Falk Symposium 164

INTESTINAL DISORDERS

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Scientific Organization:
Z. Tulassay, Budapest (Hungary)
P. Ditě, Brno (Czech Republic)
G.J. Krejs, Graz (Austria)
J. Schölmerich, Regensburg (Germany)
H.-J. Schulz, Berlin (Germany)
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Session I

Diseases of the rectum and the perianal region
Outlet obstruction: Diagnosis and treatment 2008

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The outlet obstruction syndrome (OOS) by definition encompasses all pelvic floor abnormalities, which are responsible for an incomplete evacuation of fecal contents from the rectum. The prevalence of constipation in adults may be as high as 28%, accounting for more than 2.5 million outpatient medical visits in the U.S. yearly. The OOS may be observed in half of constipated patients. The types of constipation cover the slow transit colonic constipation, the outlet obstruction and the combination of the previous two.

The causes of outlet obstruction can be divided into functional and morphological origin. The outlet obstruction with morphological causes mainly should be treated surgically. The diagnosis of outlet obstruction is basically achieved by barium X-ray defecography, anorectal manometry, electromyography (EMG) and dynamic MR imaging. Treatment of OOS is dependent on the causes of the syndrome. OOS originating from functional causes (anismus, Hirschprung’s disease, hereditary internal sphincter myopathy, central nervous lesions, Parkinson's disease) are treated conservatively (botulinum toxin directly into the puborectal muscle) There is place to progressive dilatation also. The standard laxative treatment consist of bulk laxatives (fiber, psyllium, polycarbophil, methylcellulose) lubricating laxatives, stimulating laxative (surface acting agents, diphenylmethan, ricenoleic acids, anthraquinones) and osmotic agents (magnesium and phosphate salts, sorbitol lactulose, polyethylene glycol PEG) The dietary fiber treatment should be conducted before investigations, which would be indicated only if fiber fails. The multimodal therapy includes PEG, colchicines, misoprostil and additionally there are neurotropic factors under investigations. Surgical interventions are numerous, covering wide range of interventions from endorectal repair of rectocele through stapler assisted transanal surgery to proctectomy with restorative ileo – anal reservoir. If the patient is unresponsive to conservative treatment, different surgical options should be taken in to careful consideration. The repair of specific anatomic defects are indicated if the absence of primarily colonic obstipation is proven. Moreover, patients with impaired sphincter function should be excluded due to the high risk of inducing definitive postoperative incontinence. Different surgical options have been proposed such as vaginal or perineal levatorplasty, open or laparoscopic retropexias, resection – rectopexy, transrectal or endorectal resection. The detailed surgical indications are hot spots in 2008. The pathophysiology of outlet obstruction syndrome is still far to be clearly understood, for this reason surgery should be taken into consideration as carefully as possible.
Fistulae and fissures – Diagnosis and treatment

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Anal Fistulae

Definition: An anal fistula is a communication between two epithelial surfaces – the perianal skin and the anal canal or rectal mucosa.

Pathogenesis: Perianal septic lesions may be the result of several etiologies like skin lesions, infection or perianal trauma (e.g. surgical wounds). However, about 90% of anal fistulas are considered to be of cryptoglandular origin; only 10% are due to a specific etiology.

Spread of Infection: Infection may spread and seek the path of least resistance spreading upwards, downwards and transsphincteric. Furthermore, circumferential extension is possible at any level in the intersphincteric, ischiorectal or supralevatoric space.

Symptoms: Typically anal fistulas produce chronic purulent, fecal or serosanguine discharge with skin irritation.

Diagnosis: On rectal digital examination induration can be felt. Fistulography is mainly replaced by anal ultrasonography and/or MRI.

Treatment: Anal fistulas do not heal spontaneously without surgery. The surgical challenge is to treat fistulae without damaging the anal sphincter complex too much to avoid anal incontinence. Crohn’s fistulae should be treated surgically only if life quality is severely compromised.

Anal Fissure

Definition: An anal fissure is a tear in the lower part of the anal canal extending from the dentate line more or less to the anal verge.

Pathogenesis: Different etiopathogenetic mechanisms have been proposed like mechanical, epithelial, vascular, infectious and neuromuscular theories. Probably most likely a fissure is not the result of a single mechanism.

Symptoms: The leading symptom is acute pain occurring during or just after defecation. Pain diminishes and disappears over several hours and reoccurs at the next bowel movement. Palpation will confirm anal spasm with the most painful site on digital palpation at the 6 or 12 o’clock position. If the lesion is off the midline specific diseases like Crohn’s colitis, malignancy, hematological conditions or tuberculosis should be considered in differential diagnosis. Chronic anal fissures have indurated edges and are often associated with a sentinel pile and a hypertrophied anal papilla. Pain compared to the acute lesion is less.

Diagnosis: History, clinical examination and endoscopy will confirm the diagnosis.

Treatment: The aim of the treating an anal fissure is to break the vicious cycle of hard stool, pain and reflex spasm. Conservative treatment options are diet, stool softeners, warm baths, nitroglycerin containing creams (to relax the internal anal sphincter) or injection of botulinus toxin. Thus surgical treatment is necessary in less than 10%.
Session II

Diverticular disease and irritable bowel syndrome
Treatment algorithms for diverticulitis

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Diverticulitis is defined as symptomatic diverticular disease with signs of inflammation. The most significant methods for the diagnosis of inflammatory reactions and complications are CT-scan and ultrasound. Both procedures, a history and physical examination are indispensable for an appropriate pretreatment evaluation. The choice of treatment is according to the disease status of the individual patient: Acute attack of diverticulitis – complicated or uncomplicated; in cases with uncomplicated diverticulitis, is it a mild, moderate or severe attack? Recurrent diverticulitis needs different therapeutic strategies, either for final solution or secondary prevention. Complicated attacks of acute diverticulitis or recurrent diverticulitis with chronic structural alterations are usually subject to interventional or surgical treatment. Acute uncomplicated diverticulitis is treated by diet restrictions up to nothing by mouth, fluid supplementation, analgesics and in moderate/severe cases with combined antibiotics while in mild cases 5-aminosalicylic acid may be sufficient. Relapses of acute attacks in diverticular disease without chronic structural alterations can be successfully prevented by physical activity and sufficient amounts of fibre additives. Recent data point towards an effective prevention with cyclically given antibiotics and/or 5-aminosalicylic acid. Probiotics may be a promise for the future. In general, the prognosis particularly for patients with asymptomatic diverticulosis but also for patients with diverticulitis is good. Complications occur in about 5% of the patients.
Diagnosis and treatment of diverticular bleeding

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Diverticula account for 25–40% of painless rectal bleeding which may be massive in 5%. It is often self-limiting. There is epidemiological/demographic overlap with angiodysplasia; the latter is more likely to be R sided but 40% of bleeding diverticula are right-sided. It is not known why diverticula bleed, but thought to represent chronic injury to the vasa recta and fragmentation of internal elastic lamina and loss of media.

The evidence base for diagnostic and therapeutic endeavours is unfortunately not strong. Initial management encompasses standard resuscitative measures and exclusion of UGI bleeding.

Diagnosis from angiography is specific but insensitive, requiring bleeding at 0.5–1.0 ml/min for detection. Diagnosis from nuclear scanning is more sensitive – detecting 0.1 ml/min – but less specific; it is difficult to localise the bleeding site and is insufficient for operative planning. Diagnosis from colonoscopy is specific and sensitive if possible, and although not dependent on continued bleeding it is technically difficult when bleeding does persist. Diagnosis accuracy probably exceeds 70% and this alone may speed discharge from hospital. Preparation is probably best with PEG lavage by nasogastric tube, typically needing > 5 L.

Therapeutic angiography can yield control of bleeding with vasoactive agents in >90% of cases but 50% rebleed. More definitive control is achieved with embolisation (40–90% control; ~20% rebleed) and the risk of major ischaemia is low. Therapeutic colonoscopy also yields transient control with vasoactive agents, and definitive control with diathermy or other thermal techniques, clips or other physical devices such as band ligation. Adrenaline and bipolar diathermy have both been associated with a negligible rebleeding rate compared to conservative therapy in which about half rebleed.

Surgery is warranted if other measures fail through lack of diagnosis in the shocked patient, failure to identify a specific bleeding site, failure to control bleeding when bleeding site identified and for complications of other treatments (e.g. ischaemia). Segmental colectomy with a primary anastomosis is usually appropriate.
Drugs treatment of IBS – Different approaches for different subgroups

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Irritable bowel syndrome is one of the commonest causes of GI consultation. The key features are abdominal pain or discomfort with disordered bowel habit. Multiple somatic complaints and previous medically undiagnosed disorders are a common feature found in around 50% of patients. Although anxiety and depression is also common in both the community and in IBS patients only around a third have abnormal levels. The multiple somatic complaints may be a manifestation of abnormal pain processing. Using stool consistency the Rome III consensus committee have subdivided IBS patients into diarrhea IBS (25%) constipated IBS (25%) and mixed IBS (50%). Management of approaches depend on what is the most prominent symptom.

Psychological approaches:
Those scoring high on somatisation, anxiety and depression may respond best to centrally acting drugs such as tricyclic anti-depressants or SSRI’s. Cognitive behavioural therapy, psychotherapy and hypnotherapy may all provide benefit to some.

Diarrhea predominant IBS:
Where diarrhea is the predominant symptom attention should be paid to the diet and exclusion of excessive fermentable oligo-, di- and monosaccharides and polyols (FODMAPs). Common examples are found in milk (lactose), wheat and onions (fructans), fruit (fructose) and root vegetables (artechoke). If dietary manoeuvres fail to relieve symptoms then treatment with loperamide may be tried. 5-HT₃ antagonists (Alosetron, Cilansetron, Granesitron and Ondansetron) have all been shown to be effective in reducing diarrhea though of these Alosetron and Cilansetron have been withdrawn owing to concerns over ischemic colitis.

Bloating:
Patients with bloating should be assessed for the presence of visceral hypersensitivity. In the absence of a barostat study the presence of multiple somatic symptoms may be a useful pointer and should suggest that use of low dose Amitriptyline. Those without such evidence should initially try an exclusion diet. 5-HT₄ agonists (Tegaserod) have been shown to benefit bloating in small proportion of patients.

Constipation:
Patients with predominately constipation may respond with an increase in dietary fibre or if this is poorly tolerated, ispaghula, which being non fermentable tends not to produce the problems of flatulence which bran and other laxative dietary agents tend to do. Failing this, 5-HT₄ agonists may be helpful though the effect is small and the number needed to treat is 14 for Tegaserod.
**Mixed bowel habit:**
Those with multiple somatic symptoms should be treated with psychological therapies or centrally acting agents. If not then ispaghula has the virtue of both relieving constipation and diarrhea by normalising stool consistency. Mebeverine is safe and in a small number of patients effective in reducing pain. Future therapies include antagonists of mast cell activation and CRF antagonists to block the effect of psychological stressors on the gut.

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Session III

Novel concepts in IBD
Defective barrier – Therapeutic implications

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The barrier function of the intestinal mucosa forms has come into focus of research on inflammatory bowel disease as it was shown that an intact barrier is of great importance for the prevention of permanent and chronic inflammation as a reaction to the commensal intestinal flora. As a part of the barrier function there need to be effective defense mechanisms when the barrier becomes locally leaky. Local inflammation that is always present to some limited extend can be regarded as one component of the mucosal defense system. Immediate recognition of bacteria by pattern recognition receptors and lysis of bacteria in (auto)phagosomes are crucial for these functions.

It is obvious that mechanisms initiating or limiting inflammation need to be tightly regulated as they themselves might alter the mechanical barrier function Nod2 variants have been identified to be a susceptibility factor for Crohn’s disease. The Nod2 protein is an intracellular sensor of the bacterial wall product muramyl dipeptide (MDP) and activates the transcription factor NF-kappaB upon MDP-binding. A reduced expression of defensins ("endogenous antibiotics") has been found in patients with Crohn’s disease and ulcerative colitis especially when Nod2 variants are present. Other genetic variants associated with Crohn’s disease also affect barrier function such as genes involved in the autophagosomal system. A defect in the induction of this acute defense response is associated with chronic inflammation. Invading bacteria that cannot be readily detected and eliminated may start a backup mechanism of inflammation finally resulting in chronic inflammatory reaction followed by further impairment of the mucosal barrier.

Therapies that improve intestinal barrier function or bacterial recognition are now needed and have to be further explored. Probiotics seem to play a role in improvement of the mucosal barrier. Lipids such as phosphatidylcholine may mediate their positive therapeutic effects via improvement of the barrier function of the mucus layer. Growth factors that help to restore an intact epithelial layer (without the risk of tumor induction) need to be evaluated. Further developments may include induction of local expression or substitution of defensins to improve the antimicrobial defense function of the mucosal barrier.
The intestinal mucosa constitutes a complex immunologic barrier of both cell and non-cell components that is constantly exposed to antigenic overloads of commensal bacteria, nutrients, and viruses. This first-line of defense must exert a rigorous process of rapid discrimination - excluding potential pathogens while allowing host-beneficial substances to permeate. Tight control of this complex network of cell and microbial interactions at multiple levels is critical to sustain intestinal homeostasis and prevent imbalanced immune responses. Any regulatory defect may predispose to intestinal inflammation.

Recently, much progress has been made in defining the mechanisms through which the gastrointestinal innate immune system mediates recognition and sorting of the broad luminal spectrum of diverse microbial products. Toll-like receptors (TLRs) have evolved as one major innate immune surveillance system which is central to efficient host defense and homeostasis of the intestinal mucosa. TLRs comprise a class of at least twelve mammalian transmembrane pattern recognition receptors (PRRs) that participate in recognition of molecular patterns present on luminal microbes, induction of antimicrobial effector pathways and control of adaptive immune responses. TLRs are widely expressed by various cell types of the gastrointestinal mucosa.

Compelling evidence suggests that the fine-tuned TLR apparatus and its combinatorial signalling repertoire with other PRRs ambiguously shape the responsive tone of the gastrointestinal immune system with both, beneficial and harmful, outcomes for the individual host. Within the healthy host, TLRs may drive distinct immune mechanisms necessary for protecting barrier integrity and eliminating the invading microorganisms, thus efficiently maintaining tolerance and homeostatic balance of the intestinal mucosa. Yet, in the susceptible host, TLRs may induce potentially inappropriate or overactive signalling pathways, thus leading to amplification and perpetuation of aggressive immune responses which contribute to detrimental tissue injury and consequently chronic inflammation.

Current therapies for inflammatory bowel diseases (IBD) mostly aim to interrupt the inflammatory cascade through agents that regulate TH1 or TH2 – cytokine responses. As recognition grows that TLR dysfunction may play a role in IBD pathogenesis, TLRs could provide another valid interventional target for novel therapy development. However, seemingly contradictory results from studying different murine models of colitis have so far confounded whether therapeutically useful modulation of TLRs is best accomplished by activating, inhibiting or rather a combination of both at different stages of mucosal disease. Potential strategies, their rationale and future prospects will be critically discussed in this presentation.
References


Subgroups of Crohn’s disease – Are there therapeutic differences?

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The phenotype of a living organism is the outward, physical expression of the internal, genetic information. The phenotype involves structures, metabolism, different tissues or organs and behaviour of an organism. The phenotype of an individual is not only the expression of the genotype, but also affected by the environment. The phenotype is actually the outcome of genotype – environment interactions on the expression of certain biological signs or symptoms. The phenotype is a classifiable biological group.

Crohn’s disease is a heterogeneous disease with various phenotypes of bowel inflammation. The classification of these different disease phenotypes has been challenged in previous years. Problems occur since no clear cut separation between the different parts of the involved bowel exists. Even simple definitions may show significant intra- and inter-observer variability. The Vienna Classification (age at diagnosis, location of disease, behaviour) tried to address such differences and to find a basis for stratifying patients within clinical trials. In 2005 some adjustments were incorporated during the Montreal meeting. It is, however, the biologic complexity of Crohn’s disease that hinders the perfect classification of biological subgroups.

All these efforts reflect the undisputed recognition that Crohn’s subgroups exist and that this entity is heterogeneous. Complex therapeutic regimens and treatment guidelines have been developed. Clinical differences exist with regard to bowel surgery, postoperative recurrence, response to 5-ASA and steroids. Prospective studies, however, are warranted.
Prediction of treatment success – Will there be genetic or serologic markers?

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There is substantial variability in efficacy and toxicity of drugs between patients. Many factors influence response to therapy including disease severity and complications, environmental factors such as smoking, and genetic factors. Variability in drug response is greater across a population than within the same patient or in monozygotic twins, therefore part of this difference is attributed to genetic factors. It is estimated that polymorphisms in genes can account for 20–95% of variability in drug effects. The goal of pharmacogenetics is to adapt drugs to a patient’s specific genetic background and therefore make them more efficacious and safe. Investigating genetic variants that influence the response to a specific drug is more difficult than finding factors that influence toxicity. Side effects are usually easy to define and identify. Efficacy scores are often less well defined and different scores to assess disease activity are used. Moreover treatment response is influenced by a lot of confounding factors such as the duration of disease, disease behavior and disease severity.

Although pharmacogenetics is a promising field that already contributed to a better understanding of some of the underlying mechanisms of action of drugs used in IBD, the only discovery translated until now into daily practice is the relation between thiopurine S-Methyltransferase (TPMT) gene polymorphisms and hematological toxicity of thiopurine treatment. In the Caucasian and African populations approximately 90% of individuals carry 2 wildtype alleles resulting in high TPMT enzyme activity, 10% are heterozygous and display intermediate activity and 0.3% are homozygous for low activity alleles and display no detectable TPMT activity. TPMT enzyme activity in the RBC correlates well with hematopoietic toxicity. Hundred percent of the compound heterozygous or homozygous IBD patients develop severe hematotoxicity when treated with a normal thiopurine dose. The inverse is not true however and suggests that other factors beside genetic and/or TPMT variants contribute to thiopurine toxicity. Monitoring of blood counts and liver transaminases remains therefore necessary in all patients. If TPMT enzyme activity is measured in patients with normal TPMT activity (or wildtype patients) can receive 2–2.5 mg/kg AZA or 1–1.5 mg/kg of 6-MP. Patients with intermediate activity (heterozygous) should have a dose reduction of 50% and patients with low or absent TPMT activity (compound heterozygous or homozygous) should not receive thiopurine drugs at all. TPMT phenotyping or genotyping is cost effective to identify patients with low or no TPMT enzyme activity (homozygous or compound heterozygous) in order not to treat them and avoid severe hematological complications.

Besides the thiopurines, resistance to corticosteroid treatment in IBD has also been subject of pharmacogenetic studies. Several mechanisms are thought to be responsible for corticosteroid refractoriness, including changes in the Multi-Drug Resistance (MDR)-1 gene coding for the drug efflux pump P-glycoprotein-170 (Pgp-170), and in the function of the glucocorticoid receptor. The MDR1 SNPs C3435T and G2677T have been correlated with altered activity and expression of P-glycoprotein-170 and have been associated with corticosteroid refractory Crohn’s disease and ulcerative colitis. Finally, pharmacogenetic studies of infliximab in IBD have reported associations of primary treatment failure with particular apoptotic
genes (Fas ligand -843C/T, Caspase 9 93 C/T) or genes involved in ADCC and cytotoxicity (FCGR3A V158F) but need to be confirmed. To further advance in this field, it is necessary to organize studies in well characterized patient cohorts who have been uniformly treated and systematically evaluated in order to quantitate drug response more objectively. An effort should be made to collect genomic DNA from all patients enrolled in clinical drug trials after appropriate informed consent for pharmacogenetic studies.
Session IV

Cases and controversies
A patient with remitting (sub)obstruction in Crohn’s disease

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Intestinal strictures are the most frequent complications of Crohn’s disease (CD). Surgical resection with reanastomosis often is required to relieve progressive obstructive symptoms in patients refractory to medical therapy, but multiple resective operations may lead to the development of short gut syndrome with attendant nutritional deficiencies.

We present a 45-year-old female patient with longstanding CD admitted in our Digestive Centre with 6 weeks of increasing abdominal symptoms, and occasional mucoid, bloody bowel movements. Her symptoms had worsened to the point where she was unable to tolerate any oral intake and had lost approximately 5 kg. On examination, she was a normal-appearing female. Her abdomen was slightly distended with normal bowel sounds and was diffusely and moderately tender to palpation, but without rebound. Laboratory tests were suggestive of a moderately active inflammatory disease. Abdominal ultrasound (US) and abdominal computed tomography (CT-scan) were suggestive for small-bowel obstruction, with small-bowel conglomerate. Radiologic evidences of abdominal abscess, fistula formation or free air were not seen. A water-soluble contrast small bowel enema disclosed multiple jejunal and ileal strictures with concomitant prestenotic dilatations. Given her good clinical and nutritional status, our team elected to pursue conservative medical therapy. The patient received high dose corticosteroid treatment, empiric antibiotic regimen, fluid and electrolyte replacement. Radiologic control revealed dramatic improvement. The patient’s symptoms progressively improved, and she tolerated a regular diet one week after therapy. She was discharged with a plan of possible definitive surgical intervention. Eight weeks after conservative therapy, the patient continued to be asymptomatic and stable on a regular diet. A follow-study showed persistent clinical and radiologic response without the need for high dose corticosteroid retreatment, hospitalisation or surgery.
Obstruction in Crohn's disease

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Most patients with Crohn's disease are in the inflammatory phase of the disease during the first 7–8 years of disease. However, after that period, most patients will evolve to either stricturing phenotype or to a penetrating or fistulizing phenotype (1).

Strictures represent long-standing inflammation and may occur in any segment of the gastrointestinal tract in which inflammation has been active. Strictures are likely to recur, most often at the anastomosis in patients who undergo bowel resection because of the stricture. Strictures are usually silent until the luminal caliber is small enough to cause relative obstruction. Symptoms may include colicky abdominal pain, bloating and vomiting, punctuated by more severe episodes and often culminating in the complete obstruction. However, it has to be recognized that not all obstructive presentations are caused by fibrotic strictures. The radiologic “string sign” of a markedly narrowed bowel segment amidst widely spaced bowel loops does not reflect fixed stenosis caused by fibrous stricture, but is an acute manifestation of edema, active inflammation and spasm. The typical string sign transiently resolves with administration of glucagon, which relieves smooth muscle spasm. These patients will recover after a few days of a clear liquid diet or IV fluids, combined with antiinflammatory therapy. Short of demonstrating a clear response to anti-inflammatory therapy or reviewing a surgical specimen, the clinician may find it extremely difficult to differentiate a fibrostenotic from an inflammatory stricture. All strictures must be considered with suspicion because some harbor cancer.

There are two different scenarios in which patients present with obstructive manifestations of Crohn's disease. The first scenario occurs during the acute flare of Crohn's disease. In this situation, obstructive manifestations may be accompanied by a “string sign”, with no significant prestenotic dilatation. That blockage will always open up with the help of antispasmodics, clear liquid diet, IV fluids combined with antiinflammatory therapy and will not require urgent surgical intervention (2). Therefore, the rule number one is to never operate for acute obstruction in Crohn's disease (3). The exception to that rule are patients who experience an acute, severe, complete, strangulating, adhesive obstruction, and they need prompt surgical intervention (3). If a Crohn's disease obstruction does not open within 2 or 3 days of conservative management, the patient is either suffering from Crohn's disease complicated by a foreign body, a food bolus, a fecalith, an enterolith, or a cancer, or else has a fixed adhesive obstruction.

By contrast, fixed fibrostenotic obstruction with chronic prestenotic dilation occurs in patients who are chronically obstructed and suffering repeated attacks. These patients are afraid to eat, they lose weight and have a severely impaired quality of life. Their problem is mechanical and so requires mechanical rather than a medical solution. The physician must not attempt to manage such a problem with medical therapy and later send a patient who is malnourished and debilitated, to a surgeon. That is rule number two, always operate for chronic obstruction in Crohn's disease (3). The surgeon's decision for a specific procedure, such as stricturoplasty or
resection, will depend on the anatomy of each case, but for this chronic, relapsing fixed obstruction, treatment is always surgical (4).

