of in-hospital Management of Acute Colonic Diverticulitis - a Nation’s Experience

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Department of Visceral Surgery, University Hospital Lausanne

Background
To evaluate the current practice of in-hospital management of acute colonic diverticulitis in Switzerland.

Methods
Prospective snapshot research during three months (and one month follow-up) of all patients hospitalized for acute colonic diverticulitis.

Results
Over a time period of three months, 74 participating hospitals treated 783 patients with acute colonic diverticulitis. 510/783 (65.1%) patients were diagnosed with uncomplicated diverticulitis using CT scans in 94.5%. Management was conservative in 99.8% with intravenous antibiotics in 98% and a failure rate of 1.4%. Patients with complicated diverticulitis (34.9%) were managed conservatively (67%), by percutaneous drainage (7%) or immediate surgery (26%). Failure of non-operative therapy was 15.3%. Laparoscopic surgery was performed in 46.2% with a conversion rate of 34.7%. Primary anastomosis was achieved in 49.1% (27.8% with protective ileostomy). Surgeons in training performed 31.5% of operations.

Conclusions
Conservative management of uncomplicated diverticulitis is very successful, questioning the need for hospitalisation. Hartmann’s procedure in emergency surgery for complicated diverticulitis is still high.

Rare Double-"Fish Eye"- Papilla Vateri in Main-Duct Intraductal Papillary Mucinous Neoplasia (IPMN): Curative Surgical Resection by Total Duodeno-Pankreatectomy.

1Reiner Wiest, 1Andrew Macpherson, 2Andreas Frenzer, 3Christian Ruiis, 1Thomas Malinka, 1Beat Gloor; 1University Hospital Visceral Surgery and Medicine, Inselspital Bern, Freiburgstrasse, 3010 Bern; 2Department Gastroenterology, Spital Thun, Krankenhaus-strasse 12, 3600 Thun

Introduction
In totally 47 patients we performed 76 DBE-ERCP. Patients had REYA for different indications (mostly orthotopic liver transplantation, OLT). DBE-ERCP was mainly performed for biliary obstruction (often with concomitant cholangitis). Overall, DBE-ERCP was technically successful in 65.8%. The success rate was 84.0% in patients with REYA from non-transplant surgery performed in adulthood, 57.8% in patients post OLT and only 20.0% in biliary atresia patients. Therapeutic interventions (e.g. biliary stenting, stent removal, dilatation) were successful in 72.1%. Complications occurred in only 2 cases, both developed cholangitis which resolved with conservative management.

Conclusion: The initial indication for REYA appears to be predictive for successfull DBE-ERCP. The procedure is most successful in patients after non-transplant adult surgery (previous bile duct injury, gastrectomy, pancreatoduodenectomy), intermediate successful in patients post OLT and least successful in patients with biliary atresia. Patients predicted to have low success rates should be initially referred for alternative procedures (PTCD or EUS-guided biliary access).
Swiss Snapshot Diverticulitis Trial: Influence of Hospital Category on the Management of Acute Colonic Diverticulitis
Seraina K Faes, Alexandre P Cuerel and Dieter Hahnloser for the Swiss Diverticulitis Study Group. Department of Visceral Surgery, University Hospital Lausanne

Background: To evaluate the influence of hospital category on the management of acute colonic diverticulitis in Switzerland.

Methods: Swiss Snapshot Diverticulitis Trial: Prospective research during 3 months of all patients hospitalized for acute colonic diverticulitis or elective diverticular resection. Subanalysis for hospital category in acute diverticulitis.

Results: Of 151 Swiss hospitals, 74 (49%) contributed 783 acute diverticulitis cases. Hospitals of category A included most patients (34%). Category distribution varied significantly between uncomplicated and complicated diverticulitis (p<0.001; 23% complicated in B1 vs 54% in U). Diagnostic use of CT scan differed significantly (100% in UP/private, P; 83% in B1, p=0.001). Prescription of iv antibiotics ranged from 80% (A) to 90% (B3) (p=0.03). Conservative treatment was applied in 99.6% of uncomplicated and 74% of complicated cases and its failure rates varied for hospital category (uncomplicated: min 0% B3, max 8% P; complicated: min 8% B3 max 43% B1). Length of hospital stay was not differing upon category (uncomplicated: median 4, range 1-34, p=0.57; complicated: median 7, range 2-74, p=0.068).

