

## Contents

### Images of the issue

- Malignancy presenting as multiple lesions in a cirrhotic liver: not always hepatocellular carcinoma**  
*W.M. van der Deure, E.P.J. Lugtenburg, R.S. Dwarkasing, K. Biermann, E.T.T.L. Tjwa*.....7
- Association between chronic HCV hepatitis, membranoproliferative glomerulopathy and cutaneous sarcoidosis**  
*L. Iliescu, V. Herlea, L. Toma, C. Orban*.....8
- Cocaine capsules in the colon: the internal concealment of illicit drugs**  
*D. Trabulo, S. Marques, E. Pedroso*.....9
- Right upper quadrant pain in a young female**  
*N. Renz, M. Baur, F. Stickel*.....10

### Editorial

- CAP: a novel era to better quantitate fatty liver?**  
*S. Mueller*.....11

### Original Papers

- Prevalence of anemia and iron deficiency in Romanian patients with inflammatory bowel disease: a prospective multicenter study**  
*A. Lupu, M. Diculescu, R. Diaconescu, M. Tantau, A. Tantau, I. Visovan, C. Gheorghe, C. Lupei, L. Gheorghe, Razvan Cerban, Roxana Vadan, Adrian Goldis*.....15
- Saccharomyces boulardii* for the prevention of hospital onset *Clostridium difficile* infection**  
*E.A. Flatley, A.M. Wilde, M.D. Nailor*.....21
- Autoimmune liver diseases and antiphospholipid antibodies positivity: a meta-analysis of literature studies**  
*P. Ambrosino, R. Lupoli, G. Spadarella, P. Tarantino, A. Di Minno, L. Tarantino, M.N.D. Di Minno*.....25
- Diagnostic accuracy of controlled attenuation parameter measured by transient elastography for the non-invasive assessment of liver steatosis: a prospective study**  
*M. Luşor-Platon, D. Feier, H. Stefănescu, A. Tamas, E. Botan, Z. Sparchez, A. Maniu, R. Badea*.....35
- Plasma lipidomic fingerprinting to distinguish among hepatitis C-related hepatocellular carcinoma, liver cirrhosis, and chronic hepatitis C using MALDI-TOF mass spectrometry: a pilot study**  
*A.M. Passos-Castilho, E. Lo Turco, M. Lúcia Ferraz, C. Matos, I. Silva, E. Parise, E. Pilau, F. Gozzo, C. Granato*.....43
- Association between portal vein thrombosis and survival of liver transplant recipients: a systematic review and meta-analysis of observational studies**  
*X. Qi, J. Dai, J. Jia, W. Ren, M. Yang, H. Li, D. Fan, X. Guo*.....51
- Serum immunoreactive collagen IV detected by monoclonal antibodies as a marker of severe fibrosis in patients with non-alcoholic fatty liver disease**  
*Y. Aida, H. Abe, Y. Tomita, T. Nagano, N. Seki, T. Sugita, M. Itagaki, H. Ishiguro, S. Sutoh, Y. Aizawa*.....61
- Diagnostic performance of endoscopic ultrasound (EUS)/endoscopic ultrasound – fine needle aspiration (EUS-FNA) cytology in solid and cystic pancreatic neuroendocrine tumours**  
*V. Mitra, M.K. Nayar, J.S. Leeds, V. Wadehra, B. Haugk, J. Scott, R.M. Charnley, K.W. Oppong*.....69