References:


A patient with refractory bleeding in proctosigmoiditis

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The authors report the case of a 30-year-old female patient with refractory proctosigmoiditis. In February 2004 she developed intestinal symptoms: bloody diarrhea and abdominal pain. Colonoscopy and biopsy established the diagnosis of ulcerative colitis (proctosigmoiditis). The disease activity was moderate at the beginning. 5-ASA at 3 g/day was initiated orally. In October 2004 a moderate relapse occurred; treatment was amended with topical 5-ASA and prednisolone 1 mg/bw kg orally. Symptoms regressed but a severe relapse occurred (14–16 x diarrhea, with a large amount of blood) during tapering of oral steroids in late November. Patient was admitted, iv. corticosteroids were initiated and stool frequency improved in 3–5 days significantly and steroids were continued orally and azathioprine was added at 2 mg/bw kg. Stool frequency returned to near normal (2–4 x) with occasional blood. In May 2006, severe anaemia (Hb 78 g/l), leucopenia (wbc 1.4 G/l) developed, Immuran was stopped. In July 2006, moderate to severe relapse (10–14 bloody diarrhea/day) occurred. Patient was admitted, i.v. corticosteroids were initiated with response and early relapse when steroids were tapered below 20 mg/day. In September disease extent was reassessed by colonoscopy and proximal extension was revealed with involvement till beyond the splenic flexure. Infliximab (5 mg/bw kg) induction therapy was initiated with planned maintenance. Surgical option was also discussed but refused by the patient. Stool frequency decreased to 3–4 x with moderate blood on week 8, treatment was amended with topical 5-ASA and 4-weeks later the patient reported that she became pregnant and refused further infliximab treatment. The course of the pregnancy was relatively uneventful, with only mild increase in disease activity that was treated with a combination of oral 5-ASA and topical treatment. After delivery the course of the disease became somewhat milder that could be managed by combined oral 5-ASA and topical treatment. Refractory/chronically active distal colitis may respond to intensive treatment with corticosteroids; however, if there is incomplete response after 3–5 days surgical options should be considered and discussed. Second line treatment with ciclosporin, infliximab or tacrolimus will often be appropriate, however third line therapy may only be considered at a specialist centre.
A patient with duodenal stenosis in CD

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L.F. was diagnosed with Crohn’s disease (CD) at age 19 in 1998. Right sided hemicolecction and partial urinary bladder resection was performed at the time of the diagnosis because of abdominal abscess and entero-vesical fistula. He has had upper gastrointestinal pain, nausea and intermittent vomiting since 2001, when duodenal CD was proved by endoscopy and histology as well. Despite the continuous immunosuppressive therapy a stricture developed the postbulbar duodenum, but the gastric emptying was judged satisfactory at that time. Baloon dilatations had to be performed several times in the next 1.5 years because of recurrent nausea and vomiting, and finally, a retrocolic posterior gastro-entero anastomosis (GEA) was performed in the end of 2002. Inflammatory stricture of the GEA was observed 3 months later and infliximab induction therapy was administered without efficacy, that’s why a new GEA had to be performed later in the same year. This third anastomosis had to be dilate several times between 2003 and 2005. At the end of 2005, a subcutaneous fistula was observed in the scar of the previous operation. Fistulotomy and drainage was performed, and infliximab reinduction therapy was administered. Cholecystectomy was performed due to acute cholecystitis at june of 2006. Entero-cutaneous fistulas evolved a few months later. These fistulas drained an abscess located close to the wall of the stomach and duodenum. Partial gastrectomy and complete fistulotomy was performed, and the patient has in remission since that time with increase of his weight of more than 15 kg.
Endoscopic and drug treatment may be successful

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Duodenal strictures are an important clinical problem in patients with Crohn’s disease and these patients are often referred for surgical therapy. For a long time surgical procedures were only one possibility. The major reasons for the endoscopical approach are: to avoid the intestinal resection; to minimalize the risk of development of short-bowel syndrome; to solve effectively the patient’s problems. TTS („through the scope”) balloons are needed for dilatation of the small bowel strictures. The diameter of the most applicable balloons are 18 mm. After introduction of the endoscope and balloon into the bowel stenosis, dilatation of no longer than 5 minutes is done. During one setting procedure one to three dilatations are performed. The most suitable for dilatation are stenosis less than 50 mm in length without deep ulcerations. In the case of severe inflammatory stenosis intensive drug therapy is needed first. The optimal therapeutic approach included biologicals [infliximab, adalimumab], because they work very fast and have a powerful effect. After induction treatment period [8–10 weeks] the second endoscopy [colonoscopy, enteroscopy] should be done. If a positive response was achieved the maintenance therapy with biologicals or immunosuppressants [thiopurins or metotrexate] together with endoscopical dilatation would be started. Technical feasibility for endoscopical dilatation is relatively high (80–86%). The major reasons for dilatation failure are the impossibility to introduce the balloon through the angulated or kinking stenotic bowel segment, or an extremely tight stricture. The pooled data including 112 patients who underwent small bowel dilatation in a few clinical studies have shown that nearly 70% of patients were free of symptoms until the end of the follow-up (39 months). In 50% of patients a single dilatation is usually enough for long time effect. No associations between the efficacy and technical and clinical variables were found. Endoscopical dilatation are not associated with mortality rate. The mean complication rate of endoscopic dilatation was 2% which makes the procedure considered relatively safe. The leading complication is a bowel perforation. Massive bleeding after dilatation is rarely detected, especially from the anastomotic region. The data regarding the local application of steroid injections is still scanty and requires further studies.
The traditional surgical treatment for Crohn’s disease was in the beginning a wide resection including the loco regional lymphatic glands. The view was that by removing all of the disease the chance of definite cure would be better. An alternative treatment that was not infrequently used some 40–50 years ago was just bypassing the diseased segment. The rationale was probably that this was a safe way to deal with an acute situation keeping operative morbidity which at that time was quite high at a reasonable level. The treatment was successful in that it frequently relieved the patients from their symptoms. A few studies comparing time until recurrence did however favor the resection over the bypass technique. There were also other problems both in the early and late phase after the bypass operations. Bacterial overgrowth in the excluded segment might cause problems but the main issue was that there is preponderance for malignancies to develop in these bowel segments that no longer are a part of the normal stream of intestinal contents with its corresponding micro biota. The problem being that these cancers were not affecting the passage of bowel contents and thus were not giving symptoms before reaching a considerable size. The rather frequent reports on cancers developing in these inaccessible parts of the bowel usually several decades after the initial surgery has lead to most surgeons to now consider this treatment option as rather obsolete.

Of course when these bypasses encompassed long segments of bowel in particular terminal ileum the patients would be at risk having the same problems as we see in long resections or extensive disease with an increase in the risk of kidney stone formation. This is due to a relative deficiency of bile in the small bowel when the enterohepatic bile circulation is grossly disturbed due to loss of the terminal meter or more of the ileum. The resulting steatorrhea will lead to the excess fat forming calcium bonds in the feces not allowing oxalic acid to bind to calcium and being excreted in the feces. Instead oxalic acid will be reabsorbed and concentrated in the urine predisposing for oxalic acid stone formation. The way of preventing this as well as relieving the patients from their incapacitating fat induced diarrhea is to minimalise oral fat intake.

A new development in surgical treatment of Crohn’s disease is in a sense related to bypass surgery in that the diseased bowel segment is not resected but it is not truly bypassed either the methods aim at widening the lumen across the diseased bowel segments. This strictureplasty technique was first advocated in the 1960ties by Emmanuel Lee of Oxford. It has now been generally accepted as a method of dealing with short strictures in the small bowel and in patients with multiple strictures it is considered the method of choice by most colorectal surgeons. Whether strictureplasty should be used in the colon is under debate the surgical risk is not clarified and the risk of missing a carcinoma is certainly higher in the colon. Likewise many surgeons would hesitate to do a small bowel strictureplasty in a first operation where the diagnosis is not firmly established. The conventional strictureplasty are used for rather short stenosed bowel segments (up to 10 cm). However there are now several reports on non conventional strictureplasty in patients with complicated Crohn’s disease with long and often several stenosed segments where traditional
surgery would put the patient at risk of ending up in a short bowel syndrome. The non-conventional strictureplasty encompass a division of the bowel in the middle of the diseased segment. The ends are the cut open along the antimesenteric aspect of the bowel all the way through the diseased segments. These open ends are then joined together using a long suture line one both sides of the longitudinally opened bowel ends thus in fact making the bowel wider and shorter but not resecting it. There are some indications that the mucosa will heal as is often seen after a conventional strictureplasty. Whether the absorptive capacity of the bowel also will be restored remains to be shown.

In a patients with duodenal Crohn’s disease and where medical therapy is insufficient and the lesions are inaccessible to resection surgery there might still be a place for a bypass in terms of a gastrojejunostomy.
Session VII

Tumors of the small and large bowel
Lymphoma – Staging and treatment 2008

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Based on new insights into aetiology and pathogenesis of gastrointestinal lymphoma and their histomorphological and molecular characteristics important progress in diagnostic and therapy has been made during recent years.

Classification
A few years ago, the WHO established an international accepted classification of gastrointestinal lymphoma. The vast majority of gastric lymphoma are extranodal marginalzone-B-cell-lymphoma of MALT (mucosa-associated-lymphoid tissue) and diffuse large B-cell lymphoma (DLBCL) previously considered as low-grade and high-grade gastric lymphoma, respectively. T-cell-lymphoma are extremely rare in the stomach but comprise a considerable part of intestinal lymphoma (table 1).

Diagnosis and staging
Grade of malignancy (MALT lymphoma – MALT lymphoma with high grade components – DLBCL with/without MALT components) and stage of the disease are the two major prognostic factors and therapeutic determinants. There is a strong need for a very thorough biopsy protocol ("gastric mapping"). In intestinal lymphoma diagnosis could be only established until recently by laparoscopy or laparotomy. Nowadays, capsule endoscopy and double balloon enteroscopy with its possibility of taking biopsies offer a diagnostic approach without surgery.

Once a lymphoma is diagnosed and confirmed by a reference pathology, a staging procedure is necessary. It comprises EUS, ileocolonoscopy, small bowel examination (in case of gastric lymphoma), abdominal and lymph node ultrasound, CT scan of the abdomen and thorax, and bone marrow puncture.

Therapy
In patients with gastric MALT lymphoma of stage I, H. pylori eradication is the initial treatment of choice offering lymphoma regression rates of up to 80%. There is a real chance of cure for the majority of these patients. Recent findings have shown that some patients with DLBCL and those with a negative H. pylori status may also respond to eradication treatment. Therefore, a probatory eradication therapy can also be recommended in these cases. If the lymphoma does not reveal regression after successful eradication of H. pylori or in stage II. radiation is the treatment of choice in gastric MALT lymphoma. However, this is not necessary in patients with minimal histological residuals of MALT lymphoma. They can be successfully managed by a watch-and-wait-strategy. The rare cases of stage III/IV MALT lymphoma should be subjects of chemotherapy plus Rituximab. Chemotherapy (CHOP) plus Rituximab is also the treatment of choice for all stages of gastric DLBCL. An open question is the potential benefit of radiation in these individuals. Table 2 summarizes the treatment recommendations in gastric MALT lymphoma and DLBCL.
Specific aspects of intestinal lymphoma
Intestinal lymphoma have a worse prognosis compared to gastric lymphoma. There are multiple reasons for that such as the difficulties in diagnosing intestinal lymphoma, the more advanced stages due to late diagnosis, comparably frequent complications such as perforation, and less experience in treating this rare disease. Contrary to gastric lymphoma, there are no well established treatment recommendations in intestinal lymphoma. However, Rituximab plus CHOP chemotherapy can be regarded as a kind of standard treatment in DLBCL of the intestine.

Table 1: WHO classification of gastrointestinal lymphoma

<table>
<thead>
<tr>
<th>B-cell-lymphoma</th>
<th>T-cell-lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>marginal zone-B-cell-lymphoma of MALT-type</td>
<td>enteropathy-associated T-cell-lymphoma (EATCL)</td>
</tr>
<tr>
<td>follicular lymphoma (grade I-III)</td>
<td>peripheral T-cell-lymphoma (non-EATCL)</td>
</tr>
<tr>
<td>mantle cell lymphoma (lymphomatous polyposis)</td>
<td></td>
</tr>
<tr>
<td>diffuse large B-cell-lymphoma (DLBCL) with/without MALT-type components</td>
<td></td>
</tr>
<tr>
<td>Burkitt lymphoma</td>
<td></td>
</tr>
<tr>
<td>immunodeficiency-associated lymphoma</td>
<td></td>
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</tbody>
</table>
### Table 2: stage adapted treatment strategies in low-grade (MALT) and high-grade (diffuse large B-cell lymphoma with/without MALT components) gastric lymphomas

<table>
<thead>
<tr>
<th>stage</th>
<th>low grade (MALT)</th>
<th>high grade (DLBCL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I1/2</td>
<td>Hp eradication</td>
<td>chemotherapy + rituximab ± radiation (surgery + chemotherapy)</td>
</tr>
<tr>
<td></td>
<td>Hp negative: probatory Hp eradication</td>
<td></td>
</tr>
<tr>
<td></td>
<td>no complete remission or relapse: radiation (surgery)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mhr: watch-and-wait</td>
<td></td>
</tr>
<tr>
<td>II1/2</td>
<td>radiation (surgery)</td>
<td>chemotherapy + rituximab ± radiation (surgery + chemotherapy)</td>
</tr>
<tr>
<td>III, IV</td>
<td>chemotherapy + rituximab (watch-and-wait)</td>
<td>chemotherapy + rituximab ± radiation</td>
</tr>
</tbody>
</table>

Hp: Helicobacter pylori; mhr: minimal histological residuals

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GISTs: The paradigm of a bench-to-bedside disease

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GISTs, characterized by c-kit mutations, are the most frequent mesenchymal tumors of the digestive tract; they seem to originate from the interstitial cell of Cajal, a cell making part of the myoenteric Auerbach's nervous plessus. The disease mainly affects adults, around the sixties. The stomach is the most commonly involved site. Most GISTs are asymptomatic at diagnosis. In this tumor, localization, size and mitotic rate are considered as reliable predictors of survival. The two milestones of GISTs treatment are surgery and imatinib. The demonstration of new mutations in the c-Kit gene and the introduction of new treatment options in addition to imatinib, a choice of treatment that will be tailored on the base of the molecular analysis of the tumor, are leading to a further increase in the run to publishing on GISTs.

We carried out an Audit, a multicenter study on the morphological and clinical aspects of the disease, on the response to treatment and the survival in relation to the time of diagnosis and the molecular features which we will report, with the additional aim to review the current clinical and pathological knowledge on GISTs.

The centres participating in the audit recruited 172 cases of GISTs (M:F = 1:1; mean age 65 with the youngest case registered in a 19 years old patient and the oldest at 94). The stomach was the most frequent target of the disease with the small bowel representing the second site in terms of prevalence. Large tumors were more frequently characterized by severe presentation symptoms but in 50% tumor size was lower than 5 cm. Major symptoms were observed in 43%. From the histological point of view in 45% of the cases the tumor cells were of spindle type, in 25% epithelioid and in 30% the tumor showed mixed histotype. The mitotic index was low (< 5/50 HPF) in about half of the cases. In our series patients with rectal, omental or esophageal localization, despite representing a small minority of the series, were characterized by a significantly (p = 0.03) more aggressive mitotic behaviour. The most frequent mutations were in-frame deletions and point mutations of c-KIT exon 11; moreover, we found others minor mutations, also rare, of c-Kit and PDGFRA genes. The disease was in the metastatic phase in over a quarter of the cases at diagnosis. When the factors impacting on the patients' prognosis were looked for, only the tumor mitotic index and size were significantly correlated with survival; on the contrary, unexpectedly, the presence of metastatic disease didn’t show any impact on the survival. Only in 1.5% of the cases there was a clear familial aggregation for the disease thus confirming that this kind of aggregation is very rare.

Our Audit confirmed in part the available data on GISTs in a consecutive series of patients recruited in Italy. It is clear that the point of view of molecular biology on this type of tumor is really important and that it will impact on patients' care in the near future. This consideration implies the need of a stricter collaboration between basic science and clinical medicine. This report also indicate how, particularly when dealing with relatively rare diseases (even though the incidence of GISTs is probably underestimated) only large collaborative multicenter studies may offer reliable data to help physicians to make opportune clinical and therapeutic choices.
Neuroendocrine tumors – New treatment options?

Guenter J. Krejs, MD
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The approximate incidence of gut endocrine tumors, including “nonfunctioning tumors,” is about 3 in 100,000 population per year. Mean age at diagnosis is 60 years. Tumors arise either from the diffuse neuroendocrine system or from pancreatic islets. In functional tumors, the pharmacological actions of the tumor product will often serve to predict clinical symptoms. Thus, gastrinomas are associated with severe peptic ulcer disease, VIPomas with large-volume secretory diarrhea and GRFomas with acromegaly. The glucagonoma syndrome is often diagnosed by dermatologists because of the characteristic necrolytic migratory erythema. Enteroglucagon is a 69-amino-acid peptide that includes the 29-amino-acid sequence of glucagon. Only three cases of enteroglucagonoma have been reported (hyperplasia of the intestinal mucosa and giant intestinal villi). In pancreatic cholera syndrome or VIPoma, the hallmark is several liters of secretory diarrhea per day, leading to metabolic acidosis and renal failure. Vasoactive intestinal polypeptide is the major mediator of the syndrome but PHM (peptide histidine methionine) and helodermin have also been found to be elevated in the circulation of such patients. Rare forms of pancreatic endocrine tumors also include PPoma, neurotensinoma and corticotropinoma. A tumor that produces the first GI hormone discovered, secretin (Bayliss and Starling, 1902), has not been convincingly described. Some tumors produce multiple hormones although the endocrine syndrome usually is determined by just one peptide. Neuroendocrine tumors (NETs) may also arise as part of hereditary syndromes such as MEN1 and von Hippel-Lindau disease. Progress in diagnosis has been made by early detection with provocation tests such as the intravenous secretin test for gastrinoma. Chromogranin A in serum can serve as a marker for neuroendocrine tumors and its release is proportional to tumor mass. Imaging has been improved by endosonography, detecting tumors of less than one centimeter in diameter, and also by PET and somatostatin-receptor scintigraphy. The latter, however, produces false-positive results with abdominal lymphomas and granulomatous disease. Treatment of gut endocrine tumors aims at resection of the primary tumor; however, in more than 50% of cases, metastases are present at the time of diagnosis. Agents that have been found to be helpful for treatment include the somatostatin analogues octreotide and lanreotide, which depress release of tumor products and are very effective in such syndromes as carcinoid and VIPoma. Rarely, they can also reduce tumor size. In a German multicenter study with ocreotide, tumor regression was found in 3%, stable disease in 53% and tumor progression in 44% of treated patients. Interferon alone or in combination with ocreotide may be beneficial. Radioligand therapy utilizes the presence of somatostatin receptors on tumor cells: a beta-radiating substance (such as 90yttrium) is attached to somatostatin and selectively docks to tumor tissue. 177Lutetium (with lesser penetration than yttrium) can also be used. Response rates for radioligand therapy, also known as PRRT or peptide receptor radionuclide therapy, are partial response in 32% and stable disease in 40% of patients. Cytotoxic chemotherapy (5-FU and streptozotocin) is also effective in about half of tumor cases. New targeted therapies such as mTOR antagonists (RAD001 or everolimus) or inhibitors of angiogenesis are currently being evaluated in clinical trials. Since tumor cells have dopamine receptors in addition to the somatostatin receptors, chimeric molecules that block both receptors have been
developed and show promising results in animal tumor models. Vaccination with dendritic cells also shows reduction of tumor size in animal models of NETs. In some selected cases when the primary tumor has been resected and disease remains limited to the liver, liver transplantation has been successful. Chemoembolization can sometimes be used to reduce tumor mass in the liver. Mean survival of NET patients in the presence of liver metastasis now stands at 6 years. The European Neuroendocrine Tumor Society (ENET) has issued very helpful guidelines for the management of gastrointestinal neuroendocrine tumors.
Session VIII

Colorectal carcinoma
Which way of secondary prevention is really feasible and useful?

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The process of colorectal cancer development extends over a considerable period of time and consists of multiple steps: Hyperproliferation, formation of hyperplastic polyps, adenomas and cancer. Some events like the loss of minute amounts of blood or the shedding of pathological epithelial cells with the stools can be used to screen persons with an average risk of developing CRC. Endoscopic methods (sigmoido- and colonoscopy) are accurate means of examining the colon. Flexible sigmoidoscopy misses up to 50% and more polypoid lesions because they are out of reach of this instrument. New tests include: Quantitative faecal immunochemical tests, faecal molecular tests including DNA tests, CT colonography and new colonoscopic modalities.

Can screening reduce the CRC mortality?
Randomized controlled trials have shown that biennial and annual screening with gFOBT reduces the mortality with 15–33%. However the sensitivity for the detection of cancers (50%) and adenomas (10%) is low with gFOBT and somewhat higher with the iFOBT. Endoscopy based screening is highly sensitive for CRC and its adenomatous precursor. Case control studies suggest that colonoscopy screening reduces cancer incidence and mortality by 50–90%. Limitations are related to the number of qualified examiners, potential complications, costs and low compliance of the population.

Cost effectiveness of screening
Modeling studies indicate that most screening modalities are cost-effective. Based on RCT’s, the costs per life year saved vary between 5691 and 17,805 USD for the gFOBT. For colonoscopy screening the estimates are between 8840 and 22,012 USD per life saved, these data are based on the assumption that endoscopy screening results in a 65–90% reduction in incidence and mortality of CRC. The validity of these estimates can be proven by RCTs. Current clinical practice indicates that treatment of advanced colorectal cancer becomes more and more expensive. Studies on treatment costs reach 80,000 USD and more. With the application of the modern biologicals as first line treatment these costs will double. It appears that high treatment costs make screening even more cost effective. It is promising that 17 out of 26 member countries of the European Union have introduced it in the last years.

High risk groups
Physicians should identify Individuals with a high risk of developing colorectal cancers by taking a careful family history. The early identification and treatment of hereditable CRC risk groups would improve the prognosis of this large group which makes up 20–30% of the entire population with colorectal cancer.

The time has come to end the discussion on the value of CRC screening and to use it.
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Can the identification of high-risk groups increase the effectiveness of colon cancer screening programmes.
J. Gastro. (in press)
When is a programmed follow-up meaningful and how should it be done?

A.J.M. Watson
Division of Gastroenterology, University of Liverpool, School of Clinical Sciences, Liverpool, UK

Colorectal cancers arise through the adenoma – carcinoma sequence in which adenomas arise from normal intestinal epithelium and then transform into invasive cancers. Interruption of this sequence by colonoscopy and clearance of adenomas by polypectomy has now become the standard method of preventing colorectal cancer. Similarly patients who have had a colorectal cancer resected are at high risk of recurrence in the remaining bowel. In general, adenomas and early cancers do not cause symptoms and patients did not seek medical attention until an invasive cancer has developed. For this reason a systematic approach for the surveillance of patients at risk of adenoma has been adopted in most western countries. Two categories of surveillance will be discussed; post-polypectomy surveillance and surveillance after resection of colorectal cancer. Screening strategies for average risk individuals without previous adenoma or carcinoma will not be discussed in this presentation. With patients with adenomas risk stratification of the first adenoma is essential for determining appropriate follow-up. Higher risk of development of subsequent advanced adenomas arise from adenomas that are great than 1 cm in diameter, are more than 3 in number or have villous architecture or high grade dysplasia on histological examination. A number of detailed protocols have been proposed for the follow-up of patients with adenomas. The majority recommend repeat colonoscopy after 5 years for patients with low risk adenomas and after 3 years for patients with adenomas great than 1 cm in diameter or with high risk histology. Incomplete removal of adenomas is a major difficulty and for this reason many authorities recommend repeat colonoscopy 2 to 6 months after removal of large sessile polyps. POST cancer.
Progress in the treatment of colorectal cancer: The impact of new drugs

Karen Geboes, M.D., Ph.D. & Eric Van Cutsem, M.D., Ph.D.
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The management of patients with metastatic colorectal cancer (CRC) has changed dramatically over the last five years, with increasing chances of prolonged survival. The development of new drugs has contributed to the better outcome of patients with metastatic colorectal cancer. Until the mid-1990s the only available drug, with limited activity in metastatic CRC, was 5-fluorouracil (5-FU). The development of the cytotoxic agents irinotecan, oxaliplatin and capecitabine and of the monoclonal antibodies against the vascular endothelial growth factor (VEGF) bevacizumab and against the epidermal growth factor receptor (EGFR) cetuximab and panitumumab have clearly increased the therapeutic options and have improved the outcome for patients with metastatic colorectal cancer. However, their introduction also raises many new questions and challenges.

In patients with resectable stage III colon cancer the outcome can be improved with an adjuvant treatment based on 5-FU/Folinic acid in combination with oxaliplatin. The benefit in stage II colon cancer is more controversial. Some patients also benefit. The biologicals are under active investigation in combination with classic cytotoxic therapy in the adjuvant therapy of colon cancer.
Session IX

State of the art lecture
The difference of a decade: Looking backward and forward in GI

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The past decade has seen significant progress in advancing our understanding of important GI disorders and incremental improvement in therapy. Most significant advances have been made in crystallizing an understanding of both the known and unknown dimensions of the pathogenesis of inflammatory bowel diseases. In a temporally frame-shifted manner, progress in understanding major pathogenetic mechanisms has also driven development of new therapeutics. This is especially well exemplified by anti-TNF. Experience in this decade also shows that an initial advance requires time to mature and in the interval since the first demonstration of efficacy, there has been substantial refinement in definition of the clinical utility of anti-TNF. Importantly, it appears that anti-TNF is a prototype of mechanistic insight leading to therapeutics but far from the only type of therapeutic advance that will begin to enter more routine practice, as exemplified by nataluzimab.

Just as important, recent progress has laid the foundation for advances that can be anticipated in the decade ahead. Thus we are on the cusp of insight into the mechanisms of inflammatory bowel disease at an even more fundamental level because the power of genetics has pointed to a rich variety of susceptibility genes which each represent a point of leverage for further study. If the past is a guide to the future, it is perfectly reasonable to expect that ten years hence will see a new wave of novel therapeutic interventions.

Although IBD is the vanguard of advances in GI tract disease, it is likely soon to be paralleled by other important digestive disease challenges. Thus genome wide association studies that have yielded important associations with IBD are also pointing to key host factors underlying celiac disease. Quite separately, the breakthroughs in the fundamental science of tumorigenesis is providing traction in the understanding of GI tract malignancy. This includes the characterization of specific signaling pathways but also conceptual paradigms exemplified by cancer stem cells. An important context for anticipated progress is the ultimate relevance of significant advances in study of related basic biological processes including stem cell biology and molecular basis of development. This can be expected to catalyze insights into the pathogenesis of GI tract disorders and serve as a potential foundation for novel and powerful therapeutic interventions a decade hence.

Progress in still other important luminal diseases promises to advance based on new functional imaging technologies. By facilitating the use of the human model, these may prove to be as powerful as any study of experimental animals or reductionist models in the delineation of the physiology of gastrointestinal tract motility and the pathophysiology of the common forms of functional bowel diseases.
The application of the therapeutic maturation of the study of pathogenesis undoubtedly will be shaped by other powerful forces having an impact on healthcare delivery. These include the infrastructure (both basic science and IS) that will bring pharmacogenetic variation as well as host susceptibility into mainstream clinical practice and the socio-economic context of clinical care. Looking backward, a decade from now we may well see that we have transitioned through a watershed in the understanding and treatment of digestive diseases.
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Increased levels of homocysteine in patients with ulcerative colitis

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Hyperhomocysteinemia is an increase in the risk of arterial and venous thrombosis in inflammatory bowel disorders.

Introduction: Hyperhomocysteinemia is an increase in the risk of arterial and venous thrombosis in inflammatory bowel disorders. Here we aimed at investigating relationship of homocystein, with levels of vitamin B₁₂ and folic acid and the risk of development of thrombosis in ulcerative colitis patients.

Methods: 55 ulcerative colitis patients and 45 healthy adults were included in study. Homocystein, vitamin B₁₂ and folic acid levels were measured. At clinical history, thromboembolic events were interrogated.

Results: Average homocystein level in the ulcerative colitis patients was 13.3 ± 10.93 µmmol/l) and was lower than the average homocystein level of the control group of 11.2 ± 3.58 µmmol/l (p < 0.001). Vitamin B₁₂ and folic acid averages also lower in the UC (p < 0.001). When regression analysis was performed, seen that folic acid deficiency was only risk factor in hyperhomocysteinemia. Frequency of thromboembolic complications had similar rates in UC and control groups (p = 0.250).

Discussion/Conclusion: Hyperhomocysteinemia is common phenomenon in IBD patients. Homocystein levels negatively correlate with serum folate. Nutritional statuses of all the IBD must be determined and vitamin deficiencies must be found, and folate and B complex vitamins must be added to their therapies. We could not find any correlations between Hcy levels and history of arterial and venous thrombosis risks in UC patients.
Evaluation of health-related quality of life in patients with inflammatory bowel disease

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Aim: In inflammatory bowel disease (IBD) patients often suffer severe symptoms that impair their quality of life. The purpose of this study was to evaluate patient’s outcome and quality of life, assessed by health-related quality of life (HRQOL) and symptoms evaluation.