Conclusions: Management of acute colonic diverticulitis in Switzerland highly varied between different hospital categories. A nationwide guideline might uniform our treatment approaches.

Esophageal work-up prior to bariatric surgery: who and how to investigate
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Background: Gastroesophageal reflux disease (GERD) is common in obese patients and bariatric operations have different influence on GERD. We assessed the prevalence of symptoms and objective findings prior to surgery.

Methods: Work-up included quantification of symptoms, upper GI endoscopy and 24-h impedance-pH (imp-pH) monitoring off PPI. Imp-pH monitoring was classified as abnormal if either %time pH<4 was abnormal, total number of reflux episodes was elevated or symptom index (SI) was positive.

Results: Among 100 consecutive patients 54% reported heartburn and/or regurgitation, 71% had objective evidence of GERD (38% esophageal lesions and 33% abnormal imp-pH results). Twenty-nine percent of patients with esophageal lesion had normal imp-pH monitoring, 45% of patients with abnormal imp-pH recordings had erosions. Esophagus was inferior to imp-pH in identifying GERD (sensitivity 54% vs. 85%, p < 0.01). Symptomatic and asymptomatic patients had similar prevalence of esophageal lesions (37% vs. 39%) and abnormal imp-pH findings (68% vs. 50%). Only 31% of patients with abnormal %time pH<4 had elevated number of reflux episodes suggesting that poor acid clearance is the main mechanism leading to GERD in obese patients.

Conclusion: Half of obese patients report typical GERD symptoms and >70% had evidence of GERD. Since symptoms don’t predict objective findings, endoscopy and reflux monitoring should be part of the pre-bariatric surgery work-up.

Endoscopic recanalization of a post-radiogenic complete esophageal occlusion by combined anterograde / retrograde esophagoscopy
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Background: Gastroesophageal stenosis is a potential side-effect after radiochemotherapy of tumors of the head and neck region. In rare cases complete luminal obstruction can result. Most of the patients tolerate this situation for some time due to PEG placement prior to this.

Methods: Retrospective analysis of long-term results after direct recanalization via fluoroscopy and combined anterograde (transoral route) and retrograde (via PEG-stoma) esphagoscopy by use of a stiff guide-wire (Eder-Puestow) or direct needle knife cutting followed by bougienage or balloon dilation after successful recanalization. Luminal patency was maintained by repeated balloon-dilation or self bougienage.


Conclusions: Recanalization of a complete postradiogenic esophageal long segment occlusion can be safely performed by combined anterograde/retrograde esophagoscopy, even in cases with long-lasting (max. 24months) and long-distance (max.4cm) esophageal occlusion.
Early colonoscopy in patients with complicated sigmoid diverticulitis even with covered perforation and abscesses: Preliminary results of a prospective study

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Background: After small bowel transplantation acute tissue rejection can occur as a “skipping lesion” in distant areas. Examining only the transplant stoma is not sufficient; a comprehensive evaluation of the whole transplant is necessary. Given their histologic heterogeneity and potential malignant behavior, gastric subepithelial tumors represent a diagnostic and therapeutic challenge, given their histologic heterogeneity and potential malignant behavior.

Aims and Methods
To evaluate the interest, efficiency and safety of endoscopic resection for subepithelial gastric lesions of size ≤ 20 mm. Single-center retrospective study in a tertiary care center.

Results
A total of 33 lesions (10 malignant/23 benign lesions) Mean histological size was 14.5 mm. 9 EMR, 18 ESD and 6 Hybrid Resection were performed. 93.9% lesions were resected in one piece. Complete and definitive resection, with a follow-up of 6 months, was obtained in 96.7% of cases. A vertical resection was insufficient in 4 cases.

