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# Performance of Routine *Helicobacter pylori* Tests in Patients with Atrophic Gastritis

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## Abstract

**Background.** Decreased density of *H.pylori* in atrophic gastritis may lead to low sensitivity of the routine tests. **Aims.** To evaluate the accuracy of routinely used *H.pylori* tests in atrophic gastritis. **Methods.** We compared 5 *H.pylori* diagnostic tests in 119 dyspeptic patients (28 males/91 females) with a mean age of 67 years (range 55-84). Patients with gastric cancer, peptic ulcer, previous gastric surgery, or those who have received eradication therapy were excluded. The following tests were performed: histology, rapid urease test (RUT), culture, <sup>13</sup>C- urease breath tests (UBT), and *H.pylori* IgG/IgA antibody test (serology). **Results.** Atrophic gastritis was diagnosed in 26.1% of the patients; *H.pylori* was present in 87.1%. In the group with atrophy, the sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy were as follows: histology (100% for all parameters); UBT (96; 100; 100; 80; 97%); serology (96; 50; 93; 67; 90%); culture (96; 100; 100; 80; 97%); and RUT (78; 100; 100; 40; 81%), respectively. **Conclusions.** Histology, UBT and culture were the three best tests for diagnosing *H.pylori* infection. We cannot recommend using serology as a single test in a case of atrophy, but it would be reasonable to combine serology with one of the above tests.

# Long-term Outcome of Patients with Distal Ulcerative Colitis and Inflammation of the Appendiceal Orifice

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## Abstract

**Background & Aims:** Skip inflammation of the appendiceal orifice has been described in distal UC (UC-IAO) but long-term clinical outcomes are poorly established. Our aim was to evaluate the long-term clinical outcomes of UC-IAO as compared to classic distal UC. **Methods:** Patients with UC-IAO were identified from the local IBD database. Disease outcome and therapeutic requirements during follow-up were accurately collected, and compared with a control group of patients with distal UC without periappendiceal involvement matched by disease extent (proctitis/distal), smoking habit, and date and age at diagnosis. **Results:** Fourteen UC patients were found to have UC-IAO, most of them with initial extent of UC limited to the rectum. All patients were initially managed with mesalazine administered orally (28.5%), topically (28.5%), or in combination (43%). After a median follow-up of 78 months (interquartile range - IQR 45-123) most UC-IAO patients were successfully managed with oral and/or topical aminosalicilates. Only one of them developed proximal disease progression. As compared to controls, no differences in clinical outcomes or therapeutic requirements were found. **Conclusions:** Patients with UC-IAO tend to present a mild course, with a low probability to develop proximal progression of disease extent or to require immunosuppressive therapy or colectomy.

# Response to First Intravenous Steroid Therapy Determines the Subsequent Risk of Colectomy in Ulcerative Colitis Patients

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## Abstract

**Background & Aims.** A severe flare-up develops in approximately 15% of patients with ulcerative colitis (UC). It is questionable whether the response to the first parenteral corticosteroid therapy decreases the risk for colectomy. Our aim was to evaluate the association between long-term colectomy rate and the efficacy of steroids in the first few days of the therapy and to assess other predictive factors for colectomy in our patients hospitalized because of the first severe attack of UC. **Patients and methods.** The records of the first hospitalization of a total of 183 UC patients with severe exacerbation were reviewed. Every patient had received parenteral corticosteroid treatment. Colectomy was performed in refractory UC or in the case of intolerable side-effects of the rescue therapy. We compared different laboratory and clinical parameters between patients undergoing colectomy and those who avoided surgery. **Results.** Clinical response to steroid therapy was achieved in 110 of the 183 patients with acute severe UC; 14.5% of steroid responder patients were operated on during the follow-up period. 39.7% of patients in the steroid-refractory group required either urgent or late colectomy. The overall colectomy rate was 24.6%. Unresponsiveness to intravenous steroid therapy, anemia, and the need for blood transfusion proved to be the major predictors for colectomy. **Conclusion.** The colectomy rate was 2.5 times higher in our patients with acute severe UC not responding to the intensive steroid therapy, suggesting that the response to the therapy of the first 3-5 days of hospitalization may determine the long-term outcome and colectomy rate in UC.