Material and method: We studied 250 IBD patients: 151 with ulcerative colitis (UC) and 99 with Crohn’s disease (CD), admitted in the Department of Gastroenterology Timisoara during a 6 years period, mean age 46.6 ± 15.6 years. HRQOL was assessed using the Inflammatory Bowel Disease Questionnaire (IBDQ) and disease activity was established using Crohn’s Disease Activity Index (CDAI) and Ulcerative Colitis Activity Index (UCDAI) for CD and UC patients respectively.

Results: In patients with CD (mean CDAI 151.2 ± 68.7), mean IBDQ was 181.6 ± 34.8; patients with moderate disease (18.1% cases, CDAI 262.7 ± 25), had a IBDQ of 164.5 ± 13.2, mild disease (30.3% cases, CDAI 177.3 ± 9.5) had a IBDQ of 182.1 ± 25.2 and and patients in remission (51% cases, CDAI 94 ± 28.2) had IBDQ of 198.2 ± 26.5. Patients with UC (mean UCDAI 7.4 ± 2.9) had a IBDQ of 179.2 ± 45.2; in patients with severe attack (19.8% cases, UCDAI = 10.3 ± 2.0) – IBDQ = 160.7 ± 25.7, moderate attack (40.4% cases, UCDAI = 8.3 ± 1.8) – IBDQ = 178.8 ± 22.7 and patients with mild attack (39.8% cases, UCDAI = 4.7 ± 2.1) – IBDQ = 199 ± 45.2.

Conclusions: 1. In our study no statistical differences were noticed between HRQOL parameters in the CD or UC subgroups patients (p = 0.87). Similarly, no statistical differences were noticed regarding the four IBDQ subscores. 2. When referred to the disease activity patients with mild/remission disease scored significantly higher than those with severe/active disease (p = 0.001), showing that IBD has a negative impact on HRQOL. 3. Patients in our study using the same instrument scored higher than previously reported studies.
System staging in the gastrointestinal lymphoma

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Introduction: The gastrointestinal tract is the most commonly involved extranodal site for non-Hodgkin lymphoma (NHL), accounting for up to half of all extranodal cases. Primary GI lymphomas can be operationally defined as lymphomas in which the main bulk of disease is confined to the GI tract, necessitating treatment directed toward that site.

Methods: During the last 10 years, there were registered 24 lymphoma lesions with gastric determinations. Staging procedures for gastric lymphoma include history physical examination, imagistic technique for thorax and abdomen, hematological, renal and liver evaluations, laboratory tests, including complete blood counts and peripheral blood smear, LDH, b2-microglobulin levels, gastroduodenal endoscopy with multiple gastric biopsies, and recently gastric ultrasound endoscopy (EUS).

Results: From the 24 cases with gastric lymphoma, 47.61% was high-grade four 40% of this with a low-grade component, 45.83% low-grade MALT lymphoma, 8.33% follicular lymphoma and 4.16% mantle zone lymphoma. The Ann Arbor Staging system is used but it is compared with the GI-lymphoma-specific Blackledge, Musoff or Ann Arbor revised system. EUS may facilitate the accurate estimation of both the depth of invasion and involvement of regional lymph nodes. It is superior to CT scan in false negative cases, but CT evaluates the non-contiguous subdiaphragmatic lymph nodes. The stadial distributions of our lot with MALT lymphoma is: IE 63%, IIE 17%, IEI 7%, III 2%, IV 10% and for the rest of lymphoma histological subtype IE 27%, IIE 24%, IIEII 17%, IIIIE 8.5%, IVE 24%.

Discussion/Conclusion: The type of staging system has no evident impact in our study, but several authors have suggested that such staging modification may be of prognostic significance.
Eradication therapy for Helicobacter pylori and systemic chemotherapy are very effective in gastric extranodal marginal zone B-cell lymphoma of MALT

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Introduction: The treatment of gastric extranodal marginal zone B-cell lymphoma of MALT type (E-MZL) is dictated primarily by stage and histological grade and optimal management requires an integrated multidisciplinary approach involving medical oncologists, radiation oncologists, pathologists, and surgeons.

Methods: During the last 15 years, there were registered eleven lesions of E-MZL with gastric determinations.

Results: From the eleventh cases with E-MZL gastric, eighth (72.72%) present themselves in localized stage, IE, IIE. Six of these ones (75%) responded the Helicobacter pillory (HP) triple eradication therapy. In evolution, two patients relapsed locally (range 25–37 months). Both patients responded to CVP chemotherapy and the estimated survival rate, of localized stage group, at 5 years being 100%. Three patients (27.27%) presented with an advanced stage of the disease (IIIE and IVE), two of them has laparotomy for diagnostic/treatment reason, with partial gastric resection. Two of the three of advanced stage patients underwent eradication therapy for HP, but only one patient presented a partial response. A whole lot of patients who was in an advanced stage/relapsed lymphoma were treated with protocols of CVP or CHOP type by rapport of the presence of confluent clusters or sheets of large cells resembling centroblasts. The rate of response was also 100%. Two of these patients presented multiple relapses, controlled by chemotherapy. The survival rate of 5 years in this lot has been of 66.67%.Median follow-up was 75 months (range, one to 116).

Discussion/Conclusion: The E-MZL therapy presents characteristics through the response to the HP eradication therapy manly in the localized stage. Systemic chemotherapy is effective in advanced and relapsed E-MZL. The 5 years survival rate for this group of patients is 90%.
Rare co-existence of celiac disease with Turner syndrome, myasthenia gravis and chronic myeloid leukemia

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The celiac disease is often complicated by other disease. This co-existence is evident in same cases but in others are not verified. We report three celiac disease cases with this infrequent co-existence.

In our first case dermatitis herpetiformis and celiac disease was diagnosed in a female patient at the age of 6. Beside strict gluten free diet her growth was slower than expected. She was observed due to delayed puberty and for primer amenorrhea by the age of 18. The examinations revealed hypergonadotropic hypogonadism and cytogenetic analysis showed Turner syndrome (45X/46XY mosaics). Female hormone replacement therapy was introduced. The prevalence of celiac disease in Turner syndrome seems to be around 6–7%. Therefore screening of these patients for celiac disease is recommended.

Our second patient was a young woman who was treated with immunosuppressive drugs because of myasthenia gravis. She was in remission and the corticosteroid therapy was stopped. After a month the patient was admitted to our department with diarrhea, abdominal distension and weight loss. Celiac disease was diagnosed. This coexistence was mentioned only once in the literature.

In our third case chronic myeloid leukemia (CML) developed in a 42-year-old women with untreated celiac disease. She was diagnosed with gluten sensitivity when she was an infant. Her abdominal symptoms – bloating, watery diarrhea – were temporary, so she did not adhere to diet. CML was diagnosed and she has been in remission for two years on imatinib therapy. There are only two similar cases in the literature.
Botulinum toxin injection as treatment for anal fissures

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Introduction: Anal fissure (AF) is a common proctologic condition characterized by a longitudinal tear extending from the dentate line to the anal verge caused by too high tension (resting pressure) of the internal anal sphincter (IAS), spasms and reduced blood flow.

Objectives: In this study we wanted to demonstrate the efficacy of Botulinum toxin injection in reducing the anal spasm and allowing the fissure to heal.

Material and methods: 24 patients (14 M, 10 F) with anal fissures received Botox® injection into the IAS after a proctologic exam (including anoscopy). 20 U of Botox® were initially injected in the IAS on each side of the AF (0.4 ml total volume). After one month, depending on the results, patients received another 20 U Botox® injection in the AF. Patients were followed up at two months and 6 months.

Results: At 1 month follow-up significant improvement was observed: 79% of patients treated with Botox® were symptom-free and AF healing was observed in 62.5%. 3 patients received a second Botox® injection (20 U) into the AF. At two months 96% of patients had relief of symptoms and 87.5% the AF healed. At 6 months only one female pt the AF didn’t healed and she was referred for anal dilatation. In all other patients AF healed. There were minor side-effects, especially flatus incontinence. No fecal incontinence was observed.

Conclusions: Along other treatment options, Botox® injection into the IAS is a safe and effective treatment for AF. It is well tolerated by patients and has almost no side-effects.
Mesalazine administration in the treatment of chronic post-radiation proctitis

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Aim: As a non-surgical approach in the treatment of post-radiation proctitis (PRP), we looked at the effect of mesalazine enema and suppositories administration.

Methods: 27 patients (11 M, 16 F) with PRP different etiologies (prostate carcinoma – 6 patients, colon [rectal & sigmoid] carcinoma – 12 patients, uterine corpus adenocarcinoma/radical hysterectomy – 9 patients) underwent colonoscopy for abdominal pain, loose stools and moderate rectal bleeding. All patients were treated with mesalazine enemas and/or suppositories (4 g/day) for three months. Follow-up colonoscopy was performed in all 27 patients at six months.

Results: After three months of mesalazine treatment symptoms improved: diarrhea & rectal bleeding decreased/stopped, abdominal pain disappeared. On the follow-up colonoscopy rectal mucosa was mildly active, without spontaneous or contact bleeding, erosions were healed and vascular pattern was almost normal.

Discussion: Patients with PRP present most frequently with hematochezia, pain and bowel habits disturbances. Especially recurrent hemorrhage is refractory to medical therapy. Surgery cannot always be recommended due to the high rate of complications. From the non-surgical approaches APC, Nd-YAG laser would be useful in coagulating erosions and bleeding teleangietasias. However, these procedures inquire also some risks (i.e. perforation). Follow-up colonoscopy revealed that mesalazine has cytoprotective & anti-inflammatory effects on rectal mucosa, is simply to administer, well tolerated and no adverse events were observed.

Conclusion: mesalazine enemas/suppositories have a beneficial cytoprotective effect on rectal mucosa in PRP. It improves the symptoms (bleeding) and contributes to repair of injured mucosa. The drug represents a treatment option of PRP.
Use of mesalazine in treatment of colonic diverticular disease

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Introduction: Uncomplicated diverticular disease is defined as the presence of diverticula in the absence of complications such as perforation, fistula, obstruction and/or bleeding. Combination treatment strategies, including antibiotics and antiinflammatory drugs represent a good therapeutic option in diverticulitis.

Objectives: the aim of this study is to compare the efficacy of combined therapy (rifaximin plus mesalazine) vs. antibiotics alone (rifaximin) in the treatment of diverticulitis. We want to evaluate 1. the rapidity of symptoms improvement and 2. the maintenance non-inflammatory status of diverticula.

Material and methods: 27 patients (15 males, 12 females, mean age 69.7 years) with diverticulitis were randomized to receive either rifaximin 400 mg bid, 7 days plus mesalazine 1000 mg bid for 14 days (group A) vs. rifaximin 400 mg bid for 7 days (group B). Colonoscopy was performed at baseline and at 3 months.

Results: Symptoms (abdominal pain, bloating, abdominal tenderness) and bowel habits improved significantly and more rapidly in group A compared to group B. Few side-effects were observed (abdominal pain/discomfort, skin rash), predominantly in group B (3 patients vs. 1 pt in group A). At 3 months colonoscopy revealed healing of diverticula in 13 of 14 patients in group A vs. 8 out of 13 patients in group B (p < 0.005).

Conclusion: 1. Combination therapy (rifaximin plus mesalazine) is certainly more effective than antibiotic therapy alone in diverticulitis; 2. Mesalazine is safe and acts probably on the chronic inflammation of the colonic wall; 3. In combination with antibiotics, mesalazine improves more rapidly symptoms and shortens the course of diverticulitis, preventing also reccurrence.
Subclinical left ventricular systolic dysfunction in patients with ulcerative colitis: Findings on pulsed tissue Doppler echocardiography

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Aims: Our objective was to evaluate regional systolic myocardial contraction properties along the long and short axes of the left ventricle (LV) in patients with ulcerative colitis (UC).

Methods and results: 26 patients with UC, and 13 healthy controls were enrolled into the study. Clinical and endoscopic activity indices, hemoglobin, white blood count and platelet values, ESR, fibrinogen, CRP, albumin, liver enzymes and renal function tests were recorded. Clinical activity index for UC was used and active and inactive groups were formed. Pulsed tissue Doppler imaging (TDI) was used to record myocardial velocities along the short and long axes in patients with UC (13 active UC-LV ejection fraction [LVEF] ≥ 50%; 13 inactive UC-LVEF ≥ 50) and healthy controls. In all cases, the systolic velocity pattern featured 2 distinct peaks (SW1, SW2). These peak velocities and the intervals from the electrocardiographic Q wave to each peak (Q-SW1, Q-SW2) were recorded for each axis, and group means were calculated. The active UC group had significantly longer long axis Q-SW1 than the controls (p < 0.01), but were not significantly different from the inactive group.

Conclusion: In conclusion, patients with active UC exhibit distinct systolic myocardial shortening velocities along the long axis of the LV. Further, these pulsed-TDI findings suggest that symptomatic patients with UC (those with normal LVEF) have subclinical myocardial dysfunction compared with the controls. This condition is considered to be due to the systemic inflammatory disease which can affect every organ system.
Relationship between disease activity and mean platelet volume in inflammatory bowel diseases

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Introduction: The aim of this study is to determine whether platelet volume would be useful in inflammatory bowel disease activity and to correlate mean platelet volume with other activity markers.

Methods: 145 patients with ulcerative colitis, 73 patients with Crohn’s disease and 92 healthy controls were enrolled into the study. Clinical and endoscopic activity indexes’, hemoglobin, white blood count and platelet values, Erthrocyte sedimentation rate, fibrinogen, C-reactive protein, albumin, liver enzymes and renal function tests were recorded. Clinical activity index for ulcerative colitis and CDAI for Crohn’s disease were used and active and inactive groups were formed.

Results: A statistically significant decrease in mean platelet volume was noted in patients with both ulcerative colitis and Crohn’s disease compared with healthy controls (p < 0.05), but there was no difference between the both disease. Mean platelet volume was significantly decreased in patients with both active (7.78 ± 0.92) and inactive (8.46 ± 0.84) ulcerative colitis compared with healthy controls (8.83 ± 0.82) (p < 0.05) and was significantly lower in active disease (p < 0.05). Mean platelet volume was significantly decreased in patients with both active (7.56 ± 0.85) and inactive (8.29 ± 0.86) Crohn’s disease compared with healthy controls (p < 0.05) and was significantly lower in active disease (p < 0.05).

Discussion/Conclusion: Mean platelet volume is rapid reliable and inexpensive test which may be useful in the course of inflammatory bowel disease, especially in the active episode.
Ülseratif kolit  Crohn  Kontrol

MPV
Celiac survey in Baranya region

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Introduction: Celiac disease (CD) is an immun-mediated enteropathy triggered by the ingestion of gluten-containing grains (including wheat, rye and barley) in genetically susceptible individuals. The pattern of incidence is changing, with a greater proportion of cases diagnosed later in adulthood. The prevalence of CD in caucasian populations is 1–5%.

Aim: In the past two years 354 patients were examined in our outpatient clinic with the suspicion of CD looking for clinical presentation, atypical symptoms, associated diseases and family screening.

Methods: Clinical symptoms, associated diseases, screening laboratory tests – serology: serum antibodies (anti-giadin IgA, IgG, anti-EMA, anti-tTG IgA, IgG), duodenum biopsy, HLA genes were determined. After the secure diagnosis of CD, gluten free diet was introduced, education of the patients started, measure of nutritive conditions, DEXA examination was done, QL questioner was obtained. Control after 3–6 and 12 months. Our results were compared to the literature. QL test was measured before and 6 months after the treatment (gluten free diet – GFD-).

Results: CD was diagnosed in 34 of 354 patients. In the remaining 320 cases the next diagnoses were found: irritable bowel syndrome, lactose intolerancy, nutritional allergy, Crohn’s disease, acute gastroenteritis, neurosis, hyperthyreosis, diverticulosis, giardiasis, steatosis hepatitis, colon carcinoma, postcolecystectomic syndrome.

Sex: 26 female/8 male (literature: 3:1). Average age at the time of diagnosis: 35 years (15–71 years) (literature: 64 years). Average elapsed time from the beginning of symptoms till the established diagnosis: 6.5 years (3 weeks–26 years) (literature: 11 years). Precipitating factors: pregnancy-post-partum: 3 cases, Giardia infestation: 1 case. CD in the family: 8 cases (23%) (literature: 10%). Histology: Marsh 1: 0%; Marsh 2: 7%, Marsh 3a: 11%, Marsh 3b: 37%, Marsh 3c: 45%. DQ2 HLA gene was present 95% of cases.

Complaints after 6 months on GFD: 54% no complain at all, 46% significant improvement.

Sixteen % of the patients kept strictly the diet, 26% strict, but involuntarily consumes gluten, 14% yes, but sometimes quit the diet.

Discussion/Conclusion: CD is far more common than previously considered. There are many individuals with undiagnosed CD. In many cases it takes years or decades untill CD is recognized. The health risk for untreated CD is greater compared with those who adhere to a GFD. Collaboration of other specialists, more widerspread use of serologic tests and screening in risk groups could result in an earlier diagnosis. Early diagnosis can prevent the onset of osteoporosis, decrease the incidence of spontanaeous abortions, lower the incidence of low birth weight infants, decrease the risk of cancer and lymphomas and avoid other consequences of delayed diagnosis.
Surgery emergency as primary manifestation of inflammatory bowel disease

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Introduction: Treatment in inflammatory bowel disease (IBD) is dominantly relied on pharmaceuticals and surgery is reserved for treatment of complications or improving the quality of life for critically ill patients. According to literature, the surgical IBD is not so common initial presentation.

Results: One hundred forty seven (147) patients with IBD presented in emergency admission of University Hospital Dubrava (UH Dubrava) in a 5-years period. Eleven patients (7.48%) were initially presented at surgical emergency. Two thirds (72.73%) of surgery emergency group had Crohn's disease (CD). Six (6) patients had severe CD and 2 intermediate disease activity according to CDAI. A single female patient age 76 presented suspected with acute appendicitis and diagnose of CD was established upon appendectomy.
Regarding three patients with UC, one female patient (age 65), with pancolitis and toxic megacolon with CRP 300 mg/l was operated because of bowel perforation. She had short history of unspecific abdominal pain and weight loss.

Discussion/Conclusion: The patients suspected on IBD presenting as acute emergencies should receive appropriate diagnose by radiology imaging, estimation of inflammatory markers and emergency endoscopy evaluations, all in order to avoid potentially unnecessary surgery.
Further studies of IBD are needed for better understanding biological course of disease in regard to population characteristics, heritage base and potential environmental predispositions for emergency situations as primary manifestation of IBD.
Patients with IBD hospitalized in university hospital settings during 5-years period

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Introduction: On behalf of lack in unique national IBD registry we started incidence/prevalence based study with patients managed through university hospital settings. Catchments population was 300,000, during a 5-years period. The aim was to define ground figures for IBD, enclosed entities and assess clinical activity in hospitalized patients. CDAI and Harvey Bradshaw score were used for CD, while DAI and Mayo score were applied for UC.

Results: One hundred forty-seven (147) patients, age 18–87 were diagnosed with IBD. There were more male than female (52.38%:47.62%) and regarding IBD type; UC, CD and ID as follows 85 (57.82%), 60 (40.82%) and 2 (1.36%) respectively. CD was more common in male (58.33%) and UC in female patients (51.76%). CD had peek incidence at age group 30–39 (n = 18; 30% of total CD; 12.24% of total IBD) with tendency of decreasing as age proportionally rise. Conversely UC was commonest in age group > 60 years (n = 29; 34.11% of total UC, and 19.73% of total IBD) with wave shaped curve through age gropes. Only in the youngest group (< 30) CD and UC were of exact equal incidence (n = 14; 23.33% of CD, 16.47% of UC, and 9.52% of IBD). Clinical activity presented as mild, moderate and severe for CD was following 41.65%, 27.0%, 31.67%, while in UC it was 47.06%, 45.0%, 8.24% respectively.

Discussion/Conclusion: Lesser number of patients hospitalized with CD than UC is partially due to different incidence/prevalence levels. Yet, patients with CD had greater relative share of clinically severe disease which implies greater number of unscheduled visits, more abundant burden in diagnostic workup and the therapeutic interventions.
Rectal cancer staging by endoluminal echography

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Introduction: The aim of the study is to estimate the contribution of endoluminal ultrasonography (EUS) for rectal cancer diagnosis and staging.

Methods: Using an Aloka SS 366 with 5 MHz and 7.5 MHz transducers, EUS has been performed to 48 consecutive patients with rectal cancer (rectoscopy + biopsy).

Results: Following the Dukes-Turnbull classification, we appreciated the degree of invasion in the rectal wall structures, obtaining: stage A = 3 cases, stage B1 = 5 cases, stage B2 = 8 cases, stage C = 32 cases. Later, intraoperatory and morphopathologic, our echographic estimation was confirmed in 42 cases (2 – 3 – 6 – 31) = 87.5%.

Discussion/Conclusion: EUS is a useful method for diagnosis and staging of rectal cancer. The majority of the patients come to the hospital in advanced stages of the disease.
Influence of experience on accuracy of the results in endoluminal ultrasonographic (EUS) staging of rectal cancer

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Introduction: The aim of this study is to assess the influence of experience on the accuracy of rectal cancer staging by EUS.

Methods: There were 172 patients (out of 345 admitted for rectal cancer in the Gastroenterology and Hepatology Institute of Iasi between 2002–2007) examined using EUS.

Results: The accuracy of the method becomes considerable after the examiner has performed over 50 procedures. The „learning curve“ over a period of 6 years has reached an acceptable level after the first 3 years (54 cases examined meantime), the accuracy improving from 64% to 83% during the last 3 years (50→68→70→82→83→84). The best accuracy (85%) was obtained for Dukes C stage, for which a major improvement occurred early, after the first year (12 cases), further variations being smaller (62→73→77→92→92→92).

Discussion/Conclusion: The experience of the examiner is very important for the quality of EUS investigation.
Correlations between disease activity and quality of life in patients with Crohn’s disease

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Aim: Both health-related quality of life (HRQOL) and decrease in disease activity are important outcomes in Crohn’s disease (CD). The aim of this study was to assess the correlations between patient’s outcome and quality of life.

Material and method: We studied 99 patients with CD admitted in the Gastroenterology Department Timisoara during a 5 years period (57 females and 42 males), mean age 40.6 ± 13.9 years. For HRQOL assessment we used the Inflammatory Bowel Disease Questionnaire (IBDQ), a 32-item, and for CD activity we used CDAI.

Results: Overall, mean IBDQ score was 181.6 ± 34.8 and mean CDAI was 151.2 ± 68.7. Regarding the disease activity, in patients with moderate disease (n = 18), IBDQ was 164.5 ± 13.2 (CDAI = 262.7 ± 25), mild disease (n = 30), IBDQ was 182.1 ± 25.2 (CDAI = 177.3 ± 9.5) and patients in remission (n = 51), IBDQ was 198.2 ± 26.5 (CDAI = 94 ± 28.2). None of the patients in our group was classified as having severe disease activity. Abdominal pain (78.7%), diarrhea (49%), weight loss (22.7%) and occlusive syndrome (16.6%) were the most frequently reported symptoms. The average number of flares per year was 1.6 ± 0.5. Patients who had a greater number of symptoms per flare showed a greater impairment in IBDQ (p < 0.05). In what concerns the IBDQ subscores these were as follows: bowel movements = 58.6 ± 11.2, systemic = 27.3 ± 7.4, emotional = 63.2 ± 15.9 and social = 28.5 ± 8.1. When referred to age, patients younger than 60 years had a IBDQ of 178.1 versus older patients 174.8.

Conclusions: IBD has a negative impact on HRQOL. Patients with active disease are more impaired than patients in remission (p < 0.001). Increases in disease activity predicted decreases in quality of life on the total IBDQ score and also in bowel symptoms subscale (p < 0.01) and systemic symptoms subscale (p < 0.05). Younger patients scored higher for the social dimension subscale (27.9 vs. 26.0, p = 0.017).
Irritable bowel syndrome in medical students: Data from a 5-years follow-up

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Background and aim: Irritable bowel syndrome (IBS) has a high prevalence and represents an economic burden for the health system. Its prevalence is largely ignored in our area. Even less data are available on the evolution of IBS symptoms in time. We looked for the prevalence of IBS in medical students in first year and investigated the same cohort after a 5 years interval, close to the end of the medical school.

Methods: A group of 200 students have been investigated with the Rome II questionnaire for IBS. A number of 191 filled questionnaires were returned (from 56 M, 135 F, median age 19 years). The same cohort was investigated after 5 years with the same questionnaire.

Results: At the beginning of the medical studies, the prevalence of IBS was 4% (2% diarrhea type, 2% constipation type) with sex ratio 1:1. After 5 years 70 subjects could be retrieved. IBS was present in 17% cases (10% D-type, 8% C-type). IBS disappeared in 5 cases (10%). 5 new cases were detected. One case showed the change from C-type to D-type.

Conclusion: IBS has a lower than expected prevalence in medical freshmen. After 5 years the prevalence increased significantly
Evaluation expression of MCM2 protein in advanced gastric cancer in correlation with Helicobacter infection and survival time

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Aim: The aim of the current study was to evaluate the expression of MCM2 in advanced gastric carcinomas and to analyze the relationship with chosen anatomo-clinical parameters and prognosis.

Material and methods: Study was performed on 100 cases of patients with advanced gastric carcinoma. Standard, immunohistochemical technique was adopted to detect the expression of MCM2 protein (goat polyclonal antibody to MCM2, Santa Cruz Biotechnology; dilution 1:300) in evaluated samples.

Results: We have not observed statistical significant correlation between the expression of MCM2 protein in main mass of tumor, in lymph node metastasis and age and gender of patients, localization of tumor or degree of histological differentiation. Moreover, there was no association between positive immunohistochemical staining for MCM2 protein in tumor, lymph node metastasis and Bormann’s, Lauren’s, Goseki’s classifications. Similarly, there were no correlation between expression of MCM2 and Helicobacter pylori infection. Strong association was found between the expression of MCM2 in main mass of tumor, lymph node presence (p = 0.000, p = 0.007, respectively) and lymph node metastasis and survival time.

Conclusion: Our results may indicate the association between expression of MCM2 protein and parameters of invasiveness in patients with advanced gastric cancers.
Rectorrhagia – Clinical and endoscopical profile

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Introduction: Lower gastrointestinal bleeding continues to represent an important cause for hospitalized morbidity and mortality. The aim of this study is to evaluate the clinical and etiological pattern in patients with rectorrhagia.

Methods: We studied 121 patients with rectorrhagia, admitted in our hospital in 2005, who underwent colonoscopy for diagnosis. We analyzed the demographical and clinical data on three different patient groups, according to etiology.