Conclusion
Endoscopic resection is safe and should be the procedure of choice for both diagnosis and definitive resection for subepithelial gastric lesions of size ≤ 20 mm.
Association between non alcoholic fatty liver disease severity and body composition in obese patients

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Background: Non alcoholic fatty liver disease, or NAFLD, is the hepatic manifestation of the metabolic syndrome. The prevalence of NAFLD in obese patients increases in an epidemic proportion. The link between overweight or obesity is well accepted, but little evidence exists on the relationship between body composition and NAFLD severity. Methods: 15 overweight or obese patients (age 51 ± 8 yrs; alcohol intake < 20g/week; BMI 35.1 ± 5 kg/m²) with NAFLD were investigated at the HUG using a liver biopsy (with determination of the NAFLD activity score (NAS, semi-quantitative): steatosis, ballooning hepatocytes, lobular inflammation), biochemical impedance analysis (BIA) for body fat assessment and liver fat content using MRI. Linear relationship among variables were computed by Spearman’s correlations. Multivariables analysis was performed with the linear regression model. Results: A positive association was observed between percent fat mass and the NAS score (r = 0.72, p = 0.002), which persisted after adding BMI to the model (β = 0.22, p = 0.002). A positive association was also found between serum C-reactive protein levels and liver steatosis as measured by MRI. Conclusion: In this small group of obese and overweight patients, the severity of NAFLD is associated with body composition. Increased fat mass is linked to a higher NAS score on liver histology. Body composition as assessed by BIA may contribute to a better patient selection for liver biopsy. However, these findings needs to be confirmed in a larger group of patients (funded by FLAGS in Geneva)

Evolution of portal haemodynamics in patients with decompensated alcoholic liver disease (ALD) and relationship with alcohol relapse

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Gastroenterology and Hepatology, HUG

Decompensated ALD presenting as acute on chronic liver failure is characterized by an increased portal pressure due to intral hepatic vascular resistance in relationship with inflammation and endothelial dysfunction. The evolution of portal haemodynamics over time, however, is ill defined. We explored the evolution of portal pressure, ascites formation and liver failure following decompensation. Methods: We selected 21 patients with cirrhosis from a cohort study (age 51 yrs; recent alcoholic intake: 135 3g/day; alcoholic hepatitis: 81%; 47% steroid treated; MELD score 17.2 ± 1.4; ascites: 71%; beta blockers: 9%) who were reevaluated after 3 months. We measured the hepatic venous pressure gradient (HVPG, wedge (WHVP) minus free PVP, mmHg) both at baseline and at 3 months, and inflammation using plasma C-reactive protein (CRP: N < 10 mg/L). Alcohol relapse was monitored over time. Results:

Baseline 3 months p value
MELD 17 ± 2.5 12.8 ± 4.4 < 0.05
HVPG (mmHg) 17 ± 4.2 15.7 ± 4.2 0.28
WHVP (mmHg) 30.2 ± 7.5 25.2 ± 5.9 < 0.05
CRP (mg/L) 22.1 ± 17.6 9.7 ± 12 < 0.001
Ascites (%) 33 ± 0.05

Nine (42%) patients return to alcohol during FU (heavy regular consumption in 7, mean 620 g/week, isolated relapse in 2). Abstinent patients compared to alcohol relapers presented a trend towards a better liver improvement (delta MELD -16 vs -3, p=0.06) but a parallel evolution of portal haemodynamics (% changes in HVPG: -2 vs -12, p=0.15; % changes in WHVP: -12 vs -15, p=0.56). Conclusion: In this selected population of patients with chronic ALD, portal haemodynamic parameters and liver insufficiency improve at 3 months after decompensation. Alcohol relapse doesn’t seem to influence the evolution of these parameters. (partially funded by FLAGS)


L Elkrief, I Morard, L Spahr, PA EltonRouge, P Morel, TBerney.

Liver transplantation for hepatocellular carcinoma (HCC) to patients with other liver diseases. Patients were included in the waiting list if they met the “Milan criteria” and since 2009 the “TTVA/AF criteria”.

Results: from 1987 to 2014, 594 adults patients were transplanted: 159 (27%) for hepatocellular carcinoma, and 434 (73%) for other causes. The other causes of were: HCV (20%), alcoholic cirrhosis (12%) and HBV (7%). There was a significant difference in survival rate: 77% at 5 years for CHC patients versus 85% for non-CHC, and 63% at 10 years for CHC versus 75% (log rank= 0.027). Among the 159 adults patients transplanted for HCC 43 died, including 11 (6.9%) from recurrence, which represents the main cause of death in this group of patients. Of the 435 patients transplanted for other causes 111 died, the main reasons of death being cancers (20%), HCV recurrence (13%) and cardiovascular diseases (13%). The causes of death were not significantly different between the 2 groups, except for CHC recurrence.