# Tumour Necrosis Factor-Alpha Expression in Segmental Colitis Associated with Diverticulosis Down-Regulates After Treatment

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## Abstract

**Background & Aims:** Tumour Necrosis Factor- $\alpha$  (TNF- $\alpha$ ) expression may be increased in Segmental Colitis Associated with Diverticulosis (SCAD). Our aim was to assess TNF- $\alpha$  expression in SCAD in relationship to the treatment. **Methods:** 10 patients affected by severe (type B and D) SCAD were studied (6 males, 4 females, mean age 60.54 years, range 43-85 years). All patients were treated with beclomethasone dipropionate 10 mg/day plus a probiotic preparation VSL#3 for 8 weeks. At that time, clinical, endoscopic and histological reassessment was performed. Controls were 5 patients with active ulcerative colitis (UC). **Results:** After treatment, all SCAD B and no SCAD D patients were in remission. The TNF- $\alpha$  expression dropped from 42.7% ( $\pm$ 7.58) to 15.7% ( $\pm$ 2.6) in SCAD B patients ( $p=0.001$ ), and from 40% ( $\pm$ 5.9) to 28.6% ( $\pm$ 5.3) in SCAD D patients ( $p=0.005$ ). In UC patients, the TNF- $\alpha$  expression dropped from 45.5% ( $\pm$ 5.09) to 22.5% ( $\pm$ 2.5) ( $p=0.001$ ). Neither SCAD B nor SCAD D patients showed a significant difference in TNF- $\alpha$  expression compared to UC after treatment. Finally, TNF- $\alpha$  was significantly overexpressed in SCAD D than in SCAD B at the end of treatment ( $p=0.048$ ). **Conclusions:** TNF- $\alpha$  expression in SCAD down regulates after treatment, and seems to be related to the clinical response to therapy. This behaviour, similar to that of Inflammatory Bowel Diseases (IBD), confirms that this disease should be considered as a subtype of IBD.

# Interleukin-16 (IL-16) Gene Polymorphisms in Iranian Patients with Colorectal Cancer

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## Abstract

**Background & Aims:** A number of theories have been put forward to clarify the etiology of colorectal cancer (CRC), such as genetic alterations and cytokine production. A combination of inflammatory cytokines has an important role in cancer development. The aim of our study was to screen for alterations located in promoter and exons of IL-16 gene sequence, to determine the distribution of genotypes in individuals with CRC and healthy controls in a sample of Iranian population. **Methods:** The case group consisted of 260 individuals with colorectal cancer and the control group included 405 healthy individuals. Three IL-16 gene polymorphisms (rs4072111, rs11556218, rs4778889) were genotyped using PCR-RFLP method. RFLP results were confirmed by direct sequencing. **Results:** A significant association between rs11556218 SNP in the IL-16 gene and the risk of CRC was found. The TG genotype of rs11556218 T/G polymorphism showed significant association with a 1.75 fold increased risk of CRC ( $P=0.005$ ; adjusted OR: 1.759; 95% CI: 1.191- 2.598). In addition a significant association between CC genotype of rs4778889 T/C polymorphism and decreased risk of CRC in male subjects ( $P=0.045$ ; adjusted OR: 0.192; 95% CI: 0.038-0.967) was determined. **Conclusion:** This study is the first report of IL-16 gene polymorphisms among CRC patients from Iran. Our results suggest an influence of rs11556218 T>G and rs4778889 T/C polymorphisms on the altered risk of CRC.