Results: A group of 121 patients were diagnosed with rectorrhagia. The male/female ratio was 0.95 with a mean age 53.74 yrs. The etiology of rectorrhagia was as follows: hemorrhoids (38.84%), hemorrhoids and other diseases (8.26%) and non-hemorrhoidal (52.89%). The last patients group have many causes: inflammatory bowel diseases (43.94%), colorectal cancer (22.73%), diverticulosis (7.58%), postpolypectomy (6.06%), irradiation (6.06%), ischemic (3.03%) and infectious (3.03%) colitis, anal fissures (3.03%) and no evident cause (1.52%). Most patients (61.98%) presented intestinal troubles, like diarrhea (49 patients) and constipation (28 patients). Diarrhea was more common in patients with non-hemorrhoidal bleeding (54.69% vs. 17.02%, p = 0.00005) and the constipation has an increased frequency in patients with hemorrhoidal bleeding (38.3% vs. 14.06%, p = 0.003). The anemia was mostly mild/moderate (27.27%) and severe (2.48%) and the antiinflammatory or anticoagulant drugs (p = 0.056, p = 0.218) are recorded mainly in non-hemorrhoidal bleeding.

Discussion/Conclusion: No significant differences in prevalence in patients with or without hemorrhoidal bleeding. The inflammatory bowel diseases and colorectal cancer were more important etiological causes in the non-hemorrhoidal bleeding. Diarrhea and anemia was more common in patients with non-hemorrhoidal bleeding and the constipation has an increased frequency in patients with hemorrhoidal bleeding.
BCRP deficiency in human colorectal adenomas and in the Apc Min mice promotes accumulation of the colon carcinogen PhIP and may represent an acquired susceptibility factor for colon carcinoma

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

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

Results: BCRP was significantly downregulated in human colorectal adenomas (35 ± 30% compared to adjacent healthy tissue). This was in line with data from Apc Min mice adenomas, where downregulation was significant as well (58 ± 34%). In parallel, quantitative RT-PCR showed mRNA downregulation in human adenomas (17 ± 31%). 48 h after oral gavage of PhIP, we could demonstrate a higher carcinogen concentration in adenomas of Apc Min mice (181 ± 113% when compared to normal tissue). Other xenobiotics transporters (MRP2/Mrp2 and MDR1/Mdr1) were unchanged.

Discussion/Conclusion: Significant transcriptional downregulation of BCRP/Bcrp leads to higher carcinogen concentrations in colorectal adenomas. This might promote the adenoma-carcinoma sequence by higher genotoxic effects. The results indicate a possible role of transporter deficiencies in susceptibility for colon carcinoma. Further studies regarding the impact on DNA adduct formation of PhIP in adenomas are ongoing.
Bleeding colonic varices: Two cases with different etiologies

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Introduction: Lower GI hemorrhage due to colonic varices is very rare in the literature and most of the cases reported are due to portal hypertension caused by liver cirrhosis. Here, we presented two cases with very rare etiologies.

Case-1: A 28-year-old young man was admitted to our hospital due to massive rectal bleeding for 8 days. He was referred from another center and had received twenty packs of blood during hospitalization there. In his past medical history, he had an operation due to abdominal trauma. Since bleeding was still going on, we planned an emergent colonoscopy. On transabdominal ultrasound performed before endoscopy, a thrombosed portal vein with surrounding cavernous transformation was revealed. On colonoscopic examination, despite existing fresh blood in the lumen, a tortiosed large column of submucous vein extending from rectum to splenic flexure was able to seen but bleeding site was not found. An immediate selective angiography showed a fistula between ascending branch of left colic artery (a branch of inferior mesenteric artery) and mesenteric venous system. Selective arterial embolisation was attempted during the procedure but it was failed. Surgical ligation of inferior mesenteric artery was seemed as the only choice and after two years from the procedure there was no complication and recurrence.

Case-2: A 39-year-old woman referred to our clinic with periumblical abdominal pain and hematochezia for 2 months. She needed two packs of blood transfusion during this period. There was no active bleeding on colonoscopic examination and large, serpiginous varices extending from rectum to the ascending colon was observed clearly. On selective mesenteric angiography, superior and inferior mesenteric arteries were normal but it was revealed on venous phase that there was no filling of venous systems of both arteries. On laboratory work up, anticardiolipin antibodies were negative and serum Antithrombin-III and Protein-S levels were in normal range but Protein-C level was found very low (33.8%, N: 70–130%) Her two sisters and one brother have also low levels of protein-C on screening (they have no history of thrombosis). With these findings, we diagnosed the patient as having hereditary type-II heterozygote Protein-C deficiency. We did not start anticoagulant therapy due to continuing bleeding. Propranolol 80 mg/ day was given and bleeding was stopped 3 days later. In 2 years follow-up, there was no recurrence.

Discussion/Conclusion: Although it is very rare, colonic varices must be considered as a cause of rectal bleeding as seen in two cases above.
Efficacy of mesalazine application in patients with irritable bowel syndrome

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Clinical picture of irritable bowel syndrome (IBS) characterize by abdominal pain with stool frequency and colon transit modification. But IBS pathogenesis still unclear, more over signs and elements of colon mucosa inflammation in IBS patients were found. In case of colon inflammation present application of anti-inflammatory treatment as a mesalazine is necessary.

Aim of this study was to investigate efficacy of mesalazine application in patients with IBS.

Materials and methods: 72 IBS patients were examined. Among them were 24 male and 48 female, middle age was 41.6 ± 0.4 years. Diagnosis of IBS was made clinically according to Rome III criterias. In all patients colon endoscopy with colon mucosa scrape’s cytological examinations were done. Among IBS patients in 22 (30.6%) - IBS with diarrhea, in 26 (36.1%) patients IBS with constipations, in 17 (23.6%) patients mixed IBS and in 7 (9.7%) indeterminate IBS were found. 32 patients received mesalazine (Salofalk®) in dose 1.0 g per day in combination with basis treatment, 40 patients obtained basis IBS treatment only and were a control group.

Results: Before treatment all patients suffered from abdominal pain with different intensity, meteorism, had stool frequency and consistency modification. In colon endoscopy 49 (68.1%) patients had normal results, but in 23 (31.9) minimal endoscopical changes such as mucosa hyperemia, vascular pattern modifications, slight edema were observed. In colon mucosa scrape’s cytological examination before treatment in 40 (55.6%) IBS patients dystrophic epithelium changes, in 44 (61.1%) leucocytes and in 12 (16.7%) macrophages were found. Those violations specified presents of colon inflammation in IBS patients.

Mesalazine application in IBS patients was effective. In 7 days of treatment in 21 (65.6%) patients of first group and 11 (27.5%) patients of second group pain syndrome was absent (p < 0.05). In 10 days of treatment 20 (62.5%) patients of first group and 14 (35.0%) patients of second group stool normalization was observed. Mesalazine were more effective in patients with diarrhea and mixed IBS. After treatment in endoscopical examination decreasing of violation intensity especially in first group patients were found.

Conclusion: In IBS patients signs of colon inflammation were found. Mesalazine application as anti-inflammatory treatment in IBS patients were effective and induced abdominal pain intensity decreasing and early stool normalization.
Anorectal function in long-standing type I diabetes mellitus

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Patients with diabetes mellitus tend to have anorectal abnormalities, some with clinical impact, but long standing type I diabetic patients were not particularly investigated.

The aim of the study was to investigate the anorectal function in long standing type I diabetes and to reveal its clinical relevance.

Material and method: Clinical examination, blood glucose, HbA1c, standard lab tests and standard anorectal manometry were performed in 17 patients (10 females and 7 males, mean age 48 ± 8.2 years), with a duration of diabetes longer than 10 years, and in 10 healthy control subjects (6 females and 4 males, mean age 48.1 ± 12.3 years).

Results: Normal digestive transit was present in 11 patients, but 4 patients had diarrhea, 1 patient fecal incontinence and 2 constipation. The majority of patients had microangiopathy (14 from 17), peripheral polyneuropathy (15 from 17) and HbA1c level was 9.5 ± 1.3. No significant difference between diabetic patients and controls was found for resting and squeeze anal sphincter subjects. Significant difference was found in diabetic and non-diabetic patients comparing the threshold distension volume for inducing defecation (171 ml ± 38.2 vs. 111.6 ml ± 42.5) and pain (246.3 ml ± 43.1 vs. 179.3 ml ± 22.4) but not for perception of distension (65.2 ml ± 19.6 vs. 60.2 ml ± 11.3).

Conclusion: Impaired rectal perception is a constant finding in type I diabetic patients, frequent associated microangiopathy and peripheral polyneuropathy.
Could the bacterial etiology be predicted in children’s acute diarrhea? Diarti Score – A fast etiological alternative in diagnosis

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Introduction: Since first started in 1980 by Koplan, elaborating the best predictive clinical and biological combination for bacterial acute diarrhea remains a constant concern for researchers worldwide. Objectives: To elaborate a fast predictive score for the bacterial etiology in children’s acute diarrhea.

Methods: 453 children with infectious acute diarrhea, from Arad and Timisoara (Diarrhea – Arad – Timisoara Score), Romania, participated in this study. They were divided in two groups: bacterial and viral. The bacterial group included 387 children with diarrhea produced by Shigella, Salmonella, Campylobacter, E. coli. The viral group included 66 children with Norovirus and Rotavirus infections. 33 clinical and biological variables were compared and the data were introduced in an Excel database and analyzed with statistical methods. The most meaningful parameters were included in the regression equation.

Results: Using the regression equation, three scores were elaborated: a general score and two individualized scores (for under and over 5 years of age).
- Diarti General Score included: admission season (summer), fever $\geq 38.5^\circ$C, dehydration $\geq 5\%$, vomiting $\geq 4$/day, tenesmus, mucus in stool.
- Diarti Score under 5 years of age contained: admission season, fever, dehydration $\geq 5\%$, vomiting $\geq 4$/day, mucus in stool.
- Diarti Score over 5 years of age used 4 parameters: mucus in stools, tenesmus, stools frequency $\geq 5$/day, ESR $\geq 25/50$.

Discussion/Conclusion: Diarti Score allows a fast etiological diagnosis in acute diarrhea and identifies the cases that require bacteriological investigation and antimicrobial therapy. Future prospective studies are needed to verify the Diarti Score.
Testing GPs’ knowledge on IBS: Comparative study between Germany and Romania

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Background and aim: Irritable bowel syndrome (IBS) is a common disorder and many patients are diagnosed and managed by general practitioners (GPs). It is necessary therefore to assess the knowledge of GPs on IBS and to find out how they manage this condition, in order to establish educational strategies for them. We undertook a comparative study in Germany and Romania.

Methods: Two samples have been investigated with a structured questionnaire, that was mailed in Germany (Mannheim area) and addressed before a 2 hours course on IBS in 2 venues.

Results: 121 answers were collected in Germany (response rate 46.5%) and 88 in Romania (response rate 88%). In both countries IBS was reported to have a similar prevalence (1–10% of patients in most sites). Diagnostic criteria were used by 18% in Germany and by 87% in Romania. 55% considered IBS a functional disorder in Germany and 97% in Romania. Colonoscopy was considered necessary in diagnosis of IBS in both countries. Psychotherapy was more frequently used in Germany than in Romania.

Conclusions: In both countries GPs seem to be well trained to recognize IBS. Differences in the use of diagnostic criteria and therapy have been encountered.

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Actinomycosis is a subacute/chronic suppurrative, granulomatous disease caused mainly by Actinomyces israelii, an anaerobic bacterium that is a normal inhabitant of the human bronchial and gastrointestinal tracts. Actinomycosis of the abdomen accounts for 15–20% of the reported cases. The ileocecal region is the most commonly involved site of the gastrointestinal tract. We report 2 cases of abdominal actinomycosis illustrating the difficulty of diagnosing the disease that can mimic both cancer and inflammation.

Case reports: 1. A 36-year-old woman with 6 years intrauterine device (IUD) use was diagnosed with a palpable epigastric and left subcostal mass after a week’s history of gradually increasing abdominal pain, anorexia and constant nausea. During laparotomy indicated by the clinical appearance of acute abdomen infiltrative tumor-like mass was detected with generalized lymphadenopathy. Exact diagnosis based on the histological examination could not be made; mesenteric panniculitis or myxoid tumor was suspected. Control computed tomography (CT) after metronidazol treatment showed the regression of the process, but the persistent generalized lymphadenopathy suggested lymphoma. Histological examination of the removed enlarged lymph nodes during the second, diagnostic laparotomy disclosed actinomycosis. The complaints and symptoms of the patient ceased after long-term metronidazol and penicillin treatment.

2. A 34-year-old female patient with 5 month’s history of nausea, vomiting, abdominal cramps and weight loss was found to have wall thickening in the ileal region with hydronephrosis on the right side. Crohn’s disease was suspected although the endoscopic and histologic findings of terminal ileum were substantially better than the clinical condition. Her symptoms gradually increased despite steroid and immunosuppressive treatment and 2 months later abdominal abscess was disclosed by CT and ultrasonography thus ultrasonographic drainage was performed. Diagnosis of actinomycosis was established by the positive culture from the drained sample. Intravenous penicillin therapy resulted in a definitive cure for the patient. Actinomycosis can imitate abdominal malignancy and chronic inflammatory processes as well, thus it is important to consider in the differential diagnosis of patients with abdominal pain, leucocytosis, intestinal wall thickening or abdominal mass.
Complex treatment of endotoxicosis at chronic colon children diseases

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Introduction: Gut endotoxicosis caused by penetration of bacterial and metabolic toxins from chime on the background of increasing permeability of gut wall is of great importance in pathogenesis of chronic colon diseases. It is accompanied by disturbance of regulating homeostasis system with the following disturbances of organs and systems of toxication. Endotoxicosis expressions depended on the character of pathological changes in colon and on condition of organs of detoxication, first of all the condition of liver.

Methods: We observed 95 children at the age from 5 to 15 years old with chronic colon diseases: 55 of them with its anomalous development (dolichocolon, dolichosigma), 15 patients with non-specific ulcer colitis (NUC), 25 patients with chronic non-ulcer colitis and dyskinesia of colon. To obtain accurate diagnostics of the degree and phase of development of endotoxicosis we defined quantitative and qualitative changes of metabolic status by LMMWP (low and medium molecular weight peptides) and OP (oligopeptides), determined in some mediums: blood plasma, erythrocytes, urine.

Results: Correlation between the extent of affection, expression of symptoms with the degree and the stage of endotoxicosis. The most prominent endotoxicosis was observed in children with NUC with extraintestinal manifestations the predominant of which was liver dysfunction. Therefore, the therapeutic complex was added natural lignin enterosorbent-polyphelan, which besides binding in gastrointestinal tract exogenous and endogenous toxic substances, rendered stimulating effect on reparation of ulcer defects, exerting positive influence on composition of gut microflora.

Discussion/Conclusion: Positive dynamics of laboratory – instrumental parameters in usage of complex therapy with inclusions of enterosorbent – polyphelan showed remarkable improvement of clinical conditions in comparison with controlgroup of children.
Clinical meaning of antibodies to proteinase-3 of neutrophils at inflammatory bowel diseases among children

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Inflammatory bowel diseases are characterized by chronic inflammatory damage of mucous membrane of bowel and by presence of out-intestinal displays, which are common for many other autoimmune processes and concern to “ANCA-associated disease”.

Methods: 41 children were examined, including 15 children with Crohn's disease, 17 – with ulcerative colitis, 9 – with undifferentiated colitis. The blood research was held by the method of immune ferment analysis, and the level of antibodies to proteinase-3 was defined, when the child was received to hospital, was discharged from hospital.

Results: It was discovered, that 2 children from 15 with the disease of Crohn's disease (13.3%) and 6 from 17 children with ulcerative colitis (35.3%, p < 0.05) had increase of the level of antibodies to proteinase-3 of neutrophils. Higher figures of this indicator during the intensification of the disease and reduction at the period of improvement and remission were noticed. However two patients didn't have any normalization of the level of antineutrophil antibodies even during liquidation of clinical laboratory displays of the main disease, but high activity of inflammatory process was defined during morphological research of bioptates of large intestine.

Conclusion: The level of antiproteinase-3 of patients with ulcerative colitis is for sure higher, than of patients with the disease of Crohn's disease. High indicators of antibodies to proteinase-3 reflect the activity of inflammatory process in mucous membrane of large intestine.
Therapeutic drug monitoring of azathioprine in patients with inflammatory bowel disease

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Azathioprine is widely used during Crohn’s disease. However, its effectiveness and its tolerance are variable from patient to another. Dosing azathioprine metabolites should help clinicians to improve response to this molecule.

Objective: the objective of our work is to correlate doses of 6 thioguanines nucleotides and 6 methyl mercaptopurines to clinical efficacy and adverse effects of azathioprine in inflammatory bowel disease disease population.

Patients and methods: we include patients with Crohn’s disease or ulcerative colitis (UC) treated by azathioprine for a duration more than 1 year (to appreciate clinical efficacy of the molecule). Each patient had a dosage of azathioprine metabolites by a chromatographic technique.

Results: we included 70 Crohn’s disease patients and 20 UC. Their mean age was 31 years. Azathioprine was indicated for steroid dependancy in 20 cases, to prevent postoperative recurrence in 21 cases, to maintain clinical remission obtained by steroids (11 cases) or cyclosporine (9 cases) for a fulminant colonic attack. A clinical response to azathioprine (obtention of remission without steroid, absence of recurrence during the following) was observed in 60 patients. A correlation between a level of 6 TGN > 235 pmol/8 108 GR and a clinical response to AZA was observed. A level of 6 TGN > 395 pmol/8 108 GR was associated with a leucopenia (defined by white blood cell < 5500/mm³).

Conclusion: Our work confirms the correlation between the doses of AZA metabolites and the response and adverse effects to this molecule.
Diverticulosis and diverticulitis form no risk for polyps and colorectal neoplasia in 4241 colonoscopies

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Introduction: There are conflicting reports concerning the association between diverticular disease and colorectal neoplasia. This study was performed to determine the prevalence and association of diverticulosis, diverticulitis, polyps and colorectal carcinoma.

Methods: In a cross-sectional, retrospective study we analyzed the colonoscopy reports of and pathohistological results of all patients referred for colonoscopy in a period of three months in eighteen hospitals in the Netherlands. Advanced neoplastic lesions were defined as polyps ≥ 10 mm in diameter and/or villous architecture, and/or adenomas with high grade dysplasia and/or an invasive cancer.

Results: A total of 4241 patients were included in the study (1996 (47%) male, mean age 59, range 18–95. Diverticula, diverticulitis and polyps were seen in 1052 (25%), 75 (2%) and 1282 (30%) patients, respectively. Polyps were seen significantly more in males than in females (703 (55%) vs. 579 (45%); p < 0.0001). Polyps were seen significantly less in patients with diverticulosis (29% vs. 35%; p < 0.0003; RR1.2). Colorectal carcinoma was present in 372 (9%) patients. There was a negative correlation between diverticular disease and colorectal carcinoma in age stratified analysis. No association was found between diverticulitis, polyps and colorectal carcinoma.

Discussion/Conclusion: Patients with diverticular disease are not at risk for (pre)malignant lesions. Patients with diverticulosis had a significantly lower incidence of polyps en carcinoma. This might be due to surveillance colonoscopies after polypectomy. Current clinical practice of performing a colonoscopy after cured diverticulitis is probably sufficient. Screening should be reserved for those with polyps or carcinoma and maybe those with continuous or recurrent diverticulitis.
No difference between 3 or 4 liters polyethylene glycol lavage solutions prior to colonoscopy: A prospective randomized controlled trial

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Introduction: It is suggested that bowel preparations for colonoscopy are easier to tolerate with smaller volumes with a better taste. We compared 4-liter PEG solution with 3-liter sulphate-free PEG solution (SF-PEG) concerning the effectiveness, patient acceptability and tolerability prior to colonoscopy.

Methods: In our out-patient clinic 110 patients scheduled for elective colonoscopy were randomized to receive either 4-liter PEG, or 3-liter SF-PEG. On the day of colonoscopy patients filled in a questionnaire. Three endoscopists blinded to the type of preparation assigned a bowel cleansing score using a validated 5-point scale to assess a cleansing effect in a colon. All endoscopic findings were noted.

Results: Data were available for 102 patients (44 [40%] male), mean age 53 (range 23–83). Compliance was better in the 3-liter SF-PEG than the of 4-liter, respectively 42 (82.5%) and 39 (76.5%) (p < 0.0001). No differences were found in taste (p = 0.12) and abdominal cramps (p = 0.62). Patients who received SF-PEG preferred the same preparation next time (17 [16.6%] vs. 3 [2.9%], (p < 0.029). Scores “excellent” or “good” of the rectosigmoid with 4-liter PEG were 35 (34%) and 3-liter SF-PEG were 40 (39%) (p = 0.17). Also, no differences were found in cleansing the complete colon. Diverticulosis was diagnosed in 39 patients (38%) and did not affect outcome nor did defecation frequency.

Discussion/Conclusion: 3 and 4 liters are comparable in their cleansing effect and toleration. Patients’ preference goes to cleansing with smaller volume. Improving the acceptability of colonic cleansing could improve patients’ compliance and the quality of the colonoscopy.
Dietary lipid intake is related to colorectal cancer in Romania

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Introduction: Migrant and temporal trend studies suggest that colon and rectal cancers are determined largely by environmental exposures. The aim of this study was to evaluate the incidence of colonic and rectoanal cancers in relation with lipid consumption by using the data available for seven Romanian statistical regions.

Methods: The rate of cancer incidence per regions (mean value for 10 years: 1994–2003) was calculated using the cancer registry of each county. The data concerning the population food intake relied on the dietary surveys performed by the Romanian National Institute of Statistics in 2001, 2002 and 2003. Statistical relationship between the rates of cancers incidence and the dietary intake was assessed by means of correlation and linear regression.

Results: For all regions, high rates of cancer incidence for rectal and anal cancer (8.29–11.89 cases at 100,000 inhabitants) and colonic cancer (7.28–9.54 cases at 100,000 inhabitants) were found. Dietary intake of lipids was between 75.76–89.83 g/day. The total consumption of dietary lipids adjusted to the energetic intake presented a strong correlation with the colon cancer (r = 0.77; p = 0.043) and rectoanal cancer (r = 0.92; p = 0.004). Margarine represented an aliment which appeared to be a strong risk factor for rectoanal cancer (r = 0.97; p = 0.0004), whereas a statistical significance of borderline value was reported for colonic cancer (r = 0.73; p = 0.06). Butter was associated only with rectoanal cancer (r = 0.76; p = 0.049).

Discussion/Conclusion: We can observe the need for decreasing the lipid intake, especially for those chemically modified unsaturated ones (such margarine).
Follow-up of fundic gland polyps: They are not preneoplastic lesion

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Fundic gland polyps (FGP) are almost common; they could be part of familial adenomatous polyposis (FAP) or sporadic. Sporadic FGS are sometimes associated with use of proton pump inhibithor (PPI). Gastric cancer has been reported in FAP, even arising from FGP. The neoplastic potential of sporadic FGP is considered poor considered the rare association with dysplasia; however longitudinal studies are lacking.

Methods: For every FGP patient, age, gender, PPI use and Hp status are recorded. Attempt to achieve complete eradication of polyps with endoscopic polypectomy is proposed to all patients with 10 or less polyps. Follow-up is made to control recurrence, or, if eradication of all polyps is not feasible, to control the development of displasia through endoscopy and biopsy every year. PPI discontinuation was encouraged. Polyps were classified for size and number (counted to 10, 10–20, 20–30, more than 30). Concomitant endoscopic feature are recorded. We have prospectively evaluated 21 patients with endoscopically ascertained FGP (14 female mean age XX, range YY–ZZ). Total amount of follow-up is 701 months/patient, mean 33 months, range 3–65 months. Results were compared with incidence data on gastric cancer in Italy.

Results: During follow-up two patients developed mild dysplasia, not confirmed in subsequent follow-up. No patients developed gastric cancer. Development of displasia was not associated with PPI use, number or dimension of polyps, and Hp status. In Italy it could be expected one case of gastric cancer every 2000 persons/year (50/100,000/year). Difference is not statistically significative.

Conclusion: As far as we know, this is the first study of follow-up in sporadic FGP. The risk of gastric cancer is, if one, very low. Dysplasia may affect sporadic FGP, but its further degenerative potential seems to be low. Given the low gastric cancer rate in Italy, comparision is difficult and therefore these data need confirmation with larger studies.
Association between dysplastic adenomatous colorectal polyps and metabolic syndrome in a population from southern Transylvania

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Introduction: The metabolic syndrome (MS) is characterized by obesity, dyslipidemia, hyperglycemia and high blood pressure. The purpose of the present study was to assess the association of MS with adenomas of the rectosigmoid colon, a well-established precancerous lesion.

Methods: A total of 849 colonoscopies and rectosigmoidoscopies were performed at the Gastroenterological Department of the Clinical County Hospital from Sibiu, Romania, during August 2004–August 2007. There were found a number of 144 rectal and colonic polyps. We have established the prevalence of the metabolic syndrome in each group, using the metabolic syndrome’s definition which was adopted by the International Federation of Diabetes (IDF). The results were statistically analyzed using the relative risk and the t Student test.

Results: The medium age of the patients presenting colorectal polyps was 63.76 ± 12.29 years of age. The gender distribution was 37.5% women, versus 62.5% men. At 35 patients (24.3%), the histological exam of the polyps showed high or moderate grade of dysplasia. At the rest of 109 patients (75.7%) the polyps had histological features of villous, tubular, tubulovillous or hyperplastic adenomas. The dimension of the polyps was, in average 9.194 mm. At 53 patients (36.8%) was performed a polypectomy. At the rest of them, biopsies were taken. The medium value of cholesterol level at the patients who proved to have dysplastic polyps was 221.31 mg/dl, comparing with 190.95 mg/dl at the patients with non-dysplastic polyps. The difference in the cholesterol level was statistically significantly (p = 0.05). The triglycerides level was, in average 226.21 mg/dl at the patients with dysplasia, comparing with only 127.05 mg/dl at the patients without dysplasia (p = 0.031). The relative risk of developing dysplastic polyps at the patients having metabolic syndrome, comparing with those not having metabolic syndrome was 1.35, which means that they are more exposed of developing polyps with high-grade dysplasia.

Discussion/Conclusion: Our study suggests that metabolic syndrome is associated with colorectal dysplasic polyps in a population from southern Transylvania. In patients with colorectal polyps, the coexistence of the metabolic syndrome may portend an increased risk of dysplasic transformation of the polyps.
Choice of treatment method of patients with anal fissures

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Aim: To study peculiarities of course of anal fissures and improve treatment methods.