In the 102 patients on the waiting list between January 2010 and January 2015, 23(22.5%) were withdrawn. 16 out 102 (15.6%) patients had tumor progression as main cause of dropout, and this represents 70% of the total dropout.

Conclusion: survival is significantly lower in our patients transplanted for HCC because of recurrence. New treatments are eagerly needed because death from recurrence is the reason for the difference in survival.

ClinicalTrials.gov Identifier
Intestinal microbiota significantly alters hepatic gene expression and plasma bile acid profile in mice with acute cholestasis.

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Background: Intestinal microbiota is recognized as a new “organ” which plays an important role in the regulation of metabolism of bile acids (BA). We were therefore interested in assessing the effects of intestinal microbiota on hepatic gene expression profile and plasma BA composition in basal conditions and in cholestasis.

Methods: We induced acute cholestasis in germ free (GF) and altered Schaedler flora colonized (ASF) mice by performing bile duct ligation (BDL) for 5 days. We evaluated the gene expression profile in the liver of these mice compared to non-cholestatic control groups using next generation sequencing and pathway analysis, and we measured the plasma concentration of 20 BA by UPLC-MS analysis.

Results: We found that acute cholestasis was associated with a significantly different expression of groups of genes involved in the regulation of the immune system, the accumulation of extracellular matrix and of oxidative processes in both ASF and GF mice. Moreover, 448 genes were significantly over expressed in the absence of intestinal microbiota involving in pathways such as organic acid catabolic and fatty acid metabolic processes, leukocyte migration, external side of plasma membrane. In non-cholestatic mice the absence of microbiota significantly induced or suppressed the expression level of 80 genes. Under basal conditions, chenodeoxycholic acid and muricholic acid were detected only in ASF mice, whereas taumuricholic acid was detected only in GF mice. The concentration of the majority of BA increased after BDL, but more markedly in ASF mice.

Conclusion: Intestinal microbiota significantly alters the hepatic gene expression profile and the plasma bile acid composition in basal conditions in mice. Changes observed after BDL suggest that microbial-induced differences may impact the course of cholestasis.

Real World Effectiveness, Safety and Costs of Direct-Acting Antiviral Agents in Chronic Hepatitis C Treatments

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Background/Aims: Second generation direct-acting antiviral agents (DAAs) have revolutionized hepatitis C virus (HCV) treatment since their introduction in Switzerland in 2014. We evaluated efficacy, safety and direct costs of current DAA regimens in comparison to therapies with first generation protease inhibitors (PI) in 2011-2013.

Methods: Single center retrospective analysis of outpatients treated for chronic Hepatitis C between 2011 and 2015.

Results: Overall 112 (28 PI vs. 84 DAA) patients received treatment. PI Group (2011-2013): 28 GT1 received first generation PI (Telaprevir or Boceprevir) with Interferon (IFN)/Ribavirin (RBV), mean age 49 (34-62), fibrosis stage F3 or F4 in 75 (89%), 28 (33%) treatment experienced. DAA Group (2014-ongoing): 84 with predominantly GT1 (56 (66%)), mean age 55 (33-83), fibrosis stage F3 or F4 in 75 (89%), 28 (33%) treatment experienced. Patients were treated according to Swiss label or within early access programs: 25 (30%) received IFN/RBV/Sofosbuvir (SOF), 16 (19%) SOF/Ledipasvir, 11 (13%) SOF/RBV, 11 (13%) DAA/RBV, 11 (13%) DAA/SOF/RBV with Simeprevir, 6 (7%) SOF/RBV with Daclatasvir.

Outcomes PI Group: 16 (57%) with SVR12, 9 (32%) stopped treatment due to futility rules, 2 (7%) due to serious adverse events (SAE). 14% due to breakthrough. SAEs occurred in 6 (21%); in addition 7 (25%) needed blood transfusion or EPO. Average treatment duration was 26 weeks (range 4-48 weeks) with mean drug costs per SVR12 of CHF 63 997.