<b>The Lauren classification highlights the role of epithelial-to-mesenchymal transition in gastric carcinogenesis: an immunohistochemistry study of the STAT3 and adhesion molecules expression</b> <i>S. Susman, R. Barnoud, F. Bibeau, F. Borini, M. Pocard, C. Tomuleasa, J.C. Sabourin</i> .....	77
<b>Reviews</b>	
<b>The role of colonoscopy in managing diverticular disease of the colon</b> <i>A. Tursi</i> .....	85
<b>A systematic review on drugs absorption modifications after eradication in <i>Helicobacter pylori</i> positive patients undergoing replacement therapy</b> <i>G. Fiorini, J.M. Bland, E. Hughes, V. Castelli, D. Vaira</i> .....	95
<b>Case reports</b>	
<b>Primary biliary cirrhosis – autoimmune hepatitis overlap syndrome associated with dermatomyositis, autoimmune thyroiditis and antiphospholipid syndrome</b> <i>C. Pamfil, E. Candrea, E. Berki, H.I. Popov, P.I. Radu, S. Rednic</i> .....	101
<b>Open biopsy guided by endoscopic ultrasonography from a gastric submucosal tumor growing outside the stomach</b> <i>H. Mori, H. Kobara, N. Nishiyama, S. Fujihara, T. Masaki</i> .....	105
<b>Gangliocytic paraganglioma: a rare cause of gastrointestinal bleeding</b> <i>A. Boeriu, D. Dobru, R. Georgescu, S. Mocan, C. Boeriu</i> .....	109
<b>Paroxysmal postprandial atrial fibrillation suppressed by laparoscopic repair of a giant paraesophageal hernia compressing the left atrium</b> <i>D.A. Cristian, A.S. Constantin, M. Barbu, D. Spătaru, T. Burcoş, F.A. Grama</i> .....	113
<b>Romanian Association for the Pancreatic Pathology Corner</b>	
<b>Romanian guidelines on the diagnosis and treatment of exocrine pancreatic insufficiency</b> <i>C. Gheorghe, A. Seicean, A. Saftoiu, M. Tantau, E. Dumitru, M. Jinga, L. Negreanu, B. Mateescu, L. Gheorghe, M. Ciocirlan, C. Cijevschi, G. Constantinescu, S. Dima, M. Diculescu</i> .....	117
<b>Calendar of events</b> .....	124
<b>Letters</b>	
<b>The relationship between inflammatory bowel disease and type 1 diabetes mellitus: a study of relative prevalence in comparison with population controls</b> <i>H.A. Penny, J.S. Leeds, M. Kurien, A. Averginos, A.D. Hopper, M. Hadjivassiliou, S. Tesfaye, D.S. Sanders</i> ..	125
<b>Does anatomical distribution of colorectal polyps show a rightward shift? Analysis of 2,372 colorectal polyps in 1,558 patients from Turkey</b> <i>S. Boga, A.R. Koksall, H. Alkim, M. Ergun, M. Bayram, A.A. Ozagari, C. Alkim</i> .....	126
<b>Neutrophil-lymphocyte ratio in Crohn’s disease patients predicts sustained response to infliximab 52-week therapy</b> <i>M.K. Wlodarczyk, A.E. Sobolewska, K. Stec-Michalska, J.J. Fichna, M.E. Wisniewska-Jarosinska</i> .....	127
<b>Appendiceal mucocele in ulcerative colitis: a rare association and a crucial preoperative diagnosis</b> <i>M. Tonolini</i> .....	128
<b>Comment to the article Gastric Cat Scratch - an Upper Endoscopy Finding?</b> <i>T. Akar, G. Dindar, K. Karagözoğlu, D. Malkoç, S. Aydemir</i> .....	129
<b>Reply</b> <i>T.M. Carvalho, V.M. Fernandes, J.M. de Freitas</i> .....	130
<b>Guidance for Authors</b> .....	131

# Prevalence of Anemia and Iron Deficiency in Romanian Patients with Inflammatory Bowel Disease: a Prospective Multicenter Study

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## ABSTRACT

**Background & Aims:** Anemia is the most frequent systemic complication in inflammatory bowel diseases. It affects the quality of life and can interact with working capacity. Our objectives were to identify the prevalence of anemia, its main causes and its management in patients with inflammatory bowel disease from Romania.

**Methods:** We conducted a multicenter prospective study from March 2013 to August 2014. We enrolled 291 patients from three referral centers: 115 (39.52%) with Crohn's disease (CD) and 176 (60.48%) with ulcerative colitis (UC). We defined anemia according to the WHO criteria.

**Results:** Median age of the patients was 41 years and the median time period since diagnosis was 3 years (0.75-7). The median activity index for UC (UCAI) was 4 and the median CD activity index (CDAI) was 96. More patients with CD were on antiTNF $\alpha$  therapy ( $p < 0.01$ ), corticosteroids ( $p = 0.18$ ) or azathioprine ( $p = 0.05$ ) and required surgery for their underlying disease at study enrollment ( $p < 0.01$ ). Anemia was present in 31.27% of the patients, more often in those with CD (35.65%) than with UC (28.41%) (not statistically significant); 53.26% of the patients had iron deficiency while 4.12% had folic acid and 8.59% vitamin B12 deficiency; 9.62% of the patients had received anti-anemic therapy at inclusion in the study or in the last three months prior to study enrollment.