# Weight-Based Dosing Regimen of Peg-Interferon $\alpha$ -2b for Chronic Hepatitis Delta: a Multicenter Romanian Trial

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## Abstract

**Background:** Antiviral therapy for chronic hepatitis D (delta) is not yet satisfactory, although it appears to be the only means to alter the progressive natural course of chronic hepatitis D virus (HDV) infection. **Aim:** To assess safety and efficacy, evaluated by virological, biochemical and histological end-of-treatment (EOT) and end-of-follow-up (EOF) response to Peg-Interferon  $\alpha$ -2b 1.5 $\mu$ g/kg body weight weekly in a Romanian cohort of naïve patients with chronic hepatitis delta. **Results:** 49 Caucasian patients (55.1% men, 44.9% females) with a mean age of 37.95 years received study medication; per-protocol population consisted of 36 subjects. Virological EOT response was present in 33.3% and EOF response was maintained in 25% of patients. 50% of study population showed normalization of ALT level at EOT and 25% at EOF. A combined biochemical and virological response was observed in 19.4% of patients at EOT and in 16.7% at EOF. At baseline, the necroinflammation quantified by histological activity index (HAI) score was 9.72 and the mean fibrosis score was 2.03; there was a significant decrease of HAI score to 7.44 ( $p=0.01$ ) at EOT, but not for fibrosis score (1.33,  $p=0.37$ ). However, only 8.3% of patients at EOT and 19.4% at EOF had progressive histological disease. **Conclusions:** Treatment with Peg-Interferon  $\alpha$ -2b succeeded in obtaining a negative HVD RNA in 25% of patients after 104 weeks of follow-up, although combined biochemical and virological response was present in only 16.7%. Necroinflammation decreased significantly in treated patients. Longer treatment periods with pegylated interferon or combination regimen peginterferon-nucleotide analogues should be tested in order to increase efficacy.

# Use of Elderly Donors for Liver Transplantation: Has the Limit Been Reached?

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## Abstract

**Background & Aim:** Several solutions have been proposed for the minimization of both organ shortage and prolonged waiting time for liver transplantation (LT): expansion of the donor pool using elderly donors represents a possible solution. However, it is still not fully explained if the use of “extreme” donors could cause unacceptable post-transplant adjunctive risks. The aim of the study is to evaluate the impact of donor age on post-LT patient and graft survival. **Methods:** A cohort of 188 LTs were stratified in four groups according to donor age (Group 1: age < 30 years: n=34; Group 2: age 30-49 years: n=51; Group 3: age 50-69 years: n=75; Group 4: age 70-89 years: n=28). Donor, recipient and transplantation characteristics were compared in the four groups. **Results:** No differences were observed among the groups with regard to initial (< 1 week) graft function; vascular thrombosis was predominantly experienced in the oldest subgroup (p-value 0.03). The oldest subgroup presented a 5-year patient survival of 47.0%, with statistically worse results with respect to the 1st and 2nd group (p-value 0.005 and 0.03, respectively). Analyzing the graft survivals, Group 4 had a 5-year survival rate of 40.7%, presenting statistically worse results with respect to the 1st and 2nd group (p-value 0.003 and 0.006, respectively). **Conclusions:** Use of > 70 year-aged donors should be considered with caution and only in selected cases.

# Clinicopathological Correlations of Nestin Expression in Surgically Resectable Pancreatic Cancer Including an Analysis of Perineural Invasion