Outcomes DAA Group: End of treatment response in 61/61 (100%) while 2 patients did not respond to treatment. Average treatment duration was 26 weeks (range 4-48 weeks) with mean drug costs per SVR12 of CHF 63 997.

Conclusions: Current DAA regimens are safe, well tolerated and show excellent cure rates even in treatment-experienced patients with advanced liver disease and advanced age. Overall SVR12 rates increased significantly with second generation DAAs while costs remain high.

Intestinal microbiota significantly alters hepatic gene expression and plasma bile acid profile in mice with acute cholestasis.

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Background: Intestinal microbiota is recognized as a new “organ” which plays an important role in the regulation of metabolism of bile acids (BA). We were therefore interested in assessing the effects of intestinal microbiota on hepatic gene expression profile and plasma BA composition in basal conditions and in cholestasis.

Methods: We induced acute cholestasis in germ free (GF) and altered Schaedler flora colonized (ASF) mice by performing bile duct ligation (BDL) for 5 days. We evaluated the gene expression profile in the liver of these mice compared to non-cholestatic control groups using next generation sequencing and pathway analysis, and we measured the plasma concentration of 20 BA by UPLC-MS analysis.

Results: We found that acute cholestasis was associated with a significantly different expression of groups of genes involved in the regulation of the immune system, the accumulation of extracellular matrix and of oxidative processes in both ASF and GF mice. Moreover, 448 genes were significantly over expressed in the absence of intestinal microbiota involving in pathways such as organic acid catabolic and fatty acid metabolic processes, leukocyte migration, external side of plasma membrane. In non-cholestatic mice the absence of microbiota significantly induced or suppressed the expression level of 80 genes. Under basal conditions, chenodeoxycholic acid and muricholic acid were detected only in ASF mice, whereas taumuricholic acid was detected only in GF mice. The concentration of the majority of BA increased after BDL, but more markedly in ASF mice.

Conclusion: Intestinal microbiota significantly alters the hepatic gene expression profile and the plasma bile acid composition in basal conditions in mice. Changes observed after BDL suggest that microbial-induced differences may impact the course of cholestasis.

One year experience in enhanced recovery pathway for colorectal surgery

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Background: Implementation of enhanced recovery after surgery (ERAS) pathways is associated with a reduction in morbidity and length of hospital stay (LOS). The complexity of current ERAS pathways has hampered their widespread use. This paper reports our first-year experience in implementing ERAS in elective colorectal surgery.

Methods: ERAS pathways were implemented along a structured process including all stakeholders. Outcome and pathway compliance were prospectively followed. Data were compared to a retrospectively analysed consecutive pre ERAS cohort.

Results: Within the first year 114 patients were operated on. They were compared to a 153-patient consecutive pre ERAS cohort. Patients’ age, morbidity and procedures performed did not differ significantly. In both groups most patients underwent colorectal resections for diverticular disease or cancer. Morbidity was halved from 45.7% in the pre ERAS group to 24.5% in the ERAS group (p = 0.007). Severe complications (Dindo-Clavien III-V) showed a decrease from 12.4% to 9.6%. Median LOS decreased from 9 (IQR 7, 13) to 7 (IQR 3, 11) days (p = 0.004). The readmission rate remained stable.

Conclusion: Successful implementation of ERAS pathway in colorectal surgery is feasible and worth the efforts. It requires significant work, close monitoring and a dedicated team.
Incidence of early postoperative complications comparing linear versus circular stapling technique in laparoscopic Roux-en-Y gastric bypass
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Background
Different surgical techniques for performing a Laparoscopic Roux-en-Y gastric bypass (RYGB) do exist. Currently there are two techniques, which have emerged as standard for the gastrojejunostomy: the linear stapling and circular stapling technique. The aim of this study was to compare the two techniques regarding postoperative morbidity and weight loss.

Methods
We compared two consecutive cohorts at a single institution between November 2012 and June 2014 assessing the incidence of postoperative complications (30d) and weight loss at one year after the operation. 109 patients underwent a RYGB with a 21-mm circular stapler. 134 patients underwent a RYGB performed by linear stapling technique.