Methods: For 25 years 1576 patients with anal fissures were under observation. Acute anal fissure was observed in 163 patients, chronic – in 1413 patients. 40 patients with Crohn’s disease had anal fissures. General clinic, endoscopic, morphological investigations were carried out. The state of contractile function of anus sphincter was determined with the help of sphincterometer. At acute anal fissure conservative treatment included suppositories (Posterizan, Salofalk®), ointments (Proctosedil, Proctozan), dilatation of anal sphincter, pararectal and presacral blockades, magnetic-laser therapy. At chronic anal fissure operations were carried out. Patients with lowered function of anal sphincter had dissection of anal fissure. With obvious inflammatory, trophic changes and spasm of anal sphincter dissection of anal fissure and open sphincterotomy were performed. Closed lateral sphincterotomy was carried out in patients without inflammatory and trophic changes.

Results: In case of conservative treatment healing of anal fissure was observed in 74.8%. After operative treatment recovery was determined in 96%. Morphological investigations of operative material revealed inflammatory and connective changes of tissues. Complications included light insufficiency of anal sphincter, paraproctitis, strictures. Recurrences appeared at high tonus of anal sphincter, heavy inflammations in wound sides after fissure dissection. In pre- and past-operative period administrations of Mucofalk® led to stool normalization.

Discussion/Conclusion:
1. Choice of treatment method depends on character of disease, type of anal fissure, condition of surrounding tissues, contractile function of anal sphincter.
2. Mucofalk® should be administered in patients with anal fissure.
3. At anal fissures patients with Crohn’s disease are recommended long-term administration of Salofalk® (9–12 months).
Role of colonoscopy in the monitoring risk of recurrence after resection of colorectal carcinoma

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University of Medicine and Pharmacy, Craiova, Romania

**Aim:** To study the recurrent rate of colorectal cancer after surgery treatment.

**Methods:** We studied 156 patients with colorectal carcinoma from Emergency Clinical Hospital Craiova, between 2004 and 2006. We monitor the evolution of disease and the risk of recurrences after surgical treatment at 6, 12, 24 and 36 months. The examination was based of clinical manifestations, colonoscopy with biopsy criteria. Statistical analysis use Wilcoxon and Kruskal-Wallis test.

**Results:** 88 patients with colorectal cancer (52 males and 36 females) underwent surgical treatment. The type of adenocarcinoma was: papillary in 15 cases, tubular (49 cases), mucinous (12 cases), villous (5 cases) and undifferentiated (7 cases). Most of those patients had Duke’s B stage (38 cases) or C stage (34 cases) tumors. The localization of carcinoma was: right colon 19 cases, transverse colon 7 cases, left colon 13 cases, sigmoid 20 cases and rectum 29 cases. The 38 patients had cancer recurrences: 3 patients after 6 months, 9 patients after one year, 16 patients after 24 and 10 patients within 36 to 40 months. All recurrences in patients with initial stage I disease were local and regional, whereas 14 of 19 recurrences in stage II disease were distant. Two recurrences were detected at six patients during separate examinations and three recurrences in two patients in one examination. Local recurrence occurs more frequently in sigmoid (55.0%) and rectal cancers (62.07%). Lower stage was associated with higher adenoma recurrence rates p = 0.04. Factors including age, sex and clinical manifestations were not significantly correlated with recurrence rates.

**Discussion/Conclusion:** Local recurrence occurs more frequently in sigmoid and rectal carcinoma. The rate of recurrence was correlated with Duke’s stage.
Therapeutic options in treatment of distal ulcerative colitis

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University of Medicine and Pharmacy, Clinical Hospital of Emergency, Craiova, Romania

Introduction: Aim was to statistically evaluate the efficiency and safety of mesalazine and azathioprine treatment in inducing remission of proctitis and left sided UC.

Methods: We studied 38 patients with distal UC. A comparative analysis was performed on 3 groups of patients. A group composed of 22 patients with left sided colitis, were treated with mesalazine (Salofalk®) and a short course of systemically active corticosteroids. In B group, 9 patients suffering for proctitis, were treated with Salofalk® suppositories twice a day for 8 weeks and oral mesalazine. C group consist of 7 patients (with contraindicated corticoids therapy) were treated with azathioprine (1.5–2 mg/kg/day). We evaluated the clinical disease activity index, Powell-Tuck index and endoscopic classification at baseline, after 3 and 6 months.

Results: In A group, therapy was used oral mesalazine 3.2–4 g/day, associated with systemic corticosteroids (40 mg/day with a reduction of 10 mg every 5 days), for six weeks. Most patients (10/22) had a rapid response to this associated treatment. The rate of clinical and colonoscopically confirmed remission was 68% (15/22 patients). In B group all patients achieved remission after three months. In C group two patients discontinued treatment with azathioprine due to adverse events: leucothrombocytopenia and increased aminotransferase levels. In A group side effect rate was 7.3%, headache and vomiting. The diminution of the mean Powell-Tuck score at 3 month compared with baseline was: -6.2 ± 0.92 in A group and -4.8 ± 1.3 in C group. At 6 month, compared with baseline, the diminution of the mean value of this index was: 6.8 ± 1.07 in A group and 5.3 ± 1.42 in C group. Similar evolution was observed at mean value of clinical disease activity index.

Discussion/Conclusion: Mesalazine associated with systemically active corticosteroids therapy achieved high remission rate in short term treatment in left sided UC. The oral and suppositories Salofalk® therapy had good efficacy and tolerance in mild to moderate distal forms.
Intestinal barrier dysfunction in Crohn’s disease assessed by increased iohexol resorption

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Introduction: Despite of extensive research, the pathogenesis of Crohn’s disease (CD) remains unknown. A defective intestinal epithelial barrier has been proposed as an important pathogenetic factor contributing to the intestinal inflammation. So, our aim was to assess the intestinal permeability (IP) in patients with CD and its relationship to disease’s activity.

Methods: 32 patients (16 males, 16 females; mean age 39) with previously documented CD, and 16 matched healthy controls consented to participate in the investigation. The clinical activity was estimated using Crohn’s Disease Activity Index (CDAI). IP was assessed using of a water-soluble contrast medium iohexol, which was administrated orally (25 ml, 175 mg) 2 hours after breakfast. Six hours later blood samples were taken, and iohexol was determined by a validated high-performance liquid chromatography technique.

Results: All patients were with colonoscopic lesions suggestive of active CD, with CDAI > 150, mean 225, range 156–344. According to CDAI mild disease was established in 17 (53.1%) patients and moderate in 15 (46.9%). IP presented as serum iohexol concentrations six hours after its ingestion (SIC-6), was significantly higher in patients with CD (SIC-6 3.25 ± 2.67 mg/l) than in the controls (SIC-6 0.86 ± 0.32 mg/l) (p < 0.05). A significant positive correlation was found between intestinal permeability and disease activity (p < 0.05).

Conclusion: Serum levels of iohexol in CD patients appear to be a reliable disease marker as they reflect increased IP and relate to disease activity.
The association between intestinal bowel disease and osteoarticular diseases

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Introduction: A substantial proportion of patients with inflammatory bowel disease (IBD) develop osteopenia and osteoporosis in the course of the disease. An association between IBD and osteoarticular diseases was observed.

Methods: The study was carried out on a group of 24 patients, diagnosed with IBD, in the IVth Medical Clinic of The University of Medicine and Pharmacy Victor Babes Timisoara in a one-year period. From all were 18 men (75%) and 6 (25%) women. The patients were aged between 25–47 years old. All patients were investigated: a complete clinical exam, biological current tests, antinuclear antibodies, rheumatoid factor, C reactive protein, HLA B27, radiology exam, CT, MRI, colonoscopy.

Results: From all 24 patients we had 8 patients (33.3%) with reactive arthritis, 6 patients (25%) with ankylosing spondilitis and 10 patients (41.66%) had none osteoarticular diseases. The osteoarticular symptoms were back pain with matinal functionally limitation.

Discussion/Conclusion: We recommend, based on current literature and our experience from this study, that all patients with IBD should be radiologic, CT and MRI screened for osteoarticular diseases.
Modulation of antioxidant capacity in ulcerative colitis patients

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Introduction: Reduced glutathione (GSH) is oxygen free radicals scavenger and thereby prevent or diminish "oxidative stress". Remicade® is an anti-inflammatory drug which reduces the amount of tumor necrosis factor alfa in the body.

Aim: the study of GSH in ulcerative colitis patients, before and after immunomodulating treatment with Remicade®.

Methods: There were examined 20 patients with ulcerative colitis (UC), which presented chronic diarrhea, abdominal pain, bloating and nausea. Blood GSH by spectrophotometric method with dithiobisnitro-benzoic acid was determined, in UC patients.

Results: In the mild form of UC blood GSH was about 439 ± 13.15 micromoles/l, but in severe ulcerative colitis GSH levels was decreased to 224.04 ± 38.55 micromoles/l. After one week of Remicade® treatment (5 mg/kg) in severe UC patients, blood GSH was increased to 280.58 ± 12.14 micromoles/l and this showed the increase of defensive and detoxifying activities of the body. Also, clinical remission was observed.

Discussion/Conclusion: Low GSH levels in these patients decrease the ability to inactivate toxic free radicals and oxidative stress could be produced. Introducing an immune-modulating treatment and a diet rich in GSH (fruits, vegetables, liver, chicken, fish) to UC patients may help to prevent oxidative stress and retard the disease.
Serologic investigations in children with inflammatory bowel disease and food allergy

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Introduction: The aim of the study was the evaluation of frequency and titre of IgA ASCA and IgG ASCA and p-ANCA, c-ANCA in children with IBD and occurrence of ASCA antibodies in relation to coexistence of FA.

Methods: The study comprised 95 children at the ages of 2 to 18 years. The diagnosis of IBD was established on the basis of Porto criteria. Tests of blood serum were performed in all children: IgA and IgG ASCA, p-ANCA, c-ANCA- using ELISA method.

Results: IgE-dependent FA was found in 32.5% children with UC and in 21% with CD. We did not observe any relation between the occurrence of FA and the frequency and ASCA titre. p-ANCA were significantly more frequent in the group of children with UC (25%) in comparison with the control group. The occurrence of ASCA antibodies was observed in 73.7% of children with CD, 17.5% with UC and almost 30% with allergic colitis. Patients with CD and the presence of ASCA revealed a significantly more frequent localization of lesions within the small bowel and a tendency towards older age. We observed a connection between the occurrence of antibodies and the examined mutations of gene NOD2/CARD15.

Discussion/Conclusion: We observed a relation between the occurrence of ASCA antibodies and localization in the small bowel, and a relation between p-ANCA and localization in the large bowel in children with CD.
Immunohistochemical evaluation expression of Fhit protein in advanced gastric carcinomas

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**Aim**: Our purpose was to evaluate the immunohistochemical expression of Fhit protein in patients with advanced gastric carcinoma in correlation with chosen clinico-pathological parameters, Helicobacter pylori infection and time of postoperative survival.

**Material and methods**: Formalin-fixed, paraffin-embedded tissue specimens from 80 patients with advanced gastric carcinoma were immunohistochemically stained with antibody Fhit (rabbit polyclonal antibody to Fhit, Abcam, UK), dilution 1:200.

**Results**: We have not observed statistical significant correlation between expression of Fhit protein in main mass of tumor and gender, depth of invasion, degree of histological differentiation, Lauren’s and Bormann’s classification. Also expression of Fhit in main mass of tumor was not associated with lymph node metastasis and Helicobacter colonization. Similarly, in lymph node metastasis, we found no correlation between chosen clinico-pathological parameters and expression of Fhit protein. Also, the expression of Fhit in main mass of tumor was not associated with positive immunohistochemical staining for Fhit protein in lymph node metastasis. However, a strong, statistically significant correlation was observed between expression of Fhit protein in main mass of tumor and age of patients (p = 0.04) and localization of tumor (p = 0.02). We have not found significant association between expression of Fhit and survival time (p = 0.26).

**Conclusion**: Our results may suggest, that loss or reduction expression of Fhit protein may be an favorable prognostic factor in advanced gastric carcinoma, but this date was not statistically significant.
Protection of duodenal and colon mucosa during table beet supplementation in rats

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Semmelweis University, *Chemical Research Center, Hungarian Academy of Sciences, Budapest, Hungary

Introduction: Changes of redox-homeostasis during gut resection by generated cytokines and free radicals influence many intracellular signaling pathways may determine postoperative patients outcome particularly in hyperlipidemia. Table beet and carrot powder (GPS-Powder Ltd. 1361/004/2003BFÁÉÉÁ) containing bioactive components such as betaine, betanins, betaxanthins, flavonoids, polyphenols, beta carotene, vitamins, folic acid might be able to change various cellular pathways. The aim of this study was to determine protecting effects of natural substances on the duodenum and colon mucosa in “short term” alimentary hyperlipidemia.

Methods: Male Wistar rats were fed with chow with or without high fat (2% cholesterol, 0.5% cholic acid, 20% sunflower oil) 0.1 and 1 g/bw kg/day natural product for ten days. Chemiluminescent intensity, H-donating ability, reducing power, and free SH-group concentration were determined by luminometry and spectrophotometry in plasma, duodenal and colon mucosa.

Results: Higher dose of natural product decreases the induced free radicals of both parts of gut mucosa significantly both in hyperlipidemia and normolipidemia. However the treatments do not exert significant changes in antioxidant parameters, favorable tendencies can be established in redox-homeostasis of bowel mucosa as well.

Discussion/Conclusion: As an awaited result, after consuming table beet and carrot lyophilisate as a “functional food” in perioperativ period of bowel resection in hyper- and normolipidemic cases, patients may have beneficial effects in the procedure of restoring the redox-homestasis.

Acknowledgement: ETT 012/2006
Altered cholesterol requirement during the acute phase of Crohn’s disease

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2Faculty of Medicine, Charles University, Hradec Králové, Czech Republic

Introduction: Crohn’s disease (CD) is a chronic relapsing disease whose acute period may be associated with metabolic disturbances. Alteration of lipid metabolism has been described in critically ill patients. Using cholesterol synthesis markers (lathosterol) and cholesterol absorption markers (sitosterol, campesterol), it is possible to assess the leading form of cholesterol acquisition. The aim of the study was to assess the association between the lipid profile in plasma and the plasma concentration of sterols in active CD patients and in control subjects.

Methods: In 24 patients with active CD (CDAI > 150) total cholesterol (T-CH), HDL and LDL cholesterol (HDL, LDL), and non-cholesterol sterols plasma levels were performed on days 0, 14 and 28. Cholesterol precursors were determined by GC/MS; cholesterol, LDL and HDL enzymatically.

Results: The serum concentrations of T-CH (p < 0.001), LDL and HDL were lower in patients with acute CD than in the control group. Lathosterol (p < 0.001), sitosterol and campesterol (p < 0.001) concentrations were also lower than in controls.

Discussion/Conclusion: Our results show substantial abnormalities in plasma lipids and non-cholesterol sterols concentrations. These findings correspond to alteration of the cholesterol synthesis/absorption process. Supported by grant IGA Ministry of Health Czech Republic No. NR 7854-3.
Ileocecal inflammation and *Mycobacterium tuberculosis* in sputum of young adult: Diagnostic and therapeutic implications

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Division of Gastroenterology, University Hospital "Dubrava", Zagreb, Croatia

**Introduction**: isolated tuberculosis (TB) of gastrointestinal tract is a very rare disease, most commonly localized in the ileocecal region (over 85% of the cases). The aim of this case report is to highlight the difficulties in the differential diagnosis and therapeutic implications of findings of ileocecal inflammation and *Mycobacterium tuberculosis* in sputum of young male adult.

**Results**: CASE REPORT: A 23-year-old man with history of weight loss, abdominal and low back pain, night sweat, fever, cough and mucous/bloody diarrhea in duration of three months was admitted to hospital. He had a positive family history (mother) of pulmonary tuberculosis. Diagnostic work up included laboratory tests, small bowel follow-through (SBFT) and endoscopy with histology of mucosal lesions. Findings revealed elevated C reactive protein levels, elevated sedimentation rate, normocytic sideropenic anemia; normal chest X-ray and positive *M. tuberculosis* in sputum and positive Mantoux test. SBFT was normal and lower endoscopy and histology showed cobble-stone appearance of ileal mucosa and dense mixed inflammatory infiltrate without granuloma in biopsy specimens. Direct microscopy and microbiological analysis of specimens did not show the presence of *M. tuberculosis* in ileal mucosa. The specific triple therapy for TB was started (rifampicin 600 mg/day, ethambutol 1200 mg/day, INH 400 mg/day, pyrazinamid 2000 mg/day) for six months, in combination with mesalamine. Upon the 3-months of antituberculous and 5-ASA treatment the patient's general condition improved with attenuation of all symptoms, and laboratory parameters of inflammation returned to normal. However, the scheduled colonoscopy showed progression of mucosal inflammatory changes and patient was started on budesonide with planned repeat endoscopy in period of three months.

**Discussion/Conclusion**: The prevalence of TB greatly differs between developed countries and countries in transition, such as Croatia. Diagnosis of gastrointestinal TB still remained a difficulty, often specific lesions resembling ileocecal mucosal changes with non-specific inflammatory findings on histology that could point to inflammatory bowel disease (IBD). On the other hand, TB could influence the general aspect of patients with IBD. Thus, TB represents complex immunological phenomena with diagnostic and therapeutic implications in patients with ileocecal inflammation resembling CD.
Doppler-guided hemorrhoid artery ligation in grade III and IV hemorrhoidal disease treatment

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Introduction: Hemorrhoidal disease is a frequent cause of pain, bleeding and anal discomforts in general population, many advances being developed for the treatment of this pathology. The aim of our study is to evaluate the efficacy of a Doppler transducer in surgical treatment of grade III and IV hemorrhoids in an outpatient clinic.

Patients and methods: We included in our prospective study 46 patients with symptomatic grade III (21 patients) and IV (25) hemorrhoids operated using a proctoscope coupled with a Doppler transducer. The role of this transducer is to identify hemorrhoidal arteries for ulceration ligation thorough a special designed space of a proctoscope. All patients were treated in outpatient conditions and we evaluated complications and treatment efficacy at three days, one and 6 months.

Results: There were no severe intraoperative complications, only moderate bleeding in 3 cases solved during the operation. At first follow-up we noted minor rectal bleeding in 24 patients (9 with grade III and 15 with grade IV) and tenesmus in 17 patients (9, respectively 8); symptoms were reduced significantly after one month (2 vs. 3 patients with bleeding and 5 vs. 7 patients with tenesmus). At long-term we noted 41 patients without symptoms or with significant symptoms relief. There were no significant differences between grade III and IV hemorrhoids patients.

Conclusions:
1. Doppler-guided hemorrhoid artery ligation is a good option for an outpatient treatment.
2. We didn’t observed differences between grade III and IV hemorrhoids treatment results on long-term.
Look for optimal bowel cleansing agent

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Department of Gastroenterology, *Türkiye Yüksek İhtisas Hospital, **Ankara Diskapi Education and Research Hospital, ***Ankara Hospital, ****Ankara Numune Hospital, Ankara, Turkey

Background: The quality of colon cleansing is important for quality of colonoscopy. Many bowel cleansing regimens are known but there is no clear consensus.

Aim: To compare efficacy of three different bowel preparation regimens.

Methods: This prospective study evaluated 177 consecutive patients requiring colonoscopic examination. Three different bowel cleansing procedures were applied. Patients were excluded if they had known or suspected renal failure, unstable angina, acute coronary syndrome, congestive heart failure, megacolon, known or suspected bowel obstruction or other comorbidities that may prevent colonoscopy. The bowel cleansing procedures were as follows:

1) Group 1 → Sennoside calcium: 300 ml of a 1 mg/ml solution given 1 day prior to colonoscopy + sodium phosphate solution 90 ml 1 day prior and 45 ml 5 hour prior to colonoscopy.
2) Group 2 → Sennoside calcium: 300 ml of a 1 mg/ml solution given 1 day prior to colonoscopy + sodium phosphate solution 90 ml 1 day prior and 45 ml 5 hour prior to colonoscopy + 3 x 60 mg alverine citrate 1 day prior to colonoscopy.
3) Group 3 → Sennoside calcium: 300 ml of a 1 mg/ml solution given 1 day prior to colonoscopy + sodium phosphate solution 90 ml 1 day prior and 45 ml 5 hour prior to colonoscopy + 3 x 10 mg domperidone 1 day prior to colonoscopy.

All patients were recommended to take a clear liquid diet three day before starting the bowel cleansing regimen. The quality of colon cleansing was assessed by the endoscopist with an empirical, clinically meaningful, 5-point scale.

Results: One hundred and seventseven patients were enrolled in the study. There were 76 (42.9%) patients in group 1, 56 (31.6%) patients in group 2 and 45 (25.4%) patients in group 3. Results were summarized on Table 1.

Conclusion: The colon cleansing ability in groups with NaP plus alverine citrate and NaP plus domperidone was better than only with NaP. The tolerability of colonoscopy in three groups were similar.
Table 1 – Demographic characteristics, colonoscopy tolerability and the success of bowel preparation

<table>
<thead>
<tr>
<th></th>
<th>Group I (n = 76)</th>
<th>Group II (n = 56)</th>
<th>Group III (n = 45)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female/male</td>
<td>47/29</td>
<td>32/24</td>
<td>26/19</td>
<td>0.837</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>39.53 ± 7.87</td>
<td>40.70 ± 7.88</td>
<td>35.22 ± 7.28</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Cleansing Category</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3 (3.9%)</td>
<td>5 (8.9%)</td>
<td>4 (8.9%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>11 (14.5%)</td>
<td>8 (14.3%)</td>
<td>12 (26.7%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>25 (32.9%)</td>
<td>11 (19.6%)</td>
<td>7 (15.6%)</td>
<td>0.042</td>
</tr>
<tr>
<td>IV</td>
<td>32 (42.1%)</td>
<td>19 (33.9%)</td>
<td>15 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>5 (6.6%)</td>
<td>13 (23.2%)</td>
<td>7 (15.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>Colonoscopy Tolerability</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bad</td>
<td>11 (14.5%)</td>
<td>7 (12.5%)</td>
<td>5 (11.1%)</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>34 (44.7%)</td>
<td>25 (44.6%)</td>
<td>15 (33.3%)</td>
<td>0.562</td>
</tr>
<tr>
<td>Good</td>
<td>31 (40.8%)</td>
<td>24 (42.9%)</td>
<td>25 (55.6%)</td>
<td></td>
</tr>
</tbody>
</table>
Clostridium difficile infection in inflammatory bowel disease
(our experiences)

Clinic of Gastroenterology and Hepatology, Clinical Centre Vojvodine, Novi Sad, Serbia

Introduction: Clostridium difficile (CD) infection has recently attracted high attention, because of its rising incidence in hospitalized patients. CD colitis is an especially important problem in patients with inflammatory bowel disease (IBD) because it complicates the management and clinical outcome of IBD. Symptoms can be confused with an exacerbation of IBD, leading to intensification of immuno-suppressive therapy and worsening of symptoms related to the infection.

Methods: A retrospective study (2005–2007), evaluating IBD hospitalized patients with CD colitis. Diagnosis was confirmed with stool cytotoxin analysis and/or colonoscopy. Relapse was confirmed by standard clinical, colonoscopic and laboratory criteria. Demographic information, diagnosis, IBD therapy, antibiotic exposure, and hospitalizations were recorded.

Results: During that period there were 268 relapses of IBD in 202 patients. CD infection was found in 9 relapses in 7 patients. There were 6 patients with ulcerative colitis (UC) and 1 with Crohn’s disease. CD toxin was detected in all patients with UC. All of IBD patients with CD infection had prior antibiotic exposure and corticosteroid therapy due to severity of IBD. All relapses resolved satisfactorily after treatment with antibiotics (vancomycin and/or metronidazole) with or without corticosteroids.

Discussion/Conclusion: IBD patients are frequently on potent immunosuppressive therapy, placing them at highest risk of developing CD colitis, with negative impact to clinical outcome, and higher risk of progression to fulminant disease. All IBD patients with an exacerbation of the disease symptoms should undergo stool testing for CD before intensification of immunosuppressive therapy.
Nutrition therapy using polymeric formula in adult active Crohn’s disease patients

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Rationale: Data comparing corticosteroids and nutrition therapy to induce clinical remission of Crohn’s disease is conflicting. Corticosteroids are considered a first-line treatment in adults. In children exclusive nutrition therapy has been shown to be more effective than corticosteroids, however this is not commonly practised in adults. The aim was to test the role of a whole-protein casein-based formula in inducing and maintaining remission in steroid refractory or steroid dependent active Crohn’s disease.

Methods: Eleven patients (5 female, 6 male) with active small bowel, ileo-colononic or anastomotic site Crohn’s disease were retrospectively studied. Selection criteria included (a) persistent symptoms, predominantly pain, despite a trial of medical treatment; (b) current active disease despite corticosteroids (or patient reluctance to restart steroids); (c) surgery not deemed imminent. All 11 patients received a whole protein casein-based, TGF-b containing formula. Subjects were asked to use the formula as their sole source of nutrition. Patient age, gender, activity level, stress factors and weight were used to calculate requirements.

Results: All 11 patients achieved clinical remission within 2 weeks of starting nutrition therapy. Minimum remission duration was 9 months. Patient satisfaction was high. Eight patients with steroid refractory disease have been tapered off steroids since beginning nutrition therapy.

Table:

<table>
<thead>
<tr>
<th>Data Before and After Nutrition Therapy</th>
<th>Abdominal Pain</th>
<th>Diarrhea</th>
<th>Weight Loss</th>
<th>High Inflamm Markers</th>
<th>Steroid Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>10</td>
<td>11</td>
<td>8</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>After</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions: Nutrition therapy is an effective treatment option to induce and maintain small bowel Crohn’s disease remission. This is a good choice for steroid resistant patients and avoiding the side effect of such therapy. This study suggests that nutrition therapy should be considered a first-line treatment for adult small bowel Crohn’s patients with ileal and/or stricturing disease.
Fecal continence and patients’ satisfaction after surgery for anal fistula

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Introduction: Anal abscess and fistula are frequent anorectal disorders, which may cause morbidity in terms of recurrence and fecal incontinence. A follow-up study was performed of patients, operated 1995 and 1996 for anal fistula.

Methods: The data of all patients operated 1995 and 1996 for anal fistula were analyzed retrospectively. Patients with Crohn’s disease were excluded. In low anal fistula a fistulotomy/-ectomy was performed, in high anal fistula an advancement flap was performed, mostly after placement of a seton. A questionnaire was sent to all patients June 2006. Follow-up data were available in 128 patients (73%). Data concerning fecal continence were available in 114 patients (65%). Mean follow-up time was 10 years.

Results: 175 patients (124 men; mean age 46 yr) were operated. The fistulas were classified as subcutaneous (9%), inter- (58%), trans- (33%), supra- (1%) and extrasphincteric (0). At the time of operation 64 patients had an abscess. The fistula could be healed in 141 patients (81%) in one single session, in 34 patients two or more sessions were necessary. Recurrence rate: 6%. Cleveland Clinic Continence Score: 0–4 100 (87%), 5–9 11 (10%), 10–14 4 (4%), 15–20 0 (0%). Patients’ satisfaction: 87% of the patients stated, that they would have the operation again if necessary. 89% of the patients stated that they would recommend the operation.

