

**ORIGINAL PAPERS**

Wilson's disease: a challenge of diagnosis. The 5-year experience of a tertiary centre

*Liana Gheorghe<sup>1</sup>, Irinel Popescu<sup>2</sup>, Speranta Iacob<sup>1</sup>, Cristian Gheorghe<sup>1</sup>, Roxana Vadan<sup>1</sup>,  
Alexandra Constantinescu<sup>3</sup>, Razvan Iacob<sup>1</sup>, Gabriel Becheanu<sup>1</sup>, Corina Angelescu<sup>1</sup>,  
Mircea Diculescu<sup>1</sup>*

Risk Factors for Colorectal Cancer: an Epidemiologic Descriptive Study of a Series of  
333 Patients

*Adina Neagoe<sup>1</sup>, Ana-Maria Molnar<sup>2</sup>, Monica Acalovsch<sup>1</sup>, Andrada Seicear<sup>1</sup>, Alexandru  
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Screening for Functional Tumor Suppressor Activity in Pancreatic Cancer\*

*Liviu Lefter<sup>1,3,4</sup>, Viorel Scripcariu<sup>1</sup>, Makoto Sunamura<sup>3</sup>, Toru Furukawa<sup>4</sup>, Seiki Matsuno<sup>3</sup>,  
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### Right Adrenal Abscess – An Unusual Complication of Acute Appendicitis

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### Ruptured Hydatid Cyst of the Liver with Biliary Obstruction: Presentation of a Case and Review of the Literature

*Zeno Spârchez<sup>1</sup>, G.Osian<sup>2</sup>, Alina Onica<sup>1</sup>, Cristina Bărbântă<sup>1</sup>, Marcel Tanțău<sup>1</sup>, Oliviu Pascu<sup>1</sup>*

### Hematemesis as a Presenting Symptom of Lung Cancer with Synchronous Metastases to the Esophagus and Stomach. A Case Report

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## ORIGINAL PAPERS

### Wilson's disease: a challenge of diagnosis. The 5-year experience of a tertiary centre

*Liana Gheorghe<sup>1</sup>, Irinel Popescu<sup>2</sup>, Speranta Iacob<sup>1</sup>, Cristian Gheorghe<sup>1</sup>, Roxana Vadan<sup>1</sup>, Alexandra Constantinescu<sup>3</sup>, Razvan Iacob<sup>1</sup>, Gabriel Becheanu<sup>1</sup>, Corina Angelescu<sup>1</sup>, Mircea Diculescu<sup>1</sup>*

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*Abstract*

**Background.** *Because molecular diagnosis is considered impractical and no pathognomonic features have been described, diagnosis of Wilson's disease (WD) using clinical and biochemical findings is still challenging.*

**Patients and method.** *We analysed predictive factors for the diagnosis in 55 patients with WD diagnosed in our centre between 1st January 1999 and 1st April 2004. All patients presented predominant liver disease classified as: 1) asymptomatic, found incidentally, 2) chronic hepatitis or cirrhosis, or 3) fulminant hepatic failure. Diagnosis was considered as classic (two*

out of the three following criteria: 1) serum ceruloplasmin < 20 mg/dl, 2) the presence of Kayser-Fleischer rings and/or 3) hepatic copper >250 mg/g dry weight liver tissue), and non-classic (clinical manifestations plus laboratory parameters suggesting impaired copper metabolism). The association between the predictive factors and non-classic diagnosis was assessed based on the level of statistical significance ( $p$  value<0.05) associated with the chi-squared test in contingency tables. Multivariate analysis was performed by logistic regression using SPSS 10.

**Results.** There were 31 males (56.3%) and 24 females (43.7%) with the mean age at diagnosis of  $20.92 \pm 9.97$  years (4-52 years); 51 patients (92.7%) were younger than 40 years. Asymptomatic WD was diagnosed in 14 patients (25.4%), chronic liver disease due to WD in 29 patients (52.8%) and fulminant hepatic failure in 12 patients (21.8%). The classic diagnosis was made in 32 patients (58.18%). In the univariate analysis the non-classic diagnosis was associated with: age>18 years ( $p=0.03$ ), increased copper excretion ( $p<0.0001$ ), Coombs-negative hemolysis ( $p=0.03$ ), absence of neurological manifestations ( $p<0.0001$ ). Multivariate analysis identified age over 18 years, increased urinary copper, and isolated hepatic involvement as independent predictors.