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## Abstract

**Background & Aims:** Nestin is considered to be a marker of stem/progenitor cells in different tissues. Nestin expression was also described in various tumors. In pancreatic ductal adenocarcinoma (PDAC), its role in cancer cell migration, invasion, and metastases has been suggested. The study aimed at examining the expression of nestin in PDAC, and to evaluate its clinicopathological correlations. **Methods:** The expression of nestin was immunohistochemically examined in 117 PDAC resection specimens, analyzed, and correlated with clinico-pathological parameters including perineural invasion (PNI). Analysis of nestin expression in nerve fibers in tissues of chronic pancreatitis (CP) was added. **Results:** Immunohistochemical analysis of nestin expression showed 79 nestin negative (67.5 %) and 38 nestin positive (32.5 %) PDACs. No significant correlations of nestin expression in tumor cells with the analyzed clinicopathological parameters were demonstrated. Tumor grade ( $p < 0.001$ ) and nodal status ( $p = 0.009$ ) proved to represent independent prognostic factors. PNI was identified in 94 PDAC (80.3 %), and did not correlate with nestin expression. Nestin immunostaining was displayed in nerve fibers of both CP and PDAC tissues. **Conclusion:** An intimate link of nestin to a biological process of pancreatic cancer was confirmed. The expression of nestin did not prove to be a valuable prognostic factor and an immunohistochemical assessment of nestin expression is not superior to conventional prognostic factors in PDAC. A correlation between nestin expression in tumor cells and PNI was not confirmed and expression of nestin in nerve fibers of both PDAC and CP tissues seems to reflect the process of neural remodeling responsible for pancreatic neuropathy.

## REVIEWS

# Hepatitis C Virus Infection and Genetic Susceptibility to Therapy

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### **Abstract**

Both response to treatment as well as spontaneous outcome of hepatitis C virus infection is critically affected by host genetic factors. However, most of the identified association genes could not be confirmed in subsequent studies and almost none of the identified risk factors had a noticeable impact on clinical decisions. In contrast, recent land-mark studies identified variations in close proximity to the interleukin 28B gene locus to be independently associated to treatment response and spontaneous viral clearance in hepatitis C genotype 1 infection. These findings and their potential role in future treatment decision-makings will be discussed here.

# Endoscopic Ultrasound: Current Role and Future Perspectives in Managing Rectal Cancer Patients

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## **Abstract**

As therapeutic regimens for rectal cancer have seen considerable changes, an accurate staging is mandatory for choosing the adequate strategy. Locoregional staging is the decisive factor in selecting patients for neoadjuvant chemoradiation therapy and for determining the extent of surgery. Endoscopic ultrasound (endorectal ultrasound - ERUS) is a very effective method for assessing the local extent of rectal cancer, especially regarding the depth of tumor infiltration. Although a significant limitation is represented by its lower accuracy for diagnosis of lymph node metastases, this is still a point of concern for other imaging tests as well. In this review we report the current data on ERUS, presenting both its advantages and limitations, and making a comparison to other staging methods. Recent developments of the technology that might enhance staging accuracy are also discussed.

# Combined Cardiac Surgery and Liver Transplantation: Three Decades of Worldwide Results

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## Abstract

**Background:** Patients with end-stage-liver-disease (ESLD) require orthotopic liver transplantation (OLT) as treatment. However, cirrhotic cardiomyopathy can be clinically revealed during OLT, with the possible development of a transient overt congestive heart failure. A number of patients require a combined procedure of liver transplantation and heart surgery, which includes heart transplantation, aortic valve replacement or coronary artery bypass grafting. Indications for combined liver-heart transplantation include heart failure with associated cardiac cirrhosis, familial amyloidosis, familial hypercholesterolemia and hemochromatosis, and homozygous  $\beta$ -thalassemia. **Methods/ Results.** We performed a thorough research of Pubmed/ Medline, gathering and discussing data concerning this clinical condition and its treatment. **Conclusion:** In patients with end-stage liver disease, who are unable to tolerate an OLT post-operatively due to cardiac dysfunction, combined cardiac surgery and OLT appears to have certain advantages.

## CLINICAL IMAGING

# Endomicroscopy for Assessing Mucosal Healing in Patients with Ulcerative Colitis

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### **Abstract**

The assessment of tissue healing has emerged as an important treatment goal in patients with inflammatory bowel disease. In patients with ulcerative colitis (UC), mucosal healing may represent the ultimate therapeutic goal due to the fact that the inflammation is limited to the mucosal layer. Mucosal and histological healing may indicate a subset of UC patients in long-term clinical, endoscopic and histological remission in whom immunomodulators, biologics, and even aminosalicylates may be withdrawn.