**Conclusions:** About one in three Romanian patients with inflammatory bowel disease has anemia, which is frequently associated with iron deficiency. About 30% of the patients with anemia are under therapy and the most frequent route for iron supplementation is the oral one. This might contribute to the high prevalence of iron deficiency and the low level of compliance.

**Key words:** anemia - iron deficiency - inflammatory bowel disease.

# *Saccharomyces boulardii* for the Prevention of Hospital Onset *Clostridium difficile* Infection

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## ABSTRACT

**Background & Aims:** Probiotics, including *Saccharomyces boulardii*, have been advocated for the prevention of *Clostridium difficile* infection. The aim of this project was to evaluate the effects of the removal of *S. boulardii* from an automatic antibiotic order set and hospital formulary on hospital onset *C. difficile* infection rates.

**Method.** Design: A retrospective chart review was performed on all patients with hospital onset *C. difficile* infection during the 13 months prior (control group) and the 13 months after (study group) removal of an automatic order set linking *S. boulardii* capsules to certain broad spectrum antibiotics. Setting: A large 800+ bed tertiary hospital

**Results:** Among all hospitalized patients, the rate of hospital onset *C. difficile* infection was 0.99 per 1000 patient days while the *S. boulardii* protocol was active compared with 1.04 per 1000 patient days ( $p=0.10$ ) after *S. boulardii* was removed from the formulary. No difference in the rate of hospital onset *C. difficile* infection was detected in patients receiving the linked broad spectrum antibiotics during and after the removal of the protocol (1.25% vs. 1.51%, respectively;  $p=0.70$ ).

**Conclusions:** Removal of *S. boulardii* administration to patients receiving broad spectrum antibiotics and the hospital formulary did not impact the rate of hospital onset *C. difficile* infection in either the hospital population or patients receiving broad spectrum antibiotics.

**Key words:** probiotics - *Saccharomyces boulardii* - *Clostridium difficile* infection.

# Autoimmune Liver Diseases and Antiphospholipid Antibodies Positivity: a Meta-analysis of Literature Studies

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## ABSTRACT

**Background & Aims:** Several studies reported an association between autoimmune liver diseases (AiLD) and antiphospholipid antibodies (aPL) positivity. We performed a meta-analysis of studies evaluating the association of primary biliary cirrhosis (PBC), autoimmune hepatitis (AIH), and primary sclerosing cholangitis (PSC) with aPL positivity and with aPL-related thrombotic events.

**Methods:** Studies evaluating the association of AiLD with aPL (anticardiolipin [aCL], anti- $\beta$ 2 glycoprotein-I [anti- $\beta$ 2GPI], lupus anticoagulant [LA] antibodies) and with aPL-related thrombotic complications were systematically searched in the PubMed, Web of Science, Scopus and EMBASE databases.

**Results:** A total of 10 studies (750 patients with AiLD and 1,244 healthy controls) were included in the analysis on the prevalence of aPL and showed that AiLD are significantly associated with the presence of aCL and anti- $\beta$ 2GPI. The association with aCL positivity was consistently confirmed in PBC (OR: 13.93, 95%CI: 4.69-41.38), AIH (OR: 23.50, 95%CI: 4.28-129.13), and PSC (OR: 18.21, 95%CI: 7.05-47.08). Similarly, anti- $\beta$ 2GPI were found more frequently in PBC (OR: 25.10, 95%CI: 4.77-132.11), AIH (OR: 48.57, 95%CI: 11.07-213.09), and PSC (OR: 36.30, 95%CI: 6.55-201.31). These findings are confirmed when separately analyzing IgM, IgG, and IgA directed against phospholipids. Two of the 10 included articles and 1 further study (67 cases and 75 controls) showed a trend – not achieving statistical significance – towards a higher prevalence of thrombotic complications in AIH patients with aPL as compared to those with only AIH (OR: 1.67, 95%CI: 0.46-6.05).

**Conclusion:** PBC, AIH, and PSC are significantly associated with aPL positivity. The association with aPL-related thrombotic complications should be further studied.

**Key words:** primary biliary cirrhosis - autoimmune hepatitis - primary sclerosing cholangitis - antiphospholipid antibodies - antiphospholipid syndrome.