**Conclusion.** In clinical practice, WD should be considered also in patients who do not fulfil classic criteria. Independent factors associated with non-classic diagnosis were age over 18 years, increased cupruresis and isolated liver disease.

#### Key words

Wilson's disease – diagnosis - ceruloplasmin - Kayser-Fleischer ring

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## Risk Factors for Colorectal Cancer: an Epidemiologic Descriptive Study of a Series of 333 Patients

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Abstract

**Aim.** The purpose of the research was to evaluate several risk factors for colonic neoplasia and to institute a specialized colorectal cancer (CRC) registry in the 3rd Medical and Surgical Clinics Cluj-Napoca.

**Material and methods.** The study comprised 333 patients, 155 women, mean age  $61,32 \pm 12,42$  years and 178 men, mean age  $64,31 \pm 10,39$  years, admitted to the 3rd Medical Clinic and 3rd Surgical Clinic Cluj-Napoca and diagnosed with CRC between January 2001 – September 2003. The diagnosis was made on the basis of clinical, endoscopical and histopathological findings. Age, geographical patterns, tumor location, family history, personal history and

several lifestyle factors: dietary habits (intake of fat and red meat), long term smoking (more than 20 years), heavy alcohol consumption were analyzed. Evaluation was made using family history and epidemiologic lifestyle questionnaires.

**Results.** CRC occurred more frequently in the 7th decade. There was a strong correlation between age and CRC development. In the 5th decade, females developed CRC more frequently than males. The median age for developing right-sided tumors was significantly higher in males. Patients living in an urban area were dominant (69%). Family history was present in 1/3 of females and 1/4 of males. Personal history of colon polyps was more common in men, particularly among smokers for more than 20 years and among those with an excessive intake of fat. The cholecystectomized women had an increased frequency of sigmoidian tumors. All the patient's information was included in a specialized colon cancer registry.

**Conclusion.** High fat intake and cigarette smoking favour colon polyp development. CRC development and location of the tumor are associated with an older age (in men) and personal history of cholecystectomy (in women). Inheritance was significant in our study group.

#### **Key words**

Colorectal cancer – risk factors – epidemiology

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## Screening for Functional Tumor Suppressor Activity in Pancreatic Cancer\*

Liviu Lefter<sup>1,3,4</sup>, Viorel Scripcariu<sup>1</sup>, Makoto Sunamura<sup>3</sup>, Toru Furukawa<sup>4</sup>, Seiki Matsuno<sup>3</sup>, Mitsuo Oshimura<sup>5</sup>, Vasile Drug<sup>2</sup>, Cristian Dragomir<sup>1</sup>, Akira Horii<sup>4</sup>

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#### Abstract

Pancreatic cancer has a well-known reputation as one of the leading causes of cancer deaths worldwide. Thus, acquisition of efficient approaches and markers for accurate detection at the earlier stages of the disease should be prioritized. We have been focusing on tumor suppressor genes (TSGs) activity in pancreatic cancer to find effective methods for its genetic diagnosis and/or treatment.

In this study, we utilized the technique of micro-cell-mediated chromosome transfer (MMCT) to introduce a normal copy of human chromosome 18 individually into some pancreatic cancer cells. Subsequently, the tumorigenic ability of the resulting hybrids was assessed in vitro and in vivo. In vitro growth of the hybrid clones was significantly delayed as compared to the parental cells. This was paralleled by the hybrid cells promotion of invasive carcinomas in nude mice at

*a significantly lower rate and with a longer latency than the parental tumor cells.*

*This study provides evidence that MMCT is an efficient tool for screening of tumor suppressor activity in pancreatic cancer. The functional data emerging from this study bring into sharp relief the implication of chromosome 18 as a putative location for new TSG(s), yet to be identified in this region.*