Discussion/Conclusion: Anal fistula can be operated with a low recurrence and incontinence rate and a high patient’s satisfaction: most patients cope better with minor incontinence than with recurrent complaints and operations in the anal region.
Conservative and operative therapy of thrombosed external hemorrhoids (anal thrombosis)

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Introduction: Thrombosed external hemorrhoid (anal thrombosis) (TEH) is one of the most frequent anorectal emergencies, causing pain and bringing patients into the emergency room or colorectal office. Treatment can be conservative and surgical. Aim of the study was to investigate differences between operative and conservative therapy of TEH.

Methods: Retrospectively all patients were examined with TEH, that were treated 2005 either surgically or conservatively. Operation: excision in local anesthesia (LA), secondary wound healing. Conservative therapy: external steroid ointment, NSAID. Patients received a questionnaire with questions concerning recurrent operations, recurrent TEH, current anorectal symptoms, satisfaction of the patient with the proposed treatment of TEH.

Results: 2005, 142 patients (72 M, median age 49 yr) were treated because of TEH. 86 patients were treated conservatively, 56 surgically. Recurrence: conservative group: 10 (17.2%), surgical group: 3 (5.4%). Complication: abscess after operation (1 patient, 1.8%). Follow-up rate and time in months: conservative group: 67.4%, 22 months; operative group: 73.2%, 18 Mon. Anorectal symptoms: after conservative therapy patients complained more about anal secretion, lumps, bleeding and pain than patients after operation. After surgery more patients would like to have the same treatment option (if necessary) than patients after conservative therapy (83 vs. 71%).

Discussion/Conclusion: Both surgical and conservative treatment of THE can be safely done and is effective in terms of recurrence and complications. Altogether the patients’ satisfaction with the treatment performed is greater after conservative therapy than after surgery. Patients after conservative treatment however have more anorectal symptoms at follow-up.
Anorectal disease after radiotherapy for urological or gynecological cancer

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Introduction: Radiation of urogenital tumors may have adverse effects in the anorectal region.

Methods: From 1992 till 2006 142 patients (73 females, 69 males), who had radiotherapy in the anorectal region, were examined in a coloproctological office. The files of these patients were reviewed to investigate the complaints after radiation. Patients, who had radiotherapy for anorectal cancer, were not included.

Results: Radiotherapy: percutaneous 92 (65%), interstitial only 2 (2%) and combined (percutaneous and interstitial) 48 (33%). Reasons for the pelvic radiotherapy in 73 men: prostate cancer (60/82%), seminoma (9/12%), rhabdomyosarcoma (1), non-Hodgkin’s disease (3/4%); in 69 women: uterine (49/71%), cervical (9/13%), ovarian (4/6%), vaginal (4/6%), bladder carcinoma (2/3%) and plasmcytoma (1).

Patients complained about: diarrhea, peranal bleeding, incontinence, perianal skin problems. Diagnoses: proctitis (96/75%), perianal skin lesions (radiodermatitis) (31/25%), anorectal ulcers (16/12%), fistulas (57/4%), anorectal stenosis or fissures (5/4%), gastrointestinal stenosis (2/2%), fecal incontinence (34/20%). Ten patients (9%) developed a colorectal carcinoma in the radiated area. Most patients could be treated medically. In 17 patients (10 M, 7 F) operations were necessary for complications related to the radiotherapy (anorectal stenosis, rectourethral, rectovaginal and anal fistula, colorectal carcinoma/adenoma).

Discussion/Conclusion: This retrospective study shows that patients can have serious and prolonged side effects on the anorectum after radiotherapy in this region. Most patients develop side effects immediately after the radiation; other patients may develop these effects many years afterwards. Most patients need local therapy, only a minority develops complications that need operation. Patients after pelvic radiotherapy are at a greater risk developing a colorectal carcinoma.
Bone loss factors in Crohn’s disease

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Introduction: Patients with Crohn’s disease (CD) are at higher risk of developing osteoporosis and osteopenia than healthy controls. The aim of the study was to determine the prevalence and risks factors of osteoporosis in patients with CD.

Methods: Forty patients were consecutively included, 26 men and 14 women with a mean age of 35.1 ± 11.2 years (15–60 years). Dual-energy X ray absorbmetry measurements of bone mineral density (BMD) were obtained at the femoral neck and at the lumbar spine.

Results: Osteoporosis was found in 32.5% and osteopenia in 47.5% of patients. Median body mass index (BMI) was lower in patients with osteoporosis than in those without osteoporosis (17.67 vs. 21.8 p = 0.001). Neither disease duration nor steroid use were associated with bone loss.

Discussion/Conclusion: Malnutrition seems to be a major risk factor of bone loss in patients with Crohn’s disease. It should deserve attention when planning treatment programs.
Indications, predictive factors and results of surgery in colonic Crohn’s disease patients: A single center results

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Introduction: The goal of the study was to assess indications and predictive factors of surgery as well as the relapse rate after surgical treatment in Crohn’s disease patients with colonic involvement.

Methods: It’s a retrospective study that concerned all Crohn’s disease patients with colonic involvement, hospitalized in our unit between 1996 and 2006.

Results: Our study included 86 Crohn’s disease patients. The localisation was exclusively colonic in 46 patients and ileocolonic in 40 cases. Surgery was performed in 12 patients (14%). The main indications were steroid refractory disease and symptomatic ileal or colonic stenosis. The ileocolonic localisation was the only predictive factor of surgery requirement: In fact, 9/40 (23%) patients with ileocolonic Crohn’s disease were operated, compared to 3/46 (7%) patients with those having Crohn’s disease involving only the colon. Postoperative relapse was observed in 22% of the cases but didn’t require a second resection in most of them.

Discussion/Conclusion: Requirement of surgical treatment in patients with pure colonic Crohn’s disease appears to be rare.
Fecal calprotectin is a reliable marker for diagnosis and follow-up in Crohn’s disease

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Introduction: Fecal calprotectin, a neutrophilic granulocyte-derived protein, is considered a promising marker of intestinal inflammation. The aim of the study was to investigate the usefulness of fecal calprotectin in the diagnosis and the follow-up of patients with Crohn’s disease (CD).

Methods: We included 68 patients with confirmed CD (51 with quiescent disease and 17 in active period) and 19 patients with gastrointestinal disorders other than inflammatory bowel disease as control group. Random stool sample were collected from all patients and blood was collected from CD patients. Fecal calprotectin was measured using a commercially available ELISA kit. Serum C-reactive (CRP) was assessed using immunoturbidimetric method.

Results: Fecal calprotectin concentrations were significantly higher in CD patients than in controls (452 ± 461 vs. 105 ± 102 µg/g; p < 0.001), and in CD patients with clinically active disease than in those with quiescent disease (1112 ± 470 vs. 232 ± 130 µg/g; p < 0.001). Calprotectin concentrations didn't significantly differ between CD patients with quiescent disease and control patients. However, among these patients, those with CD disease had more frequently elevated calprotectin value (> 50 µg/g) (90.2% vs. 68.4%; p = 0.03). In CD patients, fecal calprotectin was significantly related to serum CRP (r = 0.37; p = 0.002).

Discussion/Conclusion: Fecal calprotectin appears to be a reliable and non-invasive biomarker of intestinal inflammation and seems helpful in differentiating between active and non-active CD and would be used in the monitoring of disease activity.
Familial cases of chronic inflammatory bowel diseases

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Introduction: The goal of the study was to compare clinical features of familial and sporadic Crohn’s disease (CD) and ulcerative colitis (UC) patients.

Methods: We underwent a retrospective study over a 17 years period (1987–2003) during which clinical features of CD and UC patients were analyzed.

Results: Our study included 670 patients (503 CD and 167 UC). Among these patients, 630 were sporadic and 40 familial cases. Compared with sporadic cases, patients with familial IBD were younger (p = 0.05) and had a higher frequency of extraintestinal manifestations (p = 0.008), specially for skin disease (p < 0.001). Among patients with CD, immunosuppressive drugs were used more frequently and introduced earlier during the course of the disease in familial cases compared to sporadic cases (p = 0.003). There were not differences between both groups with regard to disease localization and severity.

Discussion/Conclusion: Familial cases of inflammatory bowel disease would constitute a subgroup of patients with a different phenotype than sporadic cases.
Apoptotic proteins – Bax and Bcl-xL correlate with connexin 26 expression in human colorectal cancer

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Introduction: Dysregulation of apoptosis plays an important role in colorectal carcinogenesis. Previous studies of apoptosis have focused mainly on the role of intracellular signalling pathways. Although some studies have demonstrated correlations between intercellular communication and apoptosis, the involvement of gap junction proteins – connexins (Cxs) in regulation of apoptosis remain unclear. Moreover, interactions between apoptotic proteins and Cxs in colorectal cancer have not been investigated. Thus, the aim of this study was to evaluate the expression of Bcl-xL, Bax and Cx26 in colorectal cancer samples as well as to estimate the correlation between assessed proteins and relationships with selected anatomic clinical features.

Methods: Immunohistochemical staining was performed to evaluate expression of Bax, Bcl-xL and Cx26 in 152 colorectal cancer samples. The control group was 30 slides with the normal colorectal mucosa.

Results: Expression of Bax, Bcl-xL and Cx26 was observed in 55.5%, 72.4% and 55.9% of evaluated colorectal cancers, respectively. In contrast to membranous immunostaining in normal epithelial cells, mainly cytoplasmic localization of Cx26 was present in colorectal cancer. We found the positive correlation between Bax and Cx26 expression (r = 0.561, P < 0.0001), Bcl-xL and Cx26 (r = 0.409, P < 0.0001) as well as between Bax and Bcl-xL (r = 0.486, P < 0.0001). Association of Bax, Bcl-xL and Cx26 expression with histological G2 grade of tumors was noted (P < 0.001, P < 0.002 and P < 0.005, respectively).

Discussion/Conclusion: The association between apoptotic proteins and Cx26 could suggest that Cxs might be a target point for modulations of apoptosis in colorectal cancer. Cytoplasmic presence of Cx26 could indicate a distinct role from physiological functions of Cx26 in cancer cells.
An atypical initial presentation of Crohn’s disease: A case report

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Introduction: Crohn’s disease (CD) is a chronic illness associated with a low bone mineral density and increased fracture risk. The increased prevalence of osteopenia and osteoporosis is a significant element in the increased morbidity of the disease. Although osteoporosis has been reported to occur in 13–42% of patients with CD, fracture has been very rarely reported as the initial presentation of CD. Herein, we report an asymptomatic case of CD who presented with osteoporotic fracture.

Case report: A 29-year-old male was admitted to the hospital with a week long symptoms of right ankle pain and hip strain which increased with movements. He had a history of right femur head fracture with minor trauma the year before. The physical examination revealed right lower quadrant tenderness with right hip and ankle pain with limited movements. He had also mild pain at his all extremities with movement. Laboratory findings were as follows: Hemoglobin: 10.0 g/dl, hematocrit 30%, MCV: 115 fL, white blood cell count 12.000/mm³, sedimentation rate: 40 mm/h, total serum calcium: 5.0 mg/dl (8.5–10.5 mg/dl), ionized calcium: 0.8 mmol/l (1.1–1.3 mmol/l), phosphorus: 2.2 mg/dl (2.8–4.6 mg/dl), magnesium: 1.3 mg/dl (1.7–2.3 mg/dl), alkaline phosphatase: 506 U/l (50–136 U/l), vitamin B₁₂: 100 ng/l (190–900 ng/l), parathyroid hormone: 651 pg/ml (15–65 pg/ml), vitamin D: 10 nmol/l (22.5–130 nmol/l). The other biochemical parameters were within the normal limits. Abdominal ultrasonography showed a thickened terminal ileum wall and fistula tract with fluid collection at right lower quadrant. X-RAY examination showed a fracture at right distal fibula. Cobblestone appearance plus strictures at the ileum with patchy, large, deep and linear ulcers throughout the colon were seen at the colonoscopy where rectum was normal. Histological examination of biopsies obtained from the terminal ileum, which revealed epitheloid granuloma, ulceration, and a moderate lymphocytic and plasmacytic inflammatory infiltrate of the lamina propria. Clinical and laboratory findings were consistent with CD complicated with osteomalacia. The patient was treated with intravenous calcium, oral mesalazine plus intramuscular vitamin D and vitamin B₁₂. He was taken to the surgery where 50 centimeters long ileum resection and ileocolectomy was performed. Pathological investigation of the resected material was consistent with the biopsy findings of colonoscopy. In the postoperative follow-up period there was no problem and he was discharged with 100 mg/day azathioprine and 4 g/day mesalazine. He was well during the 2 months follow-up period.

Conclusion: CD may be presented with osteoporosis as a first manifestation of the disease and gastrointestinal symptoms may not dominate the complaints even in the complicated CD. When the patient is diagnosed as CD, the patient should be evaluated for osteoporosis and calcium, magnesium and vitamin D should be started promptly when the levels are low.
Evaluation of psychological disorders in Tunisian patients with inflammatory bowel disease: A comparative case-control study

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Introduction: The aim of the study was to evaluate the psychological state in Tunisian patients with inflammatory bowel disease using the general health questionnaire in 12 items.

Methods: A prospective case-control study was performed, including 60 cases of Crohn's disease, 60 cases of ulcerative colitis and 60 healthy control subjects. The total score of the general health questionnaire was calculated on the basis of 0 – 0 – 1 – 1 system.

Results: The total score of the general health questionnaire was significantly higher in inflammatory bowel disease patients compared to control group (3.70 + 3.57 vs. 0.16 + 0.52, p < 0.0001). In inflammatory bowel disease patients, the total score of the general health questionnaire was significantly higher in Crohn's disease patients compared to ulcerative colitis patients (4.40 + 3.84 vs. 3.01 + 3.18, p = 0.03) and in case of active disease compared to quiescent disease (5.57 + 3.18 vs. 1.64 + 2.78, p < 0.0001).

Discussion/Conclusion: Psychological disorders are frequent in Tunisian patients with inflammatory bowel disease, essentially in patients with Crohn's disease or in case of active disease.
Predictive factors of colectomy among patients with severe acute colitis

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Introduction: The aim of the study was to identify risk factors of early and late colectomy during severe acute colitis in Crohn’s disease and ulcerative colitis patients.

Methods: A retrospective study was conducted over a 10 years period. All patients who had developed severe acute colitis initially treated with intravenous steroids were included.

Results: Our study included 78 patients among which 32 underwent colectomy. Predictive factors of colectomy in multivariate analysis after logistic regression were: a severe relapse (p = 0.004), the absence of azathioprine’s use (p < 0.0001), the non-response to steroid treatment (p < 0.0001) and the absence of decrease of inflammatory biochemical markers 3 days after starting intravenous steroid treatment (p = 0.03).

Discussion/Conclusion: Our study confirmed the value of monitoring biochemical inflammation markers during treatment to select patients at a higher risk of colectomy and showed that introducing azathioprine after intravenous steroid’s induced remission should decrease the rate of colectomy.
Long-term outcome and predictive factors of relapse in patients on azathioprine after a severe acute colitis successfully treated with intravenous steroids

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Introduction: The aim of the study was to determine the rate and the predictive factors of relapse in patients who had a severe acute colitis successfully treated with steroids and in whom azathioprine was introduced as a maintenance therapy.

Methods: It’s a retrospective opened study that involved all the patients who had developed a severe acute colitis successfully treated with intravenous steroids and in whom azathioprine was systematically introduced as a maintenance therapy.

Results: Our study included 33 patients (12 men, 22 women) with an average age of 31.2 years (16–53 years). Among these patients, 23 had Crohn’s disease and 10 had an ulcerative colitis. The mean duration of the follow-up was of 30.5 months (3–70 months). Azathioprine was stopped in 5 patients because of side effects. During the period of the follow-up, a relapse happened in 7 patients. The relapse was a severe acute colitis in 2 cases. The predictive factors of relapse were the number of Truelove and Witts’ criteria (4.5 + 0.7 vs. 3.8 + 0.9; p = 0.05) and stopping azathioprine (57% vs. 4%; p = 0.004).

Discussion/Conclusion: Azathioprine as a maintenance therapy prevents relapses after a first severe acute colitis. In case of side effects requiring azathioprine stopping, alternative treatments should be proposed.
Relationships among the insulin-like growth factor-I receptor, connexion 26 and antiapoptotic protein Bcl-xL in human colorectal cancer

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Introduction: Overexpression of insulin-like growth factor-I receptor (IGF-IR) in colorectal cancer mediates proliferation and migration as well as increases cell survival. Previously we reported about relationships between IGF-IR and apoptotic markers.
Gap junctional intercellular communication (GJIC) is mediated by gap junctions (GJs), which are formed from transmembrane proteins called connexins. Some studies have demonstrated association between connexins and programmed cell death.
Recently, it has been shown that IGF-I may increase gap junctional communication (GJC) and connexin protein expression. Therefore, the aim of this study was analysis of relationships between IGF-IR and Cx26 as well as Bcl-xL expression.

Methods: A total number of 115 cases of colorectal cancer were examined by immunohistochemistry, using the avidin-biotin-peroxidase method. Associations among IGF-IR and Cx26 as well as Bcl-xL were assessed in the entire group of colorectal cancer patients and its subgroups depending on lymph node involvement (N0 and N1), histological grade (G2 and G3), extent of tumor growth (pT1 + pT2 and pT3 + pT4), histopathologic type (adenocarcinoma and mucinous carcinoma), sex, age (≤ 60 and > 60) and tumor site (colon and rectum).

Results: The expression of IGF-IR, Cx26 and Bcl-xL was noted in 47%, 56.5% and 75.6% of the tumors, respectively. In the entire group of patients we found the positive correlation between IGF-IR and Cx26 (p < 0.0001, r = 0.374) as well as between IGF-IR and Bcl-xL (p < 0.0001, r = 0.344).

Discussion/Conclusion: It might be suggested that IGF-IR is involved in regulation of apoptosis and probably connexin expression in colorectal cancer cells.
“Gunpowder appearance” in the upper small intestine

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Case report: A 63-year-old man was admitted to our department with epigastric pain. He had been well until four weeks earlier when epigastric pain developed and was accompanied by nausea. He had been working as a coal miner for 25 years. Physical examination and laboratory findings including blood tests and abdominal ultrasonography were within normal limits. Endoscopic examination of the upper gastrointestinal tract revealed multiple purple-black, 3–7 mm diameters lesions that extend from cardia to whole duodenum (Figure 1). Specimens were analyzed histologically.

Discussion/Conclusion: Although endoscopic appearance thought us anthracosis among the most possible differential diagnosis in our case, pathology of the specimens confirmed a diagnosis of metastatic malignant melanoma and the patient was further analyzed for the primary origin of melanoma. In ophthalmologic examination, there was a dark color lesion at the right side of conjunctiva of the right eye. It could be seen when the patient looked at left. He underwent computed tomography of the head, chest, abdomen, pelvis which showed metastasis to the lung. The patient was diagnosed with ocular melanoma metastatic to the stomach, duodenum and the lung. The most common sites of gastrointestinal organ metastases are small bowel, stomach and colon. Ocular malignant melanoma mainly metastasizes to liver. Although the typical feature of melanoma metastases at gastroduodenoscopy is a hemispherical submucosal nodule with central ulceration resembling a “doughnut”, in our case there were multiple purple-black, 3–7 mm diameters lesions that diffusely involve whole stomach and duodenum. Melanosis, anthracosis and erosive gastritis are among the differential diagnosis.

Figure 1
Spectrum of (auto)antibodies in Brazilian patients with Crohn’s disease

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Introduction: The link between Crohn’s disease (CD) and other autoimmune diseases is not well established. Common immunogenetic bases have been assigned as possible causes for these associations. The aims of the study were to perform a broad spectrum of (auto)antibodies in patients with CD and correlate the results with clinical findings.

Methods: Thirty-six patients with CD diagnosed by clinical, endoscopic and histological criteria, 23 F and 13 M, age range 16 to 83 years, was enrolled in the study. All serum samples were tested by indirect immunofluorescence (anti-endomysium antibodies [EMA], anti-neutrophil cytoplasmic [ANCA], anti-mitochondrial [AMA], anti-nuclear [ANA], anti-liver-kidney microsomal [LKM], anti-gastric parietal cells [GPCA], anti-smooth-muscle [SMA]), or by ELISA (anti-transglutaminase [tTG] and anti-Saccharomyces cerevisiae [ASCA]). The charts of the patients were reviewed for the presence of autoimmune disorders.

Results: All the samples were negative for EMA, AMA, GPCA, SMA and LKM. ANA was positive in 8.3% (3/36), ANCA in 5.5% (2/36) and tTG in 11.1% (4/36). ASCA IgA was positive in 36.1% (13/36), ASCA IgG in 44.4% (16/36) and both ASCA IgA and IgG in 36.1% (13/36).

Discussion/Conclusion: The high positivity for ASCA and the low positivity for ANCA in CD were expected, since both antibodies are used to differentiate CD from ulcerative colitis. ANA was positive in 3 aged women with arthritic complaints. The positivity for anti-tTG could be related to the more aggressive presentation of the CD with surgical procedures in the 4 patients.
Anti-Saccharomyces cerevisiae antibodies in Brazilian patients with celiac disease and their relatives

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Introduction: Antibodies against Saccharomyces cerevisiae (ASCA), a serologic marker for Crohn’s disease, were showed in patients with celiac disease (CD), disappearing after a gluten-free diet (GFD). The study aimed to evaluate the positivity of ASCA in untreated and treated patients with CD, and in their relatives.

Methods: CD was diagnosed by histological findings, the presence of antiendomysial antibodies (EmA) (indirect Immunofluorescence) and anti-transglutaminase (anti-tTG) (ELISA). ASCA IgA and IgG were evaluated by ELISA.

Results: Fifty-one patients with CD were divided: CI (n = 34) at diagnosis, ASCA IgA positive in 61.7%, IgG in 88.2%, and both in 55.8%; CII (n = 12), adherence to a GFD, ASCA IgG positive in 58.3%; CIII (n = 5), transgressions to GFD, ASCA IgA positive in 40.0% and IgG in 60.0%. Seventy-one relatives were divided: RI (n = 45), negative EmA and tTG, ASCA IgA positive in 8.9%, IgG in 2.2%, and both in 4.4%; RII (n = 14), EmA and anti-tTG positive, ASCA IgA positive in 7.1%, IgG 28.6%, and both in 7.1%; and RIII (n = 12), negative EmA and positive anti-tTG, ASCA IgA positive in 8.3% and IgG in 25.0%.

Discussion/Conclusion: ASCA IgA and/or IgG presented higher incidence in patients untreated and with transgressions to a GFD, and in the relatives positive for CD markers. After a GFD, ASCA IgA was not found and IgG decreased. Immune response to food allergens, increased permeability of the intestinal mucosa, and genetic background can be considered. The results presumed that ASCA positivity is not only a specific marker of Crohn’s disease, but correlates with the (auto)immune inflammation of intestine.
11 year audit of the management of severe ulcerative colitis in a DGH

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In 2000 we reported a 6 year audit into the outcome of patients treated with severe ulcerative colitis (UC) in our hospital. We found an unexpectedly high mortality, 6 deaths in 32 cases (19%). Factors associated with this high mortality included care by non gastroenterologists and delays to surgery. Changes in practice were implemented. Furthermore, intravenous cyclosporin was introduced as an option for patients who failed to respond to intravenous steroids.

We now report on a re-audit of the next 5 years (2000–2005). All inpatients coded as having UC were identified, the notes reviewed and data collected on a proforma. Patients were considered to have severe UC as defined by Truelove and Witt’s criteria. 88% (352/400) of the identified notes were reviewed. There were 32 episodes of severe colitis in 30 patients (median 42.25, range 18–80). In these patient episodes, 96% of patients had stool cultures and abdominal X rays on admission. All patients not known to have colitis were treated with antibiotics. All patients received IV steroids within 72 hours and all patients had subcutaneous heparin. The table below shows outcome data from 1994–1999 compared with 2000–2005.

<table>
<thead>
<tr>
<th>Years</th>
<th>Episodes</th>
<th>Steroid Complete Responders</th>
<th>Cyclosporin</th>
<th>Colectomy</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994–2000</td>
<td>32</td>
<td>10</td>
<td>0</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>2000–2005</td>
<td>32</td>
<td>15</td>
<td>12</td>
<td>14</td>
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In the current audit, at day 10 there were 17 cases who failed to achieve complete response to steroids, 5 went directly to colectomy and 12 received intravenous cyclosporin. Of these patients, only 3 responded to cyclosporin but 9 went on to colectomy. At final outcome, 18 patients left hospital without surgery, 14 had colectomy but there were no deaths.

Following the first audit, changes introduced included the care of all inpatient UC by gastroenterologists with formal shared care with colorectal surgeons. This has led to early identification of patients not responding to medical therapy and expedited surgery. This has resulted in improved mortality outcome. The use of intravenous cyclosporin as salvage therapy was disappointing as a means of avoiding surgery in our cohort.
Treatment of local-disseminated rectal cancer

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Introduction: The aim of the study was to improve the quality and prolong patient's life with local-disseminated cancer of rectum (LDCR) by using the combined approach in diagnostic and tactic of surgical treatment.

Methods: During 2000–2007 years we operated 1468 patients, among them 124 patients had LDCR. We carried out 420 radical operations (68 cases with LDCR). The diagnostic methodics included: endoscopy, histological, laparoscopy, abdominal and rectal ultrasonography, computer and magnetic-resonance tomography, cytogenetical and ghematological analysis.

Results: We diagnosed 28 (41.2%) cases of cancer in regio supraampularis, 21 (30.8%) – ampularis, 19 (28.8%) - infraampularis. Histologically 59 (86.7%) tumors were high-differentiated and moderate-differentiated adenocarcinomas, 4 (5.9%) – low-differentiated adenocarcinomas, 5 (7.4%) were colloid and squamous cell carcinomas. Metastases were revealed neither in liver nor in other organs in all cases. All tumors satisfy the criteria T4 N1-2 M0 or T4 N3 M0. The course of treatment included 20–24 seances of the radiotherapy (RT) with total focal dose 42–56 Gy. The RT, the chemotherapy (CT) with 5-FU and the immunotherapy (IT) with laferon was conducted simultaneously; CT and IT was repeated in postoperative period. It was followed by 4–6 week pause, which was necessary for the realization of effect of anti-blastomal therapy (ABT). We assessed the character of side-effect of ABT, level of tumor regression, possibility of surgical treatment and duration of postoperative period. Early postoperative mortality was decreased from 7.7% (2000) to 5.9% (2007).