# Diagnostic Accuracy of Controlled Attenuation Parameter Measured by Transient Elastography for the Non-invasive Assessment of Liver Steatosis: a Prospective Study

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## ABSTRACT

**Background & Aims:** A novel non-invasive tool based on the evaluation of ultrasound attenuation using transient elastography (TE) has been developed, called controlled attenuation parameter (CAP). We aim to establish the histopathological parameters that significantly influence CAP, the cutoff values and their performance in predicting each steatosis grade on a group of biopsied patients with chronic liver diseases (CLD) from Romania.

**Methods.** We prospectively analyzed 201 consecutive CLD patients who underwent CAP measurements using TE. Steatosis, liver fibrosis and necroinflammatory activity were staged and graded during the pathological analysis of bioptic specimens. Univariate and multivariate regression analyses were applied to identify the variables correlated with CAP values. The diagnostic performance of CAP for steatosis prediction was assessed using an AUC analysis.

**Results.** Among the histopathological factors correlating with CAP, the multivariate analysis found steatosis as the only factor independently influencing CAP values ( $p < 0.001$ ). Maximal diagnostic accuracy (DA) was obtained for the prediction of  $\geq 34$ -66% (S2) fatty load and of 67-100% (S3) fatty load (82.06%, respectively 81.59%) while, for the prediction of  $\geq 11$ -33% (S1) fatty load, DA reached only 76.11%. The negative predictive value for the exclusion of  $\geq S2$  and S3 was 93.5% and 98.7%, respectively. AUCs calculated between each two steatosis grades were: 0.772 (S0 vs S1), 0.874 (S0 vs S2), 0.904 (S0 vs S3), 0.659 (S1 vs S2), 0.777 (S1 vs S3), and 0.665 (S2 vs S3).

**Conclusion.** Steatosis is the only histopathological factor independently influencing CAP. Maximal DA could be obtained for the prediction of  $\geq S2$  and S3 (82.06% and 81.59%), while for the prediction of S1, the accuracy reached only 76.11%.

**Key words:** steatosis - noninvasive - Fibroscan - vibration-controlled transient elastography - controlled attenuation parameter (CAP).

# Plasma Lipidomic Fingerprinting to Distinguish among Hepatitis C-related Hepatocellular Carcinoma, Liver Cirrhosis, and Chronic Hepatitis C using MALDI-TOF Mass Spectrometry: a Pilot Study

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## ABSTRACT

**Background & Aims:** Hepatitis C (HC) is a major cause of hepatocellular carcinoma (HCC), and a late diagnosis is the main factor for the poor survival of patients. There is an urgent need for identifying sensitive and specific biomarkers for HCC diagnosis. In the present study, plasma lipid patterns of patients with HC-HCC, HC-liver cirrhosis (LC), and chronic HC (CHC) were assessed by matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS).

**Methods.** Plasma samples of 25 patients with HC-HCC, 15 patients with HC-LC, and 25 patients with CHC were evaluated by MALDI-MS using a Q-ToF premier (Synapt) mass spectrometer (Waters, Manchester, UK) equipped with a 200-Hz solid-state laser in the mass range between m/z (mass-to-charge ratio) of 700–1200.

**Results.** A total of 2205 ions were initially obtained and 7 ions (m/z) were highlighted as corresponding to the most important lipids to differentiate HCC patients from LC and CHC patients. The specific lipidomic expression signature generated resulted in an overall predictive accuracy of 93% of HC-HCC and HC-LC, and 100% of HC-HCC and CHC. The 7-peak algorithm distinguished HCC from LC with a sensitivity of 96% and a specificity of 87%, and HCC from CHC with both sensitivity and specificity of 100%.

**Conclusion.** MALDI-MS-specific signature peaks accurately distinguished patients with HC-HCC from those with HC-LC and CHC. The results indicate the potential of MALDI-MS and the selected peaks to improve HCC surveillance in patients with viral C cirrhosis and chronic hepatitis C.

**Key words:** hepatocellular carcinoma - hepatitis C - lipidomics - fingerprints - lipids - MALDI-MS.

# Association between Portal Vein Thrombosis and Survival of Liver Transplant Recipients: a Systematic Review and Meta-analysis of Observational Studies

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## ABSTRACT

**Background & Aims:** Portal vein thrombosis (PVT) increases the technical complexity of liver transplantation (LT). This systematic review and meta-analysis aim to analyze the association of pre-LT PVT with the overall survival after LT.