Confocal laser endomicroscopy allows the assessment of residual cellular inflammation, crypt and vessel architecture distortion during ongoing endoscopy, and therefore permits a real-time evaluation of histological healing in patients with ulcerative proctitis. Images of conventional optical microscopy and confocal laser endomicroscopy in patients with ulcerative proctitis in remission are presented.

## CASE REPORTS

# Small Cell Carcinoma: an Unusual Location in a Young Healthy Female

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### Abstract

Small cell carcinoma (SCC) is most commonly found in the lung but is occasionally found in the gastrointestinal tract and other extrapulmonary sites. Incidences of SCC in the esophagus and stomach are rare and have been reported almost exclusively in older individuals. The following case presents the discovery of small cell carcinoma of the stomach and esophagus in a 35 year old woman, which is the youngest reported incidence of this to date. Additionally, her course reflects the importance of early diagnostic endoscopy with biopsy and adequate sampling with appropriate immunohistochemical staining when malignancy is in the differential diagnosis, regardless of age or risk factors.

# Esophageal Xanthoma – Report of Two New Cases and Review of the Literature

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## Abstract

**Background:** Esophageal xanthoma is a very rare lesion which can be incidentally discovered during endoscopy. Only eleven cases have been reported, including ours. **Case reports:** We present two new cases of esophageal xanthoma localized in the lower esophagus in a 56-year-old woman and a 62-year-old man. Endoscopically, esophageal xanthoma appears as yellowish granular spots or a slightly elevated lesion. Microscopically, it consists of fat accumulation in foamy histiocytes beneath the squamous epithelium. **Conclusions:** The clinical and pathological importance of these lesions and what they mean in patients is discussed, along with a review of the literature.

# **Gastric Ulcer Bleeding from a Variant Left Gastric Artery Accompanied by Congenital Absence of the Splenic Artery Successfully Treated With Coil Embolization: a Case Report and Review of the Literature**

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## **Abstract**

Endoscopic hemostasis is a useful treatment modality for gastric ulcer bleeding. However, it is sometimes difficult to achieve hemostasis in cases with arterial bleeding, especially those complicated with vascular abnormalities. We describe a case with gastric ulcer bleeding from a variant left gastric artery accompanied by congenital absence of the splenic artery. A 50-year-old female was admitted to our hospital with dizziness and tarry stools. Upper gastrointestinal endoscopy revealed bleeding from a gastric ulcer, and endoscopic hemostasis by endoscopic clipping was carried out. Computed tomography and abdominal angiography revealed the variant left gastric artery running below the gastric ulcer. In spite of endoscopic hemostasis and medication, re-bleeding from the gastric ulcer occurred. A transcatheter coil embolization for the variant left gastric artery was performed and successfully achieved hemostasis. This case was accompanied by congenital absence of the splenic artery, which is an extremely rare condition. We herein describe this rare case and review previously reported cases.

# Well-Differentiated Neuroendocrine Carcinoma Mimicking an Echinococcus Cyst of the Liver in CT – MRI Findings with Hepatocyte Specific Contrast Material

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## Abstract

Gastroenteropancreatic neuroendocrine tumors and their metastases have an inconsistent appearance with only a small percentage of lesions appearing as cystic masses in computed tomography (CT) and magnetic resonance imaging (MRI) and can therefore be mistaken as benign or infectious lesions, leading to a false diagnosis with delayed and inadequate treatment. We report a patient with upper abdominal pain lasting for several months, caused by a huge cystic neuroendocrine carcinoma of the liver which was mistakenly interpreted as an echinococcus cyst and present the findings in the initial CT and the subsequently performed MRI under application of hepatocyte specific contrast material, which led to distinct differential diagnoses and therefore had a capacious impact on the therapeutic strategy.