Discussion/Conclusion:
1. Usage of nominally-radical operations is rational in patients with LDCR.
2. Preoperative ABT (RT, CT and IT) is necessary method of treatment, which can considerably prolong and improve the quality of life.
Ileo-rectal anastomosis prognostic in Crohn’s disease patient: About 10 cases

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Introduction: Colectomy with ileo-rectal anastomosis is usually performed for acute colitis after medical treatment failure, symptomatic colic stenosis, dysplasia or colic cancer. In this study, we report functional results of the ileo-rectal anastomosis in Crohn’s disease patients.

Patients and methods: Ten Crohn’s disease patients with acute colitis have first subtotal colectomy with ileostomy and sigmoidostomy. Then, an ileo-rectal anastomosis was performed.

Results: 6 men and four women with a mean age of 34.7 years (17–45 years) were enrolled. Disease location was colic in 6 cases and ileocolic in the remaining 4 cases. All patients had subtotal colectomy with ileostomy and sigmoidostomy. Surgery was performed with a mean delay of 16.3 months after diagnosis (15 days–118 months). Ileorectal anastomosis was done 4.5 months later (3–7 months). After anastomosis patients have 5 stools/24 h. Only one patient complained of fecal and gas incontinence. Four patients remained asymptomatic after a mean follow-up of 44.5 months. Six patients relapsed once in a mean follow-up of 79.8 months. No patient needed further surgery.

Conclusion: Through this series and a review of the literature, we try to find out advantages and disadvantages of this surgical technique.
Conversion of ulcerative colitis to Crohn’s disease after coloproctectomy and ileo-anal anastomosis. About 5 cases

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Introduction: differential diagnosis between Crohn’s disease (CD) and ulcerative colitis (UC) may be difficult. Diagnostic of CD can be made secondarily in 2 to 10% patients with confirmed diagnostic of UC. In this study, we report cases of patients who had coloproctectomy and ileo-anal anastomosis for UC and in whom diagnosis of CD was later established.

Observations: Our study concerns 5 patients (4 men and one woman) with a mean age of 26 years at the initial diagnosis of UC. Coloproctectomy was indicated for steroid refractory fulminant colitis in 4 patients (previously to cyclosporine use), and for medical treatment failure (using steroid then ciclosporine) in 1 patient. CD was secondarly diagnosed when patients present evocatives features: chronic pochitis in a case, extensive ileitis in 3 cases, perineal fistulae in 2 cases and anal stenosis in another case. The mean time to CD diagnosis was 7 years (3–12 years). Treatment was anal dilatation in a case, medical treatment (steroids, salicylates, antibiotics and azathioprine) in 2 cases and a definitive ileostomy in 2 remaining cases.

Conclusion: Theses observations pointed in the difficult differential diagnosis between UC and Crohn’s disease despite surgical specimen study.
Prognostic impact of lesion’s topography in ulcerative colitis patients

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Introduction: The goal of the study was to determine the prognostic and the evolving impact of the topography of colonic lesions in ulcerative colitis (UC) patients.

Methods: We included 115 consecutive patients with UC followed up for at least 6 months.

Results: The initial distribution of the disease was limited to the rectum in 13 patients and to the recto sigmoid in 46 patients whereas the disease initially involved the left colonic in 23 patients and was pancolitic in the remaining 33 cases. The average follow-up was 39.2 months (6–145 months). During the follow-up period, an extension of the lesions was observed in 18 patients (16%). Patients with an initial pancolitic form were characterized by a more frequent surgery requirement (10/33: 30% vs. 10/82: 12%; p = 0.02) and by a greater risk of severe acute colitis attacks. (12/33: 36% vs. 15/82: 18%; p = 0.05). Patients who had secondary extended their lesions to a pancolitis were also characterized by a greater risk of surgery (14/45: 31% vs. 6/64: 9%; p = 0.003) and by a major risk of severe acute colitis attacks (20/45: 44% vs. 7/70: 10%; p < 0.0001). In these patients, the use of oral steroids was more frequent (22/45: 48% vs. 13/70: 18%; p = 0.001) as well as intravenous corticoids (22/45: 48% vs. 7/70: 10%; p < 0.0001). In the group of patients having initially a disease limited to the rectum or to rectosigmoid, the extension of the lesions during the follow-up was also associated with a greater risk of severe acute colitis attacks (6/12: 50% vs. 1/46: 2%; p < 0.0001), immunosuppressive drug’s use (4/12: 33% vs. 0/46; p = 0.001) and surgery requirement (3/12: 25% vs. 2/46: 4%; p = 0.05).

Discussion/Conclusion: The determination of the exact topography of the lesions in UC patients seems to be important at the time of the diagnosis as well as during further flares. In fact, the disease’s topography may have an important prognostic impact.
Segmental colic resection prognostic in colic Crohn’s disease

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Segmental colic resection in Crohn’s disease colic is controversial. However, some authors recommend this resection, that wouldn’t be at high risk of surgery, or postoperative relapse. It would also avoid definite stoma in some patients.

Patients were 2 men and three women (mean age: 39.6 years) with colic Crohn’s disease. Surgery was indicated for colic stenosis in 2 patients, distal acute colitis in one patient, corticodependent disease in one patient and colic perforation in another patient.

Mean follow-up was 24 month. Disease course was favorable in four patients. The remaining patient suffered from postoperative sepsis complications. For this patient, lesions extension led to subtotal colectomy 18 months later.

Through this series and a review of the literature, we try to find out benefits and risks of this type of surgery in Crohn’s disease patients. We also tried to define a patient subgroup that can benefit from it.
Is fecal incontinence after surgical treatment of anal fissure a surgeon or technique-related complication?

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Introduction: Anal fissure is associated with a grade of fecal incontinence, but lateral internal sphincterotomy is considered as major factor for incontinence after surgery. In this study we try to determine the role of sphincterotomy in fecal incontinence comparing with the level of disease involvement.

Patients and method: We involved in this prospective study 64 consecutive patients with anal fissure. In all patients we assessed severity of incontinence clinically, using a questionnaire and objective by endoanal ultrasonography. In 32 patients we achieved lateral internal sphincterotomy and in the rest of 32 patients only a conservative internal sphincterotomy below the fissure apex. Patients were assessed postoperatively and at one month and 6 months clinically and by endoanal ultrasonography.

Results: Endoanal ultrasonography showed minor lesions in 7 patients (10.94%) preoperatively even clinically we discover minor incontinence in 12 patients (18.75%). After the sphincterotomy 4 patients (12.5%) from “radical” group and only one patient (3.12%) from conservative group developed incontinence (p < 0.01). During the late assessment (at 1 and 6 months) only 2 patients from each group presented minor incontinence and two patients from conservative group presented relapsing of fissure (p = NS).

Conclusions:
1. We consider lateral internal sphincterotomy as treatment of choice of anal fissure.
2. Anal fissure may be associated with a grade of fecal incontinence, symptom being remitted after surgical intervention.
3. On short term sphincterotomy below the fissure apex is associated with less complications, but on long-term there were no differences between these two groups in terms of complications.
Experimental studies in vivo regarding the effect of resveratrol extracted from vine in colorectal cancer

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Resveratrol (3,4',5-Trhydroxy-stilbene) belongs to a class of polyphenolic compounds called stilbene, a fat soluble compound, found with the vegetable rank, being considered a response to stress (fungal infections, ultraviolet radiations, ozone) with vine it occurs in leaves and grapes as a response to botrytis cinerea. The highest concentrations of resveratrol can be found in red wine, grape juice, red grapes, dry peanuts and in China in polygonus cuspidatum. Besides its benefic cardiovascular effects resveratrol is considered the first product in natural medicine with certain data about its efficiency in certain stages of cancer not only does resveratrol prevent cancer but it is also proposed as additional therapy in forms of cancer already diagnosed.

Aim of study: Testing the cytogenetic effect and the potential of inducing apoptosis of resveratrol on adenocarcinoma cell cultures.

Methods: There will be used standard cell lines CaCo2 or initiated from cells obtained from intestinal biopsy from colorectal cancer injuries or from surgical samples.
Testing the cytogenetic effect of the resveratrol preparation observed the frequency of poliploide cells in the cultures, the frequency of aneuploide cells in the cultures, the types of structural chromosomal changes and their frequency. The cytogenetic evaluation of the treated cell cultures and of the witnesses ones will be done at 4 or 5 passage and to each passage we added resveratrol. In the begining we utilized the use concentrations 0.1, 1, 10, 100 mmol/l. In the same time we studied the witness culture, which be undercultivated together with the tested culture. For chromosomial analysis we used standard cytogenetic techniques. For keeping cell cultures we used a medium MEM or RPMI supplemented with 10% fetal bovine serum, penicillin, streptomycin and L-glutamine. Studying the apoptotic effect of resveratrol was made on cell cultures, too. There observed the citoplasmatic changes, nuclear changes (tahicromy, picnosis) formation of apoptotic corpuscle and the process of eating away of the cell residue.

Results and discussion: Treatment with resveratrol arrested CaCo2 cells in the G0 and G1 phase of the cell cycle and eventually induced apoptotic cell death, but had a minimal effect on cell lysis. The cytogenetic evaluation of the treated cell cultures was regarded high frequency of poliploide cells in the cultures and the frequency of aneuploide cells in the cultures. The apoptotic index determined by COMET assay was high after resveratrol.

Conclusions: Results indicate that resveratrol has potential as a chemopreventive agent against colorectal cancer because it exerts an overall deactivating effect on human colorectal adenocarcinoma cells. Evaluation of anticarcinogenic effect of resveratrol extracted from local natural sources on cell cultures of colorectal cancer with possible preventive and even curative medical implications.
Distal colonic tuberculosis with clinical features of Crohn’s disease. A case report

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A 27-year-old male patient Caucasian accused diffuse abdominal pain, important loss weight, anemia, sometimes diarrhea with blood. He was investigated clinically by laboratory and microbiological (stool culture) examinations and by lower endoscopy with histology.

Clinical we detected an abdominal tumor localized in left quadrant. Laboratory examinations present: high ESR, increased level of fibrinogen and C reactive protein, anemia, lower serum iron, negative tests to infections causes. First lower endoscopy showed a lumen stenosis of descendent colon that not permitted to continue the endoscopy. The histopathology showed the presence of inflammation and granulomas. Our diagnosis was Crohn’s disease. The patient received the treatment for CD but without any improvement of the symptoms. After 1 month he suffered segmentar resection of the descendent colon; we practiced a new histological exam and bacteriological and cultures from the secretion and found Mycobacterium tuberculosis. Standard therapy induced rapid clinical and biological remission. We considered this case interesting due to the very rare localization of intestinal tuberculosis and to the similitudes with a distal Crohn’s disease.
Intestinal inflammation effect on chronic dermatosis

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Intestines inflammatory diseases caused by the changes in protozoan microflora make skin diseases chronic and adequate therapy (treatment) difficult.

**Objective**: Investigate the changes of the intestines bacterial and protozoan clumping resulting from chronic dermatosis.

**Materials and methods**: Examination of 190 chronic dermatosis patients (96 male and 94 female aged from 20 to 72) showed the symptoms of a chronic skin disease of all the examined became more intense (eczema, psoriasis). In the period of remission and exacerbation of dermatosis the patients’ feces were tested for bacteria and parasites.

**Results**: Discharge of bacterial and protozoan associations of the chronic dermatosis patients proved the microflora substantially changed, namely, in the period of exacerbation the number of the elementary bodies like *Entamoeba*, *Blastocystis*, *Lamblia* largely increased. Consequently decreased in number became the bodies of normoflora (*coliform bacterium*, *lactobacillus* from the normal lg10.78 ± 0.08 KOE/g, lg8.96 ± 0.05 KOE/g to lg8.96 ± 0.33 KOE/g, lg6.85 ± 0.14 KOE/g respectively [p < 0.01]). The number of atypical *E. coli* bacteria including hemolytic and lacto-negative ones grew. *Bacteroids* increased from the normal lg8.85 ± 0.04 KOE/g to lg10.26 ± 0.01 KOE/g, as well as *Candida* and *Klebsiella* from the normal lg0.43 ± 0.17 KOE/g, lg0.92 ± 0.12 KOE/g to lg2.47 ± 0.43 KOE/g, lg3.12 ± 0.05 KOE/g respectively. Intestines microflora improved notably in the period of remission, namely, the elementary bodies like *Blastocystis*, *Lamblia* drastically decreased in number.

**Discussion**: The changes of the intestines bacterial and protozoan associations have an adverse effect on chronic dermatosis that is a pluricausal disease. The changes in microflora appear long before chronic dermatosis recrudesces and, therefore, may diagnose recrudescence of dermatosis.
Are symptoms constant in patients with irritable bowel syndrome during a longer period?

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Introduction: Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal pain and altered bowel habits in the absence of specific and unique organic pathology. The aim of this study is to establish if the symptoms of IBS are constant in one patient during an 18 months period.

Methods: The study was carried out on a group of 76 patients diagnosed with IBS (ROME III criteria), hospitalized in the IVth Medical Clinic of the University of Medicine and Pharmacy “V. Babes” Timisoara, in a one-year period. The patients were aged between 19–79 years, the mean age was 49 years; 51 were women and 25 were men. We followed up those patients for 18 months.

Results: In our group, 20 patients had predominant constipation, 18 had predominant diarrhea, 25 had mixed diarrhea and constipation, and 13 had alternating diarrhea and constipation. In the 18 months period 16 of the patients with constipation, developed also diarrhea, 12 of those having diarrhea developed constipation, 20 of those with mixed symptoms, and 5 of those with alternating symptoms had either diarrhea or constipation.

Discussion/Conclusion: In a year and a half 69.7% of our patients with IBS changed their predominant symptoms of the disease. 26% of the patients switched between IBS with predominant constipation to IBS with predominant diarrhea.
Anemia secondary to intestinal bleeding in elderly patients

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Introduction: In elderly patients, anemia is frequent present, and in many cases it is due to intestinal bleeding. The aim of this study is to establish if intestinal bleeding is a frequent cause of anemia in elderly patients.

Methods: The study was carried out on a group of 84 elderly patients with anemia, admitted in the IVth Medical Clinic in a 12 months period. The patients were aged between 60–91 years; the mean age was 75.5 years. Of them 53 were women and 31 were men. We performed in all patients: haemocult tests, upper endoscopies to eliminate a gastroduodenal bleeding, a barium enema, or a colonoscopy. In women, we also performed a gynecological screening.

Results: 48.8% of the patients developed just symptoms of anemia, 15.5% had intestinal bleeding, 10.7% had diarrhea, 13% had constipation and 11.9% of them had alternation of constipation and diarrhea. In 16 patients, the diagnosis was hemorrhoidal bleeding, 23 patients had diverticulosis, 14 patients were diagnosed as having colorectal cancer, and the rest of them had other causes of anemia.

Discussion/Conclusion: 63% of the patients included in our study had anemia secondary to intestinal bleeding.
**Irritable bowel disease. Is personality and stress playing a role?**

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Irritable bowel disease (IBD) is a common finding in young, active people. The aim of this study is to establish the role of the personality and the importance of stress in young patients with IBD.

**Introduction:** The study was carried out in a group of 46 patients diagnosed with IBS, hospitalized in the IVth Medical Clinic of the University of Medicine and Pharmacy “V. Babes” Timisoara, in a 6 months period. The patients were aged between 19–38 years; the mean age of those patients was 28.5 years. Of them 30 were woman and 16 were men. We applied in all patients a psychological test for personality (E.P.Q.), and a stress test.

**Methods:** The study was carried out in a group of 46 patients diagnosed with IBS, hospitalized in the IVth Medical Clinic of the University of Medicine and Pharmacy “V. Babes” Timisoara, in a 6 months period. The patients were aged between 19–38 years; the mean age of those patients was 28.5 years. Of them 30 were woman and 16 were men. We applied in all patients a psychological test for personality (E.P.Q.), and a stress test.

**Results:** Stress was present in all patients. In 26% of patients, the stress was very high, in 52.2% of patients stress was medium and in 21.8% the stress was normal but not absent. From the 46 patients 29 patients had an introversive personality and 17 had an extraversive personality. The symptoms in the introverts were: abdominal pain in 26 patients, constipation in 23 patients, bloating in 18 patients and diarrhea in 6 patients. In the extraversive patients, the symptoms were: abdominal pain in 13 patients, bloating in 10 patients, diarrhea in 14 patients and constipation in 3 patients.

**Discussion/Conclusion:** Stress seems to play a role in the etiology of the IBD; stress was present in all patients. The most frequent symptom in introverts was constipation, and in those with extraverts diarrhea was the most frequent symptom.
Detection of small bowel differentiated carcinoid tumors: Usefulness of F-DOPA PET scan

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Introduction: Detecting the primary tumor in carcinoid malignancies is a critical challenge, because surgical removal influences patient’s prognosis. Numerous endoscopic/imaging techniques are available, but localization remains difficult and sometimes unsuccessful. Limitations are small tumor size, inaccessibility of some tumor sites to endoscopy, and dedifferentiation of tumor cells, especially low receptor expression, which may hinder functional imaging.

Methods: We report the case of a 25-year-old male patient with a typical clinical carcinoid syndrome. Metastatic carcinoid malignancy was easily diagnosed by very high plasma chromogranin, plasma serotonin, and urinary 5-hydroxy-indol-acetic-acid, and the detection of multiple liver metastasis by ultrasound.

Results: Despite intense fixation of radio-labeled octreotide by liver metastasis, somatostatin receptor scintigraphy (SRS) failed to detect the primary lesion, as did upper and lower gastrointestinal (GI) tract endoscopy, bronchoscopy, total body CT, MRI, and GI tract video-capsule endoscopy. A small ileal lesion was suspected using multidetector CT with double contrast enterography but only F-DOPA PET scan ascertained, and accurately localized the primary ileal tumor. Surgery confirmed the localization, and pathology revealed a 3 cm highly differentiated carcinoid tumor with low proliferation grade (Ki67 < 2).

Discussion/Conclusion: F-DOPA PET scan is usually proposed to detect poorly differentiated neuroendocrine tumors, and may also provide a higher sensitivity than SRS for the detection of differentiated (especially serotonin synthesizing) tumors. Our report shows that it may also be superior for the detection of small differentiated primary carcinoid tumors expressing somatostatin receptors, possibly because high octreotide captation by multiple metastasis may reduce fixation on the primary tumor.
Is dysplasia the only certain marker for the colorectal cancer risk in ulcerative colitis?

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**Background:** Dysplasia is considered the only subclinical marker for the suspicion of malignant transformation in the evolution of ulcerative colitis. The evolution over a longer period of time, the fact that it affects the entire colon and the onset at an early age also represent important signs for the risk of developing colorectal cancer in the patients with ulcerative colitis.

**Aim:** In a retrospective study, we assessed the potential clinical markers that, in association with dysplasia, might indicate a higher risk of colorectal cancer (inflammatory bowel diseases family history, dominant extraintestinal manifestations, important morbid associations).

**Results:** Out of 117 patients with ulcerative colitis, 6 developed colorectal cancer. In 3 patients, the disease was located on the level of the rectum, in 2 on the level of the sigmoid and in 1 on the level of the ascending colon. In all 6 patients, the inflammatory bowel disease evolved over a period of over 15 years. In 4 patients, the inflammatory bowel disease was diagnosed before the age of 40. None of them had inflammatory bowel disease family history. None of the patients with colorectal cancer had extraintestinal manifestations. In 2 cases we discovered autoimmune associated diseases: 1 patient suffered from rheumatoid poliarthritis and 1 patient had psoriasis.

**Conclusions:** None of the investigated clinical markers was highlighted as a risk factor for the emergence of colorectal cancer in the patients with ulcerative colitis. However, in the case of patients with ulcerative colitis, the association of the disease with autoimmune diseases demands closer surveillance in order to prevent colorectal cancer. This approach is necessary especially in the presence of dysplasia.
Introduction: We report preliminary experience of the use of video capsule endoscopy (VCE) (Olympus Video Capsule System) in University Hospital Dubrava, Zagreb, Croatia (catchment area of 300,000 people), that included 29 VCE small bowel procedures.

Methods: The indications for VCE use have been restricted to the investigation of obscure GI bleeding (n = 10), iron deficiency anemia (n = 2), suspected IBD (n = 1), assessment of known small bowel Crohn’s disease (n = 5), unexplained diarrhea (n = 5), chronic abdominal pain (n = 3), suspected ganglioneurinomas (n = 1) and suspected polyposis syndrome (n = 2). To be eligible for VCE, patients had to have undergone upper endoscopy, small bowel follow through, and colonoscopy without discovering explanation for their symptoms. Findings were considered diagnostic if the observed finding could explain the symptomatology of the patient. Capsule retention was defined as capsule present and confirmed by plain abdominal radiograph at two weeks after ingestion.

Results: A definite diagnosis was made in 15 patients (51.7%). Suspicious findings were noted in 2 patients (6.9%). No diagnosis was obtained in 12 patients (41.4%). VCE has proved to be a safe device to use – we recorded capsule retention in only one of our patient (3.4%).

Discussion/Conclusion: VCE is an important diagnostic tool which allows a direct visualization of small bowel lesions that may go unrecognized by traditional radiologic or endoscopical procedures. However, according to our experience, definite diagnosis could be established in only 51.7% of the patients. The highest diagnostic yield is obtained in patients with OGIB (60%).
Unusual summer rotavirus outbreak in Bulgaria

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Introduction: In the countries with mild climate, rotaviruses cause annual winter epidemics of acute gastroenteritis in children under five. They are the single most common cause of dehydrating diarrhea which requires hospital admission. However, this study tries to characterize retrospectively the clinical spectrum of rotavirus diarrhea, which occurred in the summer.

Methods: The study covered children with acute diarrhea, residents of Ihtiman, southwest Bulgaria. They were hospitalized in the Infectious Diseases department of St. Anna University Hospital, Sofia, between July and August 2007. Stool samples were tested for rotaviruses by enzyme immunoassay (EIA) and polyacrilamide gel electrophoresis (PAGE). Genetic characterization of detected rotavirus strains were performed using reverse transcription-polymerase chain reaction (RT-PCR). All samples were also culture to exclude the presence of enteropathogenic bacteria i.e. \textit{Shigella} spp., \textit{Salmonella} spp. and \textit{E. coli}.

Results: Forty-eight children, male/female 12/10 from 4 to 36 months of age, were evaluated during the study period. Rotavirus was detected in 22/48 (45.8\%) stool specimens. Diarrhea, vomiting and fever were the commonest symptoms, usually in combination in 10 (45.5\%) patients. Dehydration occurred in 15 (68.2\%). Fourteen children had watery, 6 – mucous and 2 bloody diarrhea. “Short” and “long” E-types of rotavirus were detected in 16/22 (72.7\%) and 6/22 (27.3\%) samples, respectively. Rotaviruses with G2P[4] specificity were the predominant genotype. One child with watery diarrhea had positive stool culture for \textit{Salmonella}. Nosocomial infection occurred in one child. All patients recovered smoothly following proper fluid treatment (supplement of) either orally or parenterally.

Discussion/Conclusion: The study described an outbreak of rotavirus gastroenteritis in children that was detected in southwest Bulgaria. Surprisingly, it occurred not in cold weather but in the summer. The changing climate, the low sanitation level and other factors in the region may have set off the epidemic.
Fecal calprotectin (MRP8/14) and TNFalfa as diagnostic markers of inflammation in gastrointestinal tract in children

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**Introduction:** Calprotectin (MRP8/14) and TNFalfa measured in stool are good factors of inflammatory processes localized in the gut. The aim of the study was to assess usefulness of calprotectin and TNFalfa as diagnostic tools which can distinguish between organic or functional gastrointestinal disorders.

Methods/Results: Study was done in 94 patients (39 boys, 55 girls mean age 11.7 years, SD ± 4.06 years). Enrolled to the study patients were divided in 4 groups. Group 1 – control with 22 health children, group 2–14 children with functional disorders (fulfilled Rome III criteria), group 3 – 29 children with organic disorders (H. pylori infection, esophagitis, duodenitis, pancreatitis and others) and group 4 – 29 children with exacerbation or newly diagnosed inflammatory bowel diseases (IBD). Calprotectin and TNFalfa were compared with CRP (C-reactive protein) values in serum.

<table>
<thead>
<tr>
<th>Group</th>
<th>Calprotectin* Mean values (mg/kg of stool)</th>
<th>TNFalfa** Mean values (pg/100 mg of stool)</th>
<th>CRP*** Mean values (mg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Control</td>
<td>25.95</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>2 Functional</td>
<td>30.06</td>
<td>6.08</td>
<td>3.38</td>
</tr>
<tr>
<td>3 Organic</td>
<td>197.11</td>
<td>66.16</td>
<td>5.03</td>
</tr>
<tr>
<td>4 IBD</td>
<td>1308.44</td>
<td>77.24</td>
<td>9.73</td>
</tr>
</tbody>
</table>

* test chi-square for variable Calprotectin, p < 0.0001
** test chi-square for variable TNFalfa, p = 0.0006
***test chi-square for variable CRP, p = 0.0042

Discussion/Conclusion: Fecal calprotectin and TNFalfa assessments are valuable methods in differential diagnosis between functional and organic gastrointestinal disorders, with highest values in IBD patients.

The highest differential value has fecal concentration of calprotectin, high value has concentration of TNFalfa but low has CRP in serum.

Calprotectin has the highest concentration in children with IBD but can not differentiate between Crohn’s disease and ulcerative colitis.
The relationship between IBS and depression

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Introduction: IBS is a very frequent disorder characterized by chronic or recurrent symptoms: lower abdominal pain or discomfort, altered bowel function (urgency, altered stool consistency, altered stool frequency, incomplete evacuation), bloating. Up to date, the symptoms are not explained by identifiable structural or biochemical abnormalities. The aim of the study was to investigate the relationship between IBS and major depression.

Methods: We included into study 40 outpatients with major depression seeking medical care, and a control group consisting of 45 patients who suffered from other conditions, with no diagnosis on Axis I. The diagnosis of IBS was established by Rome III criteria.

Results: Criteria for IBS were met by 13 patients (32.5%) and only by 3 controls (6.66%), the difference being statistically significant (p < 0.05). The extraintestinal symptoms (urinary symptoms, dyspareunia, dysmenorrhea, increased urinary frequency, back pain, joint pain) were more frequent in patients with IBS and major depression compared to patients with IBS and no major depression.

Discussion/Conclusion: IBS is frequently found in patients seeking treatment for major depression. This psychiatric comorbidity may influence the subjective severity of IBS and consultation behavior.
Screening for colorectal cancer: The attitude of Romanian postgraduate medical trainees

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**Aim:** Colorectal cancer has a good prognosis if early diagnosed. Therefore it is important to develop skills in screening for colorectal cancer in medical undergraduate and postgraduate students. We lack reliable data in this country on the efficiency of our education strategy in this field.