**Methods.** PubMed, EMBASE, and Cochrane library databases were used to search for papers related to the association between pre-LT PVT and survival of LT recipients. The differences in the survival rates between the LT recipients with and without pre-LT PVT were expressed as odds ratios (ORs) with 95% confidence intervals (CIs).

**Results.** Twenty-seven papers were included. Overall meta-analysis showed that the total LT recipients with pre-LT PVT had a significantly lower 1-year survival rate than those without pre-LT PVT (OR=0.733, 95%CI=0.621-0.865; P=0.0002). But no statistically significant difference was observed in the in-hospital (OR=0.713, 95%CI=0.343-1.482; P=0.365), 1-month (OR=0.679, 95%CI=0.345-1.333; P=0.261), or 5-year survival rate (OR=0.788, 95%CI=0.587-1.058; P=0.113). Additionally, the 1-year survival rate was significantly lower in the LT recipients with complete PVT than in those without PVT (OR=0.503, 95%CI=0.295-0.858; P=0.012). However, no statistically significant difference in the 1-year survival rate between them was observed in the meta-analysis of high-quality studies (OR=0.899, 95%CI=0.657-1.230; P=0.505) or that of studies in which LT was performed after 2000 (OR=0.783, 95%CI=0.566-1.083; P=0.140).

**Conclusion.** Pre-LT PVT, especially complete PVT, decreased the 1-year survival rate after LT. However, the detrimental effect of pre-LT PVT on the survival of LT recipients became inconclusive in high-quality studies. Additionally, further well-designed cohort studies should validate the association in patients undergoing LT during the latter years.

**Key words:** prognosis - survival - portal vein thrombosis - liver cirrhosis - liver transplantation.

# Serum Immunoreactive Collagen IV detected by Monoclonal Antibodies as a Marker of Severe Fibrosis in Patients with Non-Alcoholic Fatty Liver Disease

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## ABSTRACT

**Background & Aims:** The incidence of non-alcoholic fatty liver disease (NAFLD) is increasing worldwide. We evaluated serum collagen IV as a direct non-invasive marker of severe liver fibrosis in NAFLD.

**Methods:** The study included 148 NAFLD and 187 chronic hepatitis C patients in whom histological severity of liver fibrosis was evaluated. The utility of serum collagen IV measured by immune-mediated agglutination using two types of monoclonal antibodies for distinguishing severe fibrosis ( $\geq$  stage 3 and  $\geq$  F3) from non-to-moderate fibrosis in NAFLD or chronic hepatitis C was assessed in comparison to serum hyaluronic acid or other indirect fibrosis markers.

**Results:** Multiple logistic regression analysis showed that serum collagen IV was significantly associated with severe fibrosis in NAFLD (odds ratio: 1.21,  $p < 0.001$ ) but not in chronic hepatitis C. For distinguishing severe fibrosis in NAFLD, collagen IV showed the largest area under the receiver-operating characteristic curve (0.827, 95%CI: 0.746–0.908) followed by FIB-4 (0.805, 95%CI: 0.728–0.890); in chronic hepatitis C, those for FIB-4 (0.813, 95%CI: 0.748–0.878) and collagen IV (0.770, 95%CI: 0.683–0.857) were the largest and smallest, respectively. To detect severe fibrosis in NAFLD, a cutoff of collagen IV  $> 177$  exhibited 77.1% sensitivity, 84.0% specificity, 76.5% positive predictive value, and 84.0% negative predictive value. Combined with a cutoff of FIB-4  $> 2.09$ , the negative and positive predictive values, and specificity for detecting severe fibrosis in NAFLD increased further.

**Conclusion:** Collagen IV is a reliable marker for distinguishing severe liver fibrosis from non-to-moderate fibrosis in NAFLD but not chronic hepatitis C.

**Key words:** non-alcoholic fatty liver disease - non-alcoholic steatohepatitis - collagen IV - FIB-4 - hepatitis C virus - liver fibrosis

# Diagnostic Performance of Endoscopic Ultrasound (EUS)/Endoscopic Ultrasound – Fine Needle Aspiration (EUS-FNA) Cytology in Solid and Cystic Pancreatic Neuroendocrine Tumours

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## ABSTRACT

**Background & Aims:** Our study aimed to assess the sensitivity of EUS and EUS-FNA for pancreatic neuro-endocrine tumors (pNETs) and compare performance over two consecutive 4 year 2 month periods, to investigate the comparative performance between solid and cystic pNETs and determine the incremental yield of EUS±FNA in individuals with a mass not diagnosed as a pNET after cross-sectional imaging.