**Keywords**

*Pancreatic cancer - tumor suppressor genes - chromosome 18*

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## Relevance of Mast Cells and Hepatic Lobule Innervation to Liver Injury

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*Abstract*

*Chronic liver diseases commonly result in liver fibrosis, and eventually liver cirrhosis. In the last decade, a new theory explaining liver fibrosis has been established. Accordingly, the development of liver fibrosis due to chronic liver diseases is thought to be mediated by inflammatory cells. They release fibrogenic mediators such as transforming growth factors (TGF)-beta, which are considered to be responsible for the activation and transformation of fat-storing cells. Recently, the involvement of mast cells and peripheral and autonomic nervous system in the fibrogenesis has been suggested. This study was aimed to establish the presence and distribution of mast cells and nerve fibers in the rat liver in the light of their implication in liver inflammatory and fibrotic disorders. Mast cells and afferent (sensory) fibers were detected immunohistochemically. An immunofluorescent method was applied to demonstrate tryptase and serotonin (SER) in the mast cells, while the primary sensory neuronal processes were identified by using antibodies against their marker calcitonin gene-related peptide (CGRP) and the proinflammatory mediator substance P (SP). The portal tracts and fibrous septa contained numerous mast cells, which exhibited strong immuno-reactivity to tryptase and SER. SER-positive nerve fibers were also found. It is generally accepted that no nerve fibers are present in the hepatic lobules, but the current investigation clearly demonstrates availability of CGRP-, SP, and SER-immunoreactive nerve fibers there.*

*Our results indicate that in the rat liver portal tracts and hepatic lobules there are numerous mast cells, sensory and autonomic nerve fibers, which may be involved in liver injury by the inflammatory mediators they release.*

**Key words**

*Rat liver - mast cells - parenchymal innervation - substance P - calcitonin gene-related peptide*

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## Pharmacokinetic Interaction Study between Ranitidine and Metoclopramide

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Abstract

### **Abstract**

The pharmacokinetics of metoclopramide in healthy volunteers was evaluated to determine if previously repeated doses of ranitidine inhibit the metabolism of the gastrointestinal prokinetic drug. Metoclopramide 20 mg (tablets) in combination with ranitidine 150 mg (tablets) were administered to 14 healthy human volunteers in a two treatment study design, separated by 5 days in which the ranitidine alone was administered in single p.o. doses twice daily. Plasma concentrations of metoclopramide were determined during a 24 hour period following drug administration. Metoclopramide plasma concentrations were determined by a validated RP-HPLC method. Pharmacokinetic parameters were calculated with compartmental and non-compartmental analysis. In the two periods of treatments, the mean peak plasma concentrations  $C_{max}$  were 44 ng/ml (metoclopramide alone) and 49.2 ng/ml (metoclopramide and ranitidine). The time taken to reach the peak,  $T_{max}$ , was 1.15 hrs, and 1.21 hrs, respectively. The total areas under the curve (AUC) was 314.3 ng.hr/ml and 354.06 ng.hr/ml, respectively. The half-life ( $T_{1/2}$ ) was 5.6 hr and 6.7 hr. A statistically significant difference was observed for both AUC and half-life of metoclopramide when administered alone or after 5 days of treatment with ranitidine. The experimental data proved the pharmacokinetic interaction between ranitidine of metoclopramide, and suggest monitoring adverse effects in patients.

### **Key words**

Metoclopramide - ranitidine - pharmacokinetics - drug interaction

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## Chronic Acalculous Gallbladder Disease: Outcomes of Treatment by Laparoscopic Cholecystectomy

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Abstract

### **Abstract**

**Background and aims.** The diagnosis and treatment of chronic acalculous gallbladder disease (CAGD) remains controversial. Laparoscopic cholecystectomy (LC) is increasingly accepted as the treatment of choice for this condition. The purpose of this study was to analyse the outcomes from LC for CAGD and to identify potential prognostic factors.