Results
Preoperative BMI and incidence of comorbidities were similar in both groups. The incidence of postoperative complications was significantly higher in the group using the circular stapling technique with 23.9% vs 4.5% (p=0.00009). Stenosis at the gastrojejunostomy occurred significantly more often in the circular stapling group with 14/13% cases versus 0 in the linear group. The rate of leakages (2 vs 1) and length of stay (5.5 vs 6.2 days) was similar in both groups. There was no significant difference regarding weight loss at one year (29.4 vs 29kg/m²).

Conclusion
Linear stapled gastric bypass displays less postoperative complications, with similar weight loss at one year and should therefore be the procedure of choice.

Six years results of revisional laparoscopic Roux-en-Y gastric bypass (rLRYGB) after failed gastric banding (LAGB)
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Background: Long-term failure of LAGB is high. At our institution we initially performed biliopancreatic diversion with duodenal switch (BPD-DS) in cases of LAGB failure as part of a staged concept, possibly over treating a number of patients. Lately, rLRYGB has become popular after failed LAGB. Most published series are based on a mean follow-up of 2-3 years.

Methods: Retrospective analysis of prospectively collected data on weight loss, co-morbidities, re-operations, complications, and quality of life including BAROS score (Bariatric Analysis and Reporting Outcome System) of rLRYGB was performed, with a mean follow up of 6 years (range 2-9 years).

Results: Overall 74 patients met our inclusion criteria. Baseline characteristics at the time of LAGB: age 40 ± 10 years, 55 women and 19 men, weight 120 ± 15 kg, BMI 42 ± 4 kg/m². On average it took 6.3 ± 3.1 years from initial LAGB to rLRYGB. The most common indications for rLRYGB were band intolerance (59%), band slippage (12%), pouch dilatation (6%), insufficient weight loss (3%) and/or secondary weight regain (9%). 53/74 patients (72%) were revised to 35.2 ± 5.6 kg/m² at the time of rLRYGB and further to 30 ± 4.8 kg/m² after a mean follow-up of 6 ± 2.2 years, resulting in an excessive BMI loss of 72.6 ± 27.9%. According to BAROS score, 60% had a good to excellent result. Remission/improvement rate for diabetes and arterial hypertension was over 50%.

Conclusion: Long-term results of rLRYGB as a revisional procedure after failed LAGB proved satisfactory concerning weight loss and quality of life/co-morbidities using BAROS score.

Long-term outcome of laparoscopic adjustable gastric banding (LAGB): results of a Swiss single-centre study of 405 patients with up to 18 years follow-up
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Background: LAGB seemed to be a very promising bariatric procedure but many studies showed high rates of re-operation due to complications or insufficient weight loss. There is lack of long-term studies with a follow-up beyond 15 years.

Methods: Retrospective analysis of prospectively collected clinical data on weight loss, co-morbidities, re-operations, complications, and quality of life including BAROS score (Bariatric Analysis and Reporting Outcome System) in a cohort of 405 patients having undergone LAGB was performed. Follow up (FU) was conducted in our outpatient clinic or via telephone interview.

Results: 405 patients (age 41 ± 10 years, BMI 44.3 ± 6 kg/m²) were treated with a LAGB between 1996 and 2010. Mean FU was 13 ± 3 years, with a FU rate of 85 % (range 8–18 years) corresponding to 343 patients. 100 patients exceeded a FU period of 15 years. In 216 patients (63%) the LAGB was removed and another bariatric procedure performed: 32 (9%) patients underwent lap. sleeve gastrectomy, 102 (30%) lap. gastric bypass and 82 (24%) biliopancreatic diversion with duodenal switch due to either band intolerance, slippage, insufficient weight loss or secondary weight regain; 27 (8%) patients refused further bariatric surgery after band removal. Total failure rate was 63%. Finally, 100 (30%) patients still have the band in place with a mean BMI of 35 ± 7 kg/m², corresponding to an extreme BMI-loss of 46 ± 27%. Of these, the failure rate was 25%, according to BAROS; 50% had a good to excellent outcome.

Conclusion: More than 10 years after LAGB 70% of patients lost their bands and only 12% have the band in place and a good to excellent result according to BAROS.

The value of extended lymphadenectomy in distal esophageal cancer
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Background: Curative esophagectomy provides the best prognosis in patients with esophageal cancer. The extent of lymphadenectomy and its potential benefit has been controversially discussed over the last 2 decades. The aim of this study was to assess the benefit of an extended lymphadenectomy regarding survival.