**Methods:** A retrospective review of a prospectively maintained database was carried out to identify all pNET patients who underwent EUS-FNA between April 2003 and September 2011.

**Results:** A final diagnosis of solid and cystic pNETs was made in 43 and 10 patients, respectively. Overall, the yield of combined EUS imaging and cytology was significantly higher than that of CT and/or MRI ( $p < 0.05$ ) across all groups [solid (83.7% vs. 41.8%), cystic (70% vs. 10%) and combined solid-cystic (81.1% vs. 35.8%)]. The yield of combined EUS imaging and cytology was significantly better than EUS imaging alone ( $p < 0.05$ ) in the solid (83.7% vs. 58%) and combined pNET cohort (81.1% vs. 52.8%) of patients. After a non-diagnostic CT and or MRI, EUS/EUS-FNA confirmed pNET in 19 out of 25 patients (76.0%) with solid pNETs and 6 out of 9 patients (66.7%) with cystic pNETs.

**Conclusion:** EUS and EUS-FNA had a significant clinical impact in the 25/34 of cases where pNET was not suspected after initial cross-sectional imaging.

**Key words:** pancreatic neuroendocrine tumour (pNET) - endoscopic ultrasound (EUS) - fine needle aspiration (FNA) - sensitivity.

# The Lauren Classification Highlights the Role of Epithelial-to-Mesenchymal Transition in Gastric Carcinogenesis: an Immunohistochemistry Study of the STAT3 and Adhesion Molecules Expression

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## ABSTRACT

**Background & Aims:** Despite some recent advances, gastric cancer remains an important cause of death at world level. This indicates an absence of therapeutic options, stemming from the limited understanding of the molecular mechanisms involved in carcinogenesis. Nearly fifty years ago Lauren classified gastric cancers, according to the morphological aspect, as intestinal or diffuse. The phenotype of the cells indicates the presence of different molecular mechanisms, which can be approached in the light of recent data and identified with the help of current techniques. The best described are the germline/somatic mutations or the hypermethylations of the E-cadherin 1 *CDH1* gene promoter.

**Methods.** We analyzed 195 gastric tumors, 120 intestinal and 75 diffuse type, using immunohistochemistry (tissue microarray TMA method) for pStat3<sup>Tyr705</sup>, E-cadherin,  $\alpha$ -catenin and  $\beta$ -catenin; 985 spots of gastric tumors, distributed on 4 TMA blocks were analyzed. For pStat3<sup>Tyr705</sup> we took the nuclear staining into account and for the adhesion molecules, membrane staining.

**Results.** In our study, in the diffuse type gastric cancer, pStat3<sup>Tyr705</sup> nuclear expression was statistically significantly increased ( $p=0.003$ ). Also we observed a decreased expression of the adhesion molecules in the same type of gastric cancer (E-cadherin  $p<0.0001$ ,  $\alpha$ -catenin  $p<0.0001$ ,  $\beta$ -catenin  $p<0.0001$ ), suggesting that epithelial-to-mesenchymal transition (EMT) may be involved not only in gastric carcinogenesis, but also in resistance to treatment.

**Conclusion.** The Stat3 role has been recently highlighted in carcinogenesis of the diffuse type of gastric cancer. We found that the morphological features of the diffuse type also suggest the involvement of EMT in this type of gastric cancer. Therefore, targeting the key molecules involved in this process may interfere with EMT process in the diffuse type of gastric cancer.

Key words: gastric cancer - Stat3 - adhesion molecule - EMT.

## REVIEWS

# The Role of Colonoscopy in Managing Diverticular Disease of the Colon

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### ABSTRACT

Diverticulosis of the colon is frequently found on routine colonoscopy, and the incidence of diverticular disease and its complications appears to be increasing. The role of colonoscopy in managing this disease is still controversial.