**Methods.** We retrospectively analysed 54 patients with a clinical diagnosis of CAGD. All patients underwent LC. The outcomes were evaluated at 12 months. Outcomes from surgery were graded on a predetermined scoring system (score 1-6) reflecting the effect of surgery on symptomatology. Histopathological analysis was systematically performed on the resection specimens.

**Results.** Post-operatively, 90.8% of patients (49/54) were satisfied with the operation (outcome score 1-2). A pathological abnormality was detected in 40 patients (74.1%). Of those in whom no abnormality detected on histopathological examination, LC achieved a successful outcome (score 1-2) in 85.7% of patients (12/14). The worst outcomes (score 5-6) were observed in 2 patients with a pathological abnormality of the gallbladder. For the 5 patients with outcome scores of 3 to 6 (poor outcome), the mean duration of symptoms was 7.1 months compared to 18.2 months for patients with score of 1 and 2 (good outcome).

**Conclusions.** There is no significant correlation between outcomes from LC for CAGD and the existence of a definable underlying pathology ( $p>0.05$ ). Patients with long-standing symptoms were more likely to benefit from LC ( $p=0.039$ ). LC is an appropriate treatment option for CAGD.

### **Key words**

Chronic acalculous gallbladder disease - laparoscopic cholecystectomy - prognostic factors - outcomes

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## REVIEWS

### Barret's Esophagus

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Abstract

### **Abstract**

*Barrett's esophagus is an alteration of the esophageal epithelium, regardless of length, evidenced by endoscopic examination (protrusion of the gastric mucosa into the esophagus in the shape of a flame) and confirmed by histological examination of the bioptic samples (intestinal metaplasia with mucosecretory cells). It develops following long-term gastro-esophageal reflux (GER). The documented risk factors are: long-term GER (duration more than 5 years), age over 50 years, male sex, Caucasian race, aggressiveness of the refluxed material, individual susceptibility of the esophageal mucosa to the refluxed material. The carcinogenic risk is 30 times higher than in the general population. Treatment targets the acid reflux, with proton pump inhibitors (PPI), prevention of carcinogenesis with cyclooxygenase 2 inhibitors, ablation of the metaplastic area by laser, plasma-argon mucosectomy, or photodynamic therapy and antireflux surgery.*

**Key words**

*Barrett's esophagus – gastro-esophageal reflux – esophageal cancer*

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## Molecular Prognostic Factors in Rectal Cancer

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*Abstract*

**Abstract**

*The prognosis of patients with rectal cancer can be assessed mainly on the basis of clinical and pathological factors among which the pTNM stage is the most valuable indicator. Recently, different combinations of molecular markers, which have prognostic significance, have been identified in an attempt to establish a “molecular staging” that would permit – along with the histopathological staging – taking optimum therapeutic decisions in colorectal cancer. An example in this respect is the attempt to classify patients with rectal cancer stage II (N-) with a view to administering adjuvant treatment to the risk subgroup.*

*The prognostic role of various factors (biological, genetic, molecular, etc.) was classified into four categories according to their predictive value. This paper reviews the most recent research, especially regarding the factors in the third category in order to assess their impact upon prognosis and to identify the most valuable factors that could change the therapeutic algorithm of rectal cancers in the future. However, more statistical studies are necessary before these factors can become the basis of new therapeutic strategies or prognostic evaluations in rectal cancer.*

**Key words**

*Rectal cancer - prognosis - molecular markers - p53 - apoptosis – oncogenes*

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## CASE REPORTS

# Blue Rubber Bleb Nevus Syndrome: Case Report and Literature Review

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Abstract

### **Abstract**

*Blue Rubber Bleb Nevus Syndrome ( BRBNS) is a rare disorder characterized by multiple cutaneous venous malformations in the skin and gastrointestinal tract associated with intestinal hemorrhage and iron deficiency anemia. Other organs may also be involved.*

*BRBNS has a potential for serious or fatal bleeding. The causes of this syndrome are unknown. Its most common presentation is in the form of sporadic cases, but dominant autosomal inheritance has been described. Although it was first recognized by Gascoyen in 1860, only one hundred years later did Bean further describe these lesions and coined the term BRBNS. A MEDLINE search yielded about 200 case reports published till 2003.*