**Methods:** We investigated 127 young medical doctors (interns and residents) by a validated structured questionnaire about colorectal cancer screening and the use of fecal occult blood testing, created and used by Sharma and Howden.

**Results:** The majority of the Romanian trainees prefer colonoscopy as the test of choice for the screening of colorectal cancer when they were asked to choose between colonoscopy, flexible sigmoidoscopy, fecal occult blood test and barium enema. These data are different from previous data obtained by the same method in an American sample, where the fecal occult blood test was indicated as test of choice to start colorectal screening. The indication of the fecal occult blood test is incorrectly known by some of the young Romanian doctors. In general the knowledge in the Romanian groups is not different from the knowledge of the American group, but strategies of screening are different. Colonoscopy is preferred as the test of choice for the further evaluation of a patient with a positive FOBT result. Our students do not think frequently to FOBT, but consider colonoscopy as the test of choice.

**Conclusions:** Our postgraduate students are generally well trained. However they still need more information on the cost – efficiency approach. They also seem not to be realistically and adequately prepared for their own future working conditions, which can sometimes be different from those offered by a tertiary health center, where they were trained during the test.
Ulcerative colitis and bacterial-protozoan intestinal associations

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Ulcerative colitis brings about changes in bacterial-protozoan intestinal associations and affects characteristics of microorganisms, which contributes to the inflammation in the intestines and increases the risk of developing a chronic condition.

Objective: Explore changes in bacterial-protozoan intestinal associations caused by ulcerative colitis to enable early detection of the disease.

Materials and methods: The study involved 176 individuals affected by non-specific ulcerative colitis including 89 male and 87 female patients aged 16–67. The diagnosis was verified by the results of colonoscopy. All patients were tested for bacteria and parasites in feces, both during a remission and a relapse.

Results: Discharges of bacterial-protozoan intestinal associations in patients affected by non-specific ulcerative colitis revealed substantial changes in bacterial and protozoal intestinal associations during a relapse, more specifically, a sharply increased number of protozoan parasites, such as Blastocystis, Lamblia, Entamoeba. At the same time, the number of representatives of normoflora, such as collibacillus, lactobacillus dropped to $\lg 7.2 \pm 0.15$ KOE/g, $\lg 6.3 \pm 0.11$ KOE/g respectively, compared to the normal $\lg 9.38 \pm 0.08$ KOE/g, $\lg 8.86 \pm 0.09$ KOE/g ($p < 0.01$). Besides, there was a growth in E. coli with atypical characteristics, including hemolytic and lactonegative ones. Bacteroids grew in number from the normal $\lg 9.0 \pm 0.6$ KOE/g to $\lg 10.3 \pm 0.1$ KOE/g, as well as Candida, Klebsiella, which went up from $\lg 3.3 \pm 0.29$ KOE/g, $\lg 3.4 \pm 0.7$ KOE/g to $\lg 6.3 \pm 0.4$ KOE/g, $\lg 5.3 \pm 0.32$ KOE/g respectively.

Discussion: A chronic inflammation developing in the intestines during the non-specific ulcerative colitis brings about changes in bacterial-protozoan associations, which are less pronounced during remissions. Minor changes in microflora may be detected long before the symptoms of the disease become clearly manifested, and, therefore, may be considered a diagnostic sign of the beginning relapse.
Functional gastrointestinal symptoms are associated with allergic diseases

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Introduction: Increased duodenal eosinophils have recently been described in patients with functional dyspepsia. Mucosal eosinophilia is more typically associated with allergic diseases such as asthma and allergic rhinitis (AR). Asthma is characterized by increased numbers of eosinophils in bronchial mucosa, airways lumen and circulating blood, in numbers correlating with asthma severity. In these patients mucosal eosinophilia is not restricted to the airways and increased eosinophils have been recorded in esophageal and small bowel mucosa. Intriguingly, increased intestinal permeability has also been documented in asthmatic patients, suggestive of physiological consequences to observed histological changes. We hypothesized that functional gastrointestinal symptoms would be more common in patients with allergic diseases.

Methods: Retrospective case control study based in a large primary care adult (aged ≥ 20 years) population in the UK. The prevalence of general practitioner diagnosed irritable bowel syndrome (IBS) and dyspepsia was calculated in 865 asthmatic patients and 647 patients with AR (without asthma). The remaining 5723 patients served as controls.

Results: The prevalence of dyspepsia in was significantly increased in asthmatic (21.2%, OR = 2.10 95% CI: 1.68–2.62, P < 0.0001), and AR patients (15.4%, OR = 1.43 95% CI: 1.10–1.84, P < 0.003), compared to controls (11.3%). Similarly, the prevalence of IBS was also significantly more common in asthmatic (9.9%, OR = 1.89 95% CI: 1.39–2.56, P < 0.0001) and AR patients (7.9%, OR = 1.47 95% CI: 1.04–2.09, P < 0.02) compared to controls (5.5%). These associations were independent of age, gender and prescribed asthma therapies.

Discussion/Conclusion: Our data suggest an increased prevalence of functional gastrointestinal symptoms in patients with allergic diseases. Whether these symptoms are potentially attributable to activated eosinophils entering gut mucosal sites merits research attention.
Z-plasty in pilonidal sinus

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Introduction: Pilonidal sinus is a common pathology in proctology, many factors (as obesity, hairy body, male sex, prolonged sitting) being implicated in this disease. Common surgical procedures involve a great rate of recurrence. Placing the surgical scar away from the middle line may produce a lower recurrence rate. The aim of our study is to evaluate Z-plasty technique comparing with classical techniques.

Patients and methods: We included in our study 78 patients with pilonidal sinus operated in our clinic during a period of 2 years, divided into two groups: group A (44 patients) in which we achieved a classical technique and group B (34 patients) operated with Z-plasty technique. Operations were made under rachidian anesthesia, single dose antibiotics being administered prior the operation. There were no differences in the operation time; all patients were evaluated during the hospitalization and at one and 6 months.

Results: There were no mortality or significant complications during the hospitalization (median hospitalization time was 3.2 days, range between 1 and 5 days). In 2 patients from group A we noted minimal skin necrosis and in another 6 patients (5 from group A and one from group B) there was wound infection, few sutures being removed for drainage. Recurrence was seen in 6 patients from group A (13.64%) and in one patient from group B (2.94%) (p < 0.01).

Conclusions: Z-plasty is a recommended technique for surgical treatment of pilonidal sinus.
Diagnostic value of beta-glucuronidase determination in serum and urine of patients with colon adenocarcinoma

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Introduction: Colorectal cancers are the second cause (and the first in gastrointestinal tract), of cancer-related deaths. Adenocarcinoma is the most common type of colorectal cancer and the third most common cancer form of men and women in North America and Western Europe. Colon adenocarcinoma often grows for long time without symptoms until a relatively advanced stage. Early detection of colon adenocarcinoma dramatically improves the chances of eradication, therefore specific and sensitive markers are urgently needed. Colon adenocarcinoma usually is accompanied by inflammation, caused by change in structure and metabolism of the tumor cells and neighboring tissues. Invasion of neighbouring and remote tissues by cancer cells with accompanying inflammation, cause damage to the tissue. In degradation of the tissue take part lysosomal hydrolases, and among them lysosomal exoglycosidases which degrade oligosaccharide chains of glycoconjugates (glycoproteins, glycolipids and proteoglycan). One of lysosomal exoglycosidases is beta-glucuronidase which releases a glucuronate from a chains of glycosaminoglycans driven from proteoglycans.

The aim of this study was to determine beta-glucuronidase activity in serum and urine of patients with colon adenocarcinoma, and assess sensitivity and specificity of this determination.

Methods: The serum and urine samples were taken from 21 patients with colon adenocarcinoma (confirmed by pathologists) and 17 healthy people. beta-glucuronidase activity was determined with colorimetric method Chatterjee as modified by Zwierz et. al. Concentration of enzyme activity in serum was expressed in pKat/ml and specific activity in urine in pKat/mg of creatinine. The urine concentration of creatinine was determined by Jaffé’s method. The results were processed with Mann-Witney test. p < 0.05 was considered statistically significant.

Results: We have found a significant increase of concentration beta-glucuronidase activity in the blood serum (p < 0.001), and specific activity in the urine (p < 0.001), of patients with colon adenocarcinoma, in comparison with beta-glucuronidase concentration of the blood serum and specific activity in urine of healthy people. Our data shows high sensitivity and specificity of beta-glucuronidase determination in blood serum and urine of patients with colon adenocarcinoma, (80.0%; 82.35%) and (95.24%; 92.86%), respectively.

Discussion/Conclusion: It was proved that the cancerous process changed the activity of beta-glucuronidase in the serum of patients with colon adenocarcinoma. Determination of beta-glucuronidase activity may be used in the diagnostic of adenocarcinoma of the large intestine.
Diagnostic value of N-acetyl-beta-hexosaminidase and its isoenzymes A and B determination in serum of patients with colon adenocarcinoma

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Introduction: Colon adenocarcinoma is the second cause of mortality in both sexes. Environmental factors like the components of tobacco smoke are toxic and carcinogenic. Cigarette smoking is known as potential colon adenocarcinoma risk factor. Damage to tissues caused by colon adenocarcinoma is accompanied by the release of metabolites and various proteins including hormones and enzymes from the focus of carcinoma with the inflammatory state, to the systemic circulation. N-acetyl-beta-hexosaminidase (HEX) is the most active of lysosomal exoglycosidases participating in catabolism of glycoconjugates. HEX catalyzes removal of N-acetylglucosamine and N-acetylgalactosamine residues from the non-reducing end of oligosaccharide chains of glycoconjugates. HEX appears in several molecular forms, and the most active are isoenzymes A and B (HEX A and HEX B), which differ in charge, subunit composition: HEX A(alpha, beta), HEX B(beta, beta), and heat stability. HEX activity changes in diseases with damage to the tissues and a coexisting inflammation. There are no reports concerning influence of smoking on the activity of HEX and its isoenzymes in serum of patients with colon adenocarcinoma. The aim of our study was to evaluate the effects of cigarette smoking on HEX, HEX A and HEX B activity in the blood serum of patients with colon adenocarcinoma.

Methods: The blood serum samples were collected from 20 healthy people and from patients with colon adenocarcinoma (confirmed histopathologically). Patients with colon adenocarcinoma were divided into cigarette smokers (n = 17) and non-smokers (n = 17). HEX activity was determined by Zwierz et al. method. The absorbancy of p-nitrophenol was measured on microplate reader ELx800, BIO-TEK at 405 nm. Serum HEX activity concentration was expressed in pKat/ml. Statistical analysis was performed by the Mann-Witney test. A value of p < 0.05 was considered to be the level of statistical significance.

Results: Our study shows increased concentration in total HEX, HEX A and HEX B activity in blood serum of patients with colon adenocarcinoma in comparison to control with p < 0.001 for all enzymes. The significant increase in total HEX and its isoenzyme HEX A activity concentration was demonstrated in patients with colon adenocarcinoma who non-smoked cigarettes, when compared to smoking patients. No significant differences were found in HEX B activity in blood serum in smoking, and no smoking patients.

Discussion/Conclusion: Our study revealed that colon adenocarcinoma increases HEX and its isoenzymes activity in blood serum of patients with colon adenocarcinoma. Cigarette smoking significantly reduces HEX activity in blood serum of patients with colon adenocarcinoma, which is unexpected result and difficult to explain.
Evaluation in changes in Crohn’s disease pattern over time, according to Vienna/Montreal classifications

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Aim: Crohn’s Disease (CD) is a disease with both genetic and environmental etiology. The aim of our study was assess the evolution over of behavior and location of CD as defined by Vienna/Montreal Classifications.

Material and method: We followed-up 115 patients (57.6% females and 42.4% males), mean age 40.63 years with CD admitted in the Gastroenterology Department Timisoara. Behavior and location of CD were assessed at diagnosis and after 10 years.

Results: Regarding the age at diagnosis (A), all our patients were older than 16, so no case was classified as Montreal A1. 51.5% patients were A1 and 48.5% A2. Colonic location (L2) occurred most frequently (27.2% cases were L1, 49.2% - L2, 18.1% - L3 and 6.2% – L4 (no differences compared with Montreal classification). Location of the disease remained stable over the course of the disease (only 14% of patients had a change in disease behavior after 10 years – p < 0.001). In our patients non-stricturing non-penetrating forms (B1) were most frequent (57.5%), compared to structuring (16.6%) or penetrating diseases (16%); 9% of cases presented a combination of strictures and penetration. When referred to Montreal classification, 6% of the cases had perianal involvement. We noticed a more significant change in disease behavior over 10 years (35.5% had a change in disease behavior – p < 0.001, this was more prominent in the non-stricturing non-penetrating disease to either stricturing (22% – p < 0.001) or penetrating disease (23.5% – p < 0.001). Ileal location was more often stricturing, colonic or ileocolonic disease were more often penetrating; this aspect became more evident after 10 years (p < 0.05).

Conclusions: Location of CD assessed by Vienna or Montreal Classifications is relatively stable and can be used as in genotype-phenotype analyses, whereas behavior varies over the course of the disease.
Phagocytic function of dendritic cells is altered in patients with Crohn's disease and colorectal cancer

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Introduction: Dendritic cells (DCs) are thought to play a crucial role in the regulation of gut immunity. Disturbances of their abilities, such as an altered endocytic activity, may therefore be involved in the initiation and maintenance of inflammatory response in Crohn's disease (CD) and in the immunoediting during the development of colorectal cancer (CC).

Methods: Blood samples were taken from 12 CD patients, 11 patients with CC and 14 healthy volunteers. Mononuclear cells were isolated and placed on a plastic plate. Adherent cells were cultured for 5 days. The culture medium was supplemented with IL-4 and GM-CSF. Immature Mo-DCs were incubated with dextran-FITC for 4 and 24 hours at 4°C and at 37°C. Endocytic activity was evaluated by flow cytometry and confocal microscopy and positive Mo-DCs percentage was calculated.

Results: Dextran endocytic ability of Mo-DCs was significantly reduced in patients with CD after 4 and 24 hours (68.2%, 85.5%) as compared to Mo-DCs generated from healthy subjects (82.21%, 99.56%; p = 0.003, p = 0.004, respectively) and from patients with CC (89.4%, 99.7%; p = 0.001, p = 0.005, respectively). Mo-DCs dextran endocytosis after 4 hours was significantly increased in CC patients (89.4%) in comparison with healthy subjects (82.21%; p = 0.006). Higher percentage of Mo-DC generated from CC patients presenting dextran endocytic activity was found also after 24 hours, but the difference appeared not significant.

Discussion/Conclusion: Our data demonstrate an impaired endocytic function of Mo-DCs from CD patients as compared to Mo-DCs from healthy subjects that may suggest disturbances in C-lectine family receptors playing a pivotal role in endocytosis of dextran particles. The dextran endocytic activity seems to be enhanced in Mo-DC generated from CC patients that might be involved in the mechanisms of immunoediting in colorectal cancer.

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Emotional, social and behavioral factors in children with functional dyspepsia. Symptoms occurrence and resistance to pharmacological treatment in school-age children

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Introduction: Functional dyspepsia (FD) is common compliant of convoluted biopsychosocial origin. Despite some evidence of depression there is shortcoming in precise assessment of the psychosocial maladjustment in adolescents with FD. The aim of this study was to assess social competence, behavioral and emotional disorders in adolescents with FD and to evaluate impact of psychosocial facets on coexistence and intensity of subjective sensations and their change during implemented pharmacotherapy.

Methods: 66 consecutive patients (aged 11–18) were diagnosed with FD following Rome II criteria. The control group consisted of 86 healthy children who denied recurrent abdominal pain. Severity of dyspeptic symptoms was measured with visual-analogue scales before and after 8 weeks of treatment implementation. Psychosocial evaluation was completed using Youth Self Report (YSR) Questionnaire, which is one of Child Behavior Checklist (CBCL) instruments.

Results: Patients with FD exposed increased level of Anxiety and depression, Somatic compliance, Social and Thought problems, Internalisation (girls) and stunted externalisation (boys). Dysmotilities were more connected with elevated Internalisation (Somatic compliance Anxiety and depression) and Total problems outcome. Ulcer-like symptoms severity correlated in boys with strongly inhibited Externalisation (aggressiveness) and Total problems outcome. Somatic compliance, Internalisation and Total problems outcome correlated positively with both ulcer- and dysmotility-like symptoms, while Anxiety and depression related positively to intensity of dysmotilities. Somatic compliance was conducive to release of Early satiety, while Externalisation components related positively with aggravation of both ulcer- and dysmotility-like symptoms, despite of implemented treatment.

Discussion/Conclusion: FD is connected with other somatic compliances, elevated anxiety and depression, and internalisation disorders. Psychosocial factors influence treatment efficacy. Further longitudinal research is needed to precise effectiveness of simultaneous pharmacological and psychosocial therapies.
Colonoscopy in elderly - A retrospective study comparing the prevalence of the colorectal diseases at different age groups of patients from Sibiu, Romania

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Introduction: Colonoscopy is currently the best diagnostic modality for evaluating colonic diseases but studies of its use in the very elderly are limited.

Methods: We have retrospectively analyzed all colonoscopies and rectosigmoidoscopies which were performed during the last 4 years in the Department of Gastroenterology from the Clinical County Hospital, Sibiu, Romania. A number of 911 investigations were performed. The aim of this study was to establish the prevalence of the colorectal diseases at elderly people (over 70 years of age) compared with those less than 70 years of age.

Results: The medium age for the whole group was 61.31 ± 14.16 years. From the total number of patients, at 9.33% there was a colorectal cancer was found. 15.9% of the patients presented colorectal polyps and 4.28% presented a diverticular disease. Hemorrhoids and hemorrhoidal disorders were found at 9% of the patients. The studied lot was divided into 2 groups: group A, formed by 318 patients which were over 70 years of age, and group B, formed by 593 patients which were less than 70 years of age. The gender distribution was equally in both groups. 16% from the older group presented a colorectal cancer, compared with only 9.27% in the younger group. The relative risk of developing a colorectal cancer at the patients older than 70, compared with those less than 70 was 1.73. From the total of polyps which were found, 36 proved to be dysplastic. The relative risk of finding a dysplastic polyp at older patients compared with younger ones was 1.31. The diverticular disease was diagnosed at 9% from the elderly, compared with only 1.63% from the younger patients. The relative risk of developing a diverticular disease in elderly patients was 5.68. Despite these, hemorrhoids and hemorrhoidal disorders appeared more often in group B (10.28%), compared with only 6.6% in group A.

Discussion/Conclusion: The colorectal cancer is almost 2 times more frequently in elderly patients. The colorectal polyps seem to be transforming more often in dysplastic lesions at older people compared with younger patients. The diverticular disease’s prevalence is 5 times higher in elderly people. In contrast, the hemorrhoidal disorders are more frequent at younger people.
Listeriolyisin O induces chloride secretion and affects barrier function in HT-29/B6 colon epithelial cells

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Introduction: *Listeria monocytogenes*, a food-borne pathogen known to cross the mucosal barrier, is the causative agent of listeriosis. We sought to clarify *listeria’s* role in diarrhea by investigating effects on ion secretion and barrier function of human intestinal epithelial cells using purified listeriolyisin O (LLO), the major extracellular virulence factor of *L. monocytogenes*.

Methods: Monolayers of human colonic cells (HT-29/B6) were functionally characterized in Ussing chambers. Besides electrophysiogical and flux measurements, we tested for putative signal transducers using inhibitory components. Potential involvement of the Ca²⁺-signalling pathway was assessed with FURA-2-Imaging.

Results: Mucosal addition of LLO induces a dose-dependent, transient increase in short circuit-current (I_SC) paralleled by a decrease of transepithelial resistance (Rₜ). Electrogenic chloride secretion accounted for the observed I_SC as shown by Tracer flux studies. While the decrease in Rₜ points to a permeability increase for monovalent ions, mannitol permeability was also slightly increased after LLO addition. FURA-2 measurements and pharmacological testing for known intracellular transducing signals showed that Ca²⁺ release from intracellular stores and PKC activation mediate LLO-induced chloride secretion.

Discussion/Conclusion: Listeriolysin induces active chloride secretion and disturbs epithelial barrier function for small solutes. Thus, the Listeria-induced diarrhea comprises two components, secretory diarrhea and leak flux diarrhea.
Global burden of intestinal helminthic diseases

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Introduction: Intestinal parasites cause significant morbidity and mortality.

Methods: Searching through authentic databases.

Results: Diseases caused by *Ascaris lumbricoides*, *Trichiuris trichura*, *Ancylostoma duodenale*, *Necator americanus*, *Enterobius vermicularis*, *Strongyloides stercoralis*, *Entamoeba histolytica* and *Giardia lamblia* arise worldwide. A vast majority of these parasites are included in neglected tropical diseases (NTP) list and a great effort is under way to estimate their Global Burden. They encompass a high global impact of disability-adjusted life years (DALYs) which solely for geohelminths is 43.5 million. Amoebiasis is prevalent in many countries and approximately 10% of the world’s population is infected with it, yet 90 percent of infected persons are asymptomatic. Of the roughly 50 million symptomatic cases of amoebiasis occurring each year, up to 100,000 are fatal. It can cause intestinal ulcerations, bloody diarrhea, weight loss, fever, gastrointestinal obstruction, and peritonitis. Regarding giardiasis about 209 million persons worldwide are infected. *Giardia* causes nausea, vomiting, malabsorption, diarrhea, and weight loss. The final estimate of global mortality due to ascariasis in the Global Burden of Disease project was 11,000 concentrated in the age group 5–14 years. *A. duodenale* and *N. americanus* are hookworms that cause blood loss, anemia, pica, and wasting. In the USA, they are the second most common helminthic infection. The anemia caused by hookworm infection is life-threatening and has been estimated to result in 65,000 deaths per year.

Conclusion: The present poster is to have a fast look on the present outcomes of intestinal helminthic diseases in the world.
Transepithelial translocation of an alpha-gliadin 33mer

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Introduction: Mechanisms of epithelial gliadin translocation as the first step in antigen presentation in celiac disease (CD) are poorly understood. The alpha2-gliadin peptide p56-89 (33mer) includes several epitopes that are recognized by CD-specific T cells and is therefore a pivotal part of the immunologic response to CD. The aim of the study is to analyze the transepithelial translocation of a 33 amino-acid alpha-gliadin-peptide.

Methods: Transcytosis of a Cy3-tagged 33 amino-acid gliadin peptide was analyzed in basal and apical compartments of Caco2 und IEC6 cells grown on filters using RP-HPLC. Caco2- und IEC6 cells transfected with rab-pEGFPN1 constructs were analyzed in vivo with confocal laser scanning microscopy (CLSM). Duodenal mucosa of celiac disease patients and healthy controls (endoscopical biopsies) were mounted in Ussing chambers. After luminal Cy3-33mer-addition biopsies the epithelial 33mer-uptake was quantified with CLSM.

Results: Inhibitors of endocytosis reduced the transepithelial 33mer-translocation (Caco2 cells: mb-cyclo dextrine -74 ± 5%, nystatine -55% ± 17%). Cy3-33mer and FITC-Dextran4000 colocalized 30 min after apical 33mer-addition. The 33mer colocalized with rab5GFP, but not with rab4-, and rab7-GFP. Live cell imaging allowed in vivo-real time analysis of the 33mer-uptake by intestinal epithelial cells. Epithelial 33mer-uptake was significantly increased in duodenal specimen of CD patients compared to healthy controls (% epithelial cells: CD patients 4.6 ± 2.2%, controls 0.1 ± 0.1%).

Conclusion: Epithelial 33mer-transcytosis involves rab5, but not rab4 and rab7 and possibly accounts for the intracellular 33mer-processing. The epithelial 33mer uptake is increased in the inflamed CD mucosa.
Bowel cleansing: A better image or a better comfort?

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Introduction: There is no good endoscopic examination without a good cleaning of the colon. But we must always remember that patient’s safety and comfort should be our first goal. Therefore the aim of our study was to evaluate the efficiency and tolerability of different dosage from the same macrogol compound available on the market.

Methods: From the patients with normal result on colonoscopy recorded in our clinic in 2007, we have selected 58 patients (group A) that received 2 L of macrogol, 60 patients (group B) that received 3 L of macrogol and 56 patients (group C) that received 4 L of macrogol solution. All study groups had a similar sex and age distribution. Patients had the same instruction regarding the fasting and the rate of drinking the macrogol solution (250 mL every 15 minutes). During the bowel preparation and 24 hours after colonoscopy we have recorded all symptoms related to the bowel cleansing.

Results: The overall most common adverse reactions were abdominal bloating (55.17%), bad taste (44.83%), insomnia (41.14%), nausea (39.08%) and abdominal pain (35.63%). By calculating Pearson correlation coefficients we found that high dosage of macrogol was statistically correlated with abdominal pain (p < 0.00000002), abdominal bloating (p < 0.0000008), nausea (p < 0.000009), vomiting (p < 0.0002) and bad taste (p < 0.0009). There was no correlation between macrogol dosage and dermatitis (p = 0.488). The best bowel cleansing was recorded in group C (92.86%) (p < 0.0003) although a good cleansing was recorded in group B also (80%).

Discussion/Conclusion: Higher dosage of macrogol achieves the best bowel cleansing but is associated with high rate of adverse events. Therefore adapting the dosage for each patient is mandatory in order to reassure the minimum discomfort.
The role of colonoscopy in colorectal cancer postoperative surveillance

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Introduction: In this study we tried to identify the most important histological and endoscopical patterns associated with 5 years postoperative prognosis in colorectal cancer patients.

Methods: Between 1999 and 2003, 174 patients were endoscopically diagnosed with colorectal cancer and underwent surgical treatment in our hospital. After surgery all patients were enrolled in a follow-up programme: first colonoscopy at 6 months (for patients without total colonoscopy at diagnosis) or 1 year (for patients with total colonoscopy at diagnosis); second colonoscopy after another 3 years and then every 5 years.

Results: According to TNM staging, 4 patients (2.3%) were in stage I, 12 (6.9%) in stage IIA, 26 (14.94%) in stage IIB, 4 (2.3%) in stage IIIA, 44 (25.29%) in stage IIIB, 2 (1.15%) in stage IIIC and 82 (47.13%) in stage IV. The overall survival rate was 57.47%. The lowest survival rate was recorded in stage IV (31.7%), in poor differentiated adenocarcinoma (16.17%) and perineural invasion. The recurrence rate was 19.54% with a maximum incidence in T4 patients (p < 0.0004) and the highest detection (70.59%) rate was recorded at first colonoscopic examination. The detection of synchronal and metachronal neoplastic lesions was 5.75% and 9.2% respectively, with a higher incidence in males (p < 0.0000002 and p < 0.00007 respectively).

Discussion/Conclusion: By using