Colonoscopy plays a key role in managing diverticular bleeding. Several techniques have been effectively used in this field, but band ligation seems to be the best in preventing rebleeding. Colonoscopy is also effective in posing a correct differential diagnosis with other forms of chronic colitis involving colon harbouring diverticula (in particular with Crohn's disease or Segmental Colitis Associated with Diverticulosis). The role of colonoscopy to confirm diagnosis of uncomplicated diverticulitis is still under debate, since the risk of advanced colonic neoplasia in patients admitted for acute uncomplicated diverticulitis is not increased as compared to the average-risk population. On the contrary, colonoscopy is mandatory if patients complain of persistent symptoms or after resolution of an episode of complicated diverticulitis. Finally, a recent endoscopic classification, called Diverticular Inflammation and Complications Assessment (DICA), has been developed and validated. This classification seems to be a promising tool for predicting the outcome of the colon harboring diverticula, but further, prospective studies have to confirm its predictive role on the outcome of the disease.

**Key words:** acute diverticulitis - colonoscopy - diverticulosis - diverticular disease - diverticular bleeding - Segmental Colitis Associated with Diverticulosis - Diverticular Inflammation and Complications Assessment (DICA) classification.

# A Systematic Review on Drugs Absorption Modifications after Eradication in *Helicobacter pylori* Positive Patients undergoing Replacement Therapy

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## ABSTRACT

**Background & Aims:** *Helicobacter pylori* (*H. pylori*) infection has been suggested as a cause of impaired drug absorption. This infection leads to alteration of the gastric acid secretion that may change the conformational characteristics of drugs and their intestinal absorption leading to uncertainties about the dose to administer and the therapeutic results. A systematic review was undertaken to clarify the implications of drug absorption during the administration of replacement therapies.

**Methods:** Electronic databases such as MEDLINE/Pubmed, EMBASE and The Cochrane Library [which includes Cochrane Database of Systematic Review (CDSR), the Cochrane Central Register of Controlled Trials (CENTRAL), the Database of Abstract of Reviews of Effect (DARE)] were searched. Grey literature databases (e.g. the International clinical trials registry platform, Trials Register, Clinical Trials.gov, Controlled Trials and TrialsCentral), Theses database, Government publication and LILACS database were also searched. No language restriction was applied.

**Results:** Infection and altered drug absorption were evaluated in patients under replacement therapies with iron, thyroxin and L-dopa. In all, seven studies included an improvement in drug absorption after eradication and an existing inverse correlation between the grade of gastric inflammation and indices of drug absorption were noticed.

**Conclusion:** This systematic review confirmed the presence of an interaction between infection and drug absorption of orally administered replacement therapies. Gastric acid reduction and subsequent alteration of drug composition seem to lead this mechanism. Clinicians should be aware of this possible interaction when starting a replacement therapy in patients and when evaluating poor clinical response.

**Key words:** *Helicobacter pylori* - absorption - replacement therapy.

## CASE REPORTS

# Primary Biliary Cirrhosis – Autoimmune Hepatitis Overlap Syndrome Associated with Dermatomyositis, Autoimmune Thyroiditis and Antiphospholipid Syndrome

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### ABSTRACT

Autoimmune liver diseases may be associated with extrahepatic autoimmune pathology. We report the case of a 52-year old woman who initially presented to the gastroenterology department for extreme fatigue, pale stools, dark urine and pruritus. Laboratory tests showed significant cholestasis and elevation of aminotransferase levels. Immunological tests revealed positive antinuclear (ANA=1:320) and antimitochondrial antibodies (AMA=1:40) with negative anti-smooth muscle and liver kidney microsomal type 1 antibodies. The biopsy was compatible with overlap syndrome type 1. The patient was commenced on immunosuppressive therapy according to standard of care (azathioprine 50mg, ursodeoxycholic acid and prednisone 0.5mg/kg), with moderate biochemical improvement. She subsequently developed proximal symmetrical weakness and cutaneous involvement and was diagnosed with biopsy-proven dermatomyositis. The immunosuppressive regimen was intensified to 150 mg azathioprine. At the three-month follow-up, her symptoms subsided and aminotransferases and muscle enzymes normalized. Upon further investigation the patient was diagnosed with autoimmune thyroiditis and antiphospholipid syndrome. To our knowledge, this is the first case of primary biliary cirrhosis – autoimmune hepatitis overlap syndrome associated with dermatomyositis, autoimmune thyroiditis and antiphospholipid syndrome.

**Key words:** autoimmune hepatitis - primary biliary cirrhosis - inflammatory myopathies - autoimmune thyroid disease - antiphospholipid syndrome.

# Open Biopsy guided by Endoscopic Ultrasonography from a Gastric Submucosal Tumor growing Outside the Stomach

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## ABSTRACT

Submucosal tunneling bloc biopsy for submucosal tumors growing inside the gastric wall is a safe and reliable method. However, it is difficult for an endoscopist to perform submucosal tunneling bloc biopsy and detect the demarcation line between the proper muscular layer and the capsule layer of submucosal tumors growing outside the gastric wall.

A submucosal tumor in the lesser curvature of the stomach was identified in a 74-year-old man by esophagogastroduodenoscopy. Computed tomography revealed hetero-density with partial calcification of the tumor growing outside the gastric wall, that connected to approximately 10 mm of the muscular layer. Almost all of the tumor body was located outside the stomach. After the small connecting area was detected by endoscopic ultrasonography, two markings were placed at the opposite ends of the tumor. The tumor was removed via snare resection between the markings located immediately above the top of the tumor. After the biopsy site was reconfirmed using endoscopic ultrasonography, a large bloc biopsy was conducted. This new “open biopsy under endoscopic ultrasonography” is a simple, safe, and reliable method to obtain samples from any type of submucosal tumor growing inside or outside the stomach.

**Key words:** submucosal tunneling biopsy - submucosal tumor - outside growth - endoscopic ultrasonography.

# Gangliocytic Paraganglioma: a Rare Cause of Gastrointestinal Bleeding

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## ABSTRACT

Duodenal neuroendocrine tumors (NETs) are rare tumors, consisting of five different types of tumors. In many cases, they may be asymptomatic, leading to delay in diagnosis. Clinical symptoms are related to local tumor growth and mucosal ulceration. We report a 38-year old man with duodenal gangliocytic paraganglioma causing overt upper gastrointestinal bleeding and anemia. We describe specific clinical and histopathological features of the tumor, and review the diagnostic and therapeutic strategy. Gangliocytic paragangliomas are regarded as benign tumors. However, the disease recurrence and the malignant potential of the tumor have also been reported.

**Key words:** gangliocytic paraganglioma - immunostaining - surgical excision - metastasis.

# Paroxysmal Postprandial Atrial Fibrillation Suppressed by Laparoscopic Repair of a Giant Paraesophageal Hernia Compressing the Left Atrium

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## ABSTRACT

We present the case of a patient with a giant paraesophageal hernia associated with paroxysmal postprandial atrial fibrillation that was suppressed after surgery. The imaging investigations showed the intrathoracic displacement of a large part of the stomach, which pushed the left atrial wall causing atrial fibrillation. The laparoscopic surgical repair acted as sole treatment for this condition.

**Key words:** giant hiatal hernia - paroxysmal postprandial atrial fibrillation - laparoscopic hiatal hernia repair.

# Romanian Guidelines on the Diagnosis and Treatment of Exocrine Pancreatic Insufficiency

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## ABSTRACT

In assessing exocrine pancreatic insufficiency (EPI), its diverse etiologies and the heterogeneous population affected should be considered. Diagnosing this condition remains a challenge in clinical practice especially for mild-to-moderate EPI, with the support of the time-consuming breath test or the coefficient of fat absorption. The fecal elastase-1 test, less precise for the diagnosis, cannot be useful for assessing treatment efficacy. Pancreatic enzyme replacement therapy (PERT) is the mainstay of treatment, whereby enteric-coated mini-microspheres are taken with every meal, in progressive doses based on an individual's weight and clinical symptoms. The main indication for PERT is chronic pancreatitis, in patients who have clinically relevant steatorrhea, abnormal pancreatic function test or abnormal function tests associated with symptoms of malabsorption such as weight loss or meteorism. While enzyme replacement therapy is not recommended in the initial stages of acute pancreatitis, pancreatic exocrine function should be monitored for at least 6-18 months. In the case of unresectable pancreatic cancer, replacement enzyme therapy helps to maintain weight and improve overall quality of life. It is also indicated in patients with celiac disease, who have chronic diarrhea (in spite of gluten-free diet), and in patients with cystic fibrosis with proven EPI.

**Key words:** exocrine pancreatic insufficiency - enzyme replacement therapy - chronic pancreatitis - guidelines.