Methods: 3087 patients with stage I-II distal esophageal cancer were identified from the Surveillance, Epidemiology, and End Results (SEER) database between 2004 and 2012. The impact of extended lymphadenectomy with 20+ retrieved regional lymph nodes (RLN) on survival was assessed using both multivariate Cox proportional hazards model and propensity score matching (PSM).

Results: In 727 patients (23.6%) 20+ RLN were retrieved. This rate increased from 14.1% in 2004 to 30.1% in 2012 (P<0.001). The 5-year overall and cancer-specific survival in patients with 20+ retrieved RLN were 48.4% (95%CI: 44.0-53.2%) and 55.2% (95%CI: 50.8-60.0%) compared to 43.3% (95%CI: 40.9-45.7%) and 48.7 (95%CI: 47.3-52.3%) in patients with less retrieved RLN. Extended lymphadenectomy of 20+ RLN was associated with an increased overall survival in unadjusted (hazard ratio (HR) of death=0.85, 95%CI: 0.75–0.97, P=0.013) and 0.85, 95%CI: 0.75–0.97, P=0.016). Similar results were observed for cancer-specific survival in unadjusted (HR=0.86, 95%CI: 0.75–0.99, P=0.037) and PSM-adjusted Cox regression (HR=0.81, 95%CI: 0.69–0.91, P=0.002).

Conclusions: Extended lymphadenectomy resulted in a significant survival benefit in unadjusted and PSM-adjusted population-based analysis. Therefore, extended lymphadenectomy should be advocated in all patients undergoing esophagectomy.
Laparoscopic Sleeve Gastrectomy and Roux-Y-Gastric Bypass are equally effective up to three years. Results of the prospective randomized Swiss Multicentre Bypass Or Sleeve Study (SM-BOSS)

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Background: Laparoscopic Sleeve Gastrectomy (LSG) is performed almost as often in Europe as laparoscopic Roux-Y-Gastric Bypass (LRYGB). We present the 3-year results of this randomized clinical trial comparing the two procedures.

Methods: Initially 217 patients (LSG, n=107; LRYGB, n=110) were randomized to receive either LSG or LRYGB at four bariatric centres in Switzerland. Mean BMI of all patients was 44 ±11 kg/m², mean age was 43 ±5.3 years, and 70% of patients were female. Minimal follow-up was three years with a rate of 97.7% at three years after surgery. Both groups were compared for weight loss, co-morbidities, quality of life according to GIQLI and BAROS score, and complications.

Results: Excessive BMI loss was similar between LSG and LRYGB at each time point (one year: 73±22% vs 77±21%, p=0.2; two years: 74±30% vs 78±30%, p=0.4; three years: 70±24% vs 74±23%, p=0.2). Prevalence of comorbidities was significantly reduced after both procedures except for GERD, which showed a higher remission rate after LRYGB. Quality of life increased significantly in both groups after one and three years post surgery.

Conclusion: Laparoscopic Sleeve Gastrectomy (LSG) is performed almost as often in Europe as laparoscopic Roux-Y-Gastric Bypass (LRYGB). We present the 3-year results of this randomized clinical trial comparing the two procedures.

Double-barreled wet colostomy following exenteration for locally advanced and recurrent pelvic cancer: early experience

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Introduction
In patients undergoing pelvic exenteration for advanced cancer, two stomas are usually required - a colostomy and ileal conduit. Whilst inconvenient for the patient, this approach limits options for perineal flap reconstruction. We describe the technique, and our early experience of, the double-barreled wet colostomy (DBWC) as an alternative option.

Methods
Exenterations were undertaken via a midline incision, with proximal vascular ligation, lymphadenectomy, en bloc organ resection and removal of specimens via the perineum. Each DBWC was constructed by anastomosing the ureters separately, over infant feeding tubes, into a 15cm blind length of colon distal to the colostomy site. Following Vertical Rectus Abdominus Muscle (VRAM) flap mobilisation and abdominal closure, the DBWC was exteriorised and matured over a bridge in the left iliac fossa, recovering the infant feeding tubes to drain into a colostomy bag.