*We present a case of this syndrome diagnosed in a 16- year – old patient with both upper and lower gastrointestinal bleeding. He had severe anemia and venous swellings on the trunk. Similar lesions were found in the stomach, bowel and on his foot. In addition, we review the available literature on the epidemiology, clinical features, associated conditions, diagnosis and treatment.*

### **Key words**

*Blue rubber bleb nevus syndrome - hemorrhage - anemia- vascular malformation - endoscopic therapy*

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## Right Adrenal Abscess – An Unusual Complication

# of Acute Apendicitis

Gabriel Dimofte<sup>1</sup>, Liviu Dubei<sup>1</sup>, Lili-Gabriela Lozneanu<sup>1</sup>, Corina Ursulescu<sup>2</sup>, Mihai Grigoraş<sup>2</sup>

1) Department of Surgery. 2) Department of Radiology, University Hospital "St. Spiridon" Iaşi, Romania Abstract

## Abstract

Acute appendicitis represents one of the most frequent abdominal emergencies encountered in everyday surgical practice. Local infectious complications are not unusual and retroperitoneal abscesses after acute retrocaecal appendicitis have been previously described. The authors present the case of a 22-years-young female patient, admitted for a right iliac fossa abscess, secondary to gangrenous appendicitis. A right adrenal mass 35/40mm was revealed during preoperative ultrasound evaluation, which evolved in an adrenal abscess that spontaneously drained 10 days after appendectomy and retrocecal drainage. Adrenal abscesses are exceptionally rare, with only a few cases being reported in the literature, but none of these after acute appendicitis.

## Key words

Adrenal gland – appendicitis – abscess

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# Ruptured Hydatid Cyst of the Liver with Biliary Obstruction: Presentation of a Case and Review of the Literature

Zeno Spârchez<sup>1</sup>, G.Osian<sup>2</sup>, Alina Onica<sup>1</sup>, Cristina Bărbântă<sup>1</sup>, Marcel Tanţău<sup>1</sup>, Oliviu Pascu<sup>1</sup>

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## Abstract

The case of a 66 year old woman admitted with a picture of jaundice acute cholangitis is reported. Ultrasonography showed a dilatation of intrahepatic bile ducts, gallbladder hydrops with several stones, enlarged common bile duct (CBD) with hyperechoic material inside and a cystic tumor with hydatid features. With a strong suspicion of a hydatid cyst ruptured in the biliary tree with biliary obstruction, endoscopic cholangiopancreatography was performed. The diagnosis was confirmed by endoscopic retrograde cholangiopancreatography and the hydatid membranes were extracted from the CBD with subsequent clinical improvement. The second step of treatment comprised the surgical cure of the cyst and cholecystectomy. The data from the literature are finally presented with a special emphasis on the ultrasound diagnosis and the

*endoscopic treatment.*

**Key words**

*Biliary obstruction – hydatid liver cyst - ultrasono-graphy– endoscopic treatment*

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## Hematemesis as a Presenting Symptom of Lung Cancer with Synchronous Metastases to the Esophagus and Stomach. A Case Report

*Panagiotis Katsinelos, George Paroutoglou, Athanasios Beltsis, Ioannis Pilpilidis, Basilis Papaziogas, Kostas Mimidis, Panagiotis Tsolkas*

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**Abstract**

*A rare case of upper gastrointestinal hemorrhage due to synchronous metastases to the esophagus and stomach from an asymptomatic lung cancer is reported. A 51-year-old white man presented with hematemesis and an emergency endoscopy revealed submucosal tumorous lesions with central ulcerations in the esophagus and stomach. A needle aspiration biopsy revealed the presence of cellular proliferation of adenocarcinoma, which led to the diagnosis of lung cancer, along with a chest radiograph revealing a tumor in the right middle lung field. The importance of conducting an upper gastrointestinal endoscopic examination for staging of patients with lung cancer is stressed.*

**Key words**

*Gastrointestinal hemorrhage - esophageal metastases - gastric metastases - lung cancer*

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