Results
Eight patients (6 males; median age 61) underwent exenteration and DBWC over a 9 month period. Pathologies were: locally advanced primary rectal cancer with prostatic invasion (5 patients); recurrent rectal cancer or anal cancer with vaginal and urethral involvement (2 patients); prostate cancer invading rectum (1 patient). Seven patients received preoperative chemoradiotherapy and 7 had perineal reconstruction with a VRAM flap. Median hospital stay was 21 days. Procedure-related complications included: urinary sepsis which resolved after ureteric stent removal (2 patients), and one collection around a VRAM flap needing drainage.

Conclusion
Early experience with DBWC following exenteration is encouraging. No major complications were seen, urinary sepsis does not appear to be a significant risk, as fecal and urinary streams do not mix, and patient satisfaction is high. Avoidance of a second stoma eliminates the risk of ileal conduit complications and allows the harvesting of a VRAM flap for perineal reconstruction.

Postoperative inflammatory syndrome after CRS/HIPEC

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Background: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is a treatment option in well-selected patients with peritoneal tumors. There is a risk of severe morbidity and even mortality; however knowledge about the complex pathophysiology of CRS/HIPEC is scarce. Here we describe the postoperative dynamics of inflammatory parameters in presence or absence of infectious complications after CRS/HIPEC.

Methods: Ninety patients after completed CRS/HIPEC between 2008-2013 were taken from the prospective Zurich database, including peroperative complications, clinical parameters and laboratory values. Patients with infectious complications (CDC Definition 1999) were compared to patients without infection. Routine diagnostics included clinical examination, chest X-ray, urine and catheter cultures, and CT scan in selected cases. To exclude the influence of postoperative management, the patients were additionally compared to patients (n=77) after esophagectomy.

Results: The majority of patients had appendix tumors (53%) and colorectal carcinomatosis (30%), with a female preponderance (61%), and a median age of 51 years. The two groups (+/- infection after CRS/HIPEC) were not different regarding the extent of the disease (median PCI 10), and surgery (splenectomy, number of colon anastomoses). Surprisingly, also the group without infection, showed a second postoperative peak in CRP levels, observed only after CRS/HIPEC but not after esophagectomy. If this CRP value was >80mg/l, it was predictive for major complications (OR 3.0, p=0.04) in patients after CRS/HIPEC. Patients after CRS/HIPEC developed less leucocytosis in case of infection compared to patients after esophagectomy. Conclusion: There is a second rise of inflammatory parameters (CRP) after uncomplicated CRS/HIPEC, and a reduced capacity for leucocytes in case of infectious complications. This observation is novel and highlights the complex pathophysiology of CRS/HIPEC.
Aepli P  2 S, 12 S, 13 S
Baumeler S  2 S
Bega H  2 S
Bochatay L  8 S, 9 S
Boudewijn Van der Weg B  6 S
Brunner F  13 S
Castro Soares P J  11 S
Csaba Horvath H  12 S
Elkrief L  16 S
Eshmuminov D  19 S
Faes S K  13 S, 14 S
Friedli B  14 S
Gan-al-Vonarburg S C  2 S
Giriens B  8 S
Godat S  3 S, 15 S
Gomez de Agüero M  11 S
Grignoli R  9 S
Guirgis M  3 S
Heimgartner B  4 S, 14 S
Juillerat P  7 S
Kaymak T  11 S
Köllner Y  7 S
Krat T  14 S, 15 S
Kraus R  4 S, 19 S
Künzler P  17 S
Künzli C  17 S
Kwong Chung C  11 S
Li H  3 S
Mechera R  19 S
Michetti P  10 S
Moghadamrad S  17 S
Moyat M  12 S
Perez-Shibayama C  4 S
Peterli R  19 S
Ronchi F  12 S
Rupp S C  10 S
Safonova E  8 S, 9 S
Schärdin A  17 S
Schneider M  4 S
Spahr L  5 S, 16 S
Steinert A  10 S
Straumann A  5 S
Stutz A  5 S
Stulz M C  5 S
Troller R  6 S
Uchimura Y  10 S
Venetz D  6 S
Vines L C  18 S
Vinzens F  6 S, 18 S
Wang Q  16 S
Wiest R  7 S, 13 S
Wolf S  18 S
Zimmermann D  8 S
Zumstein V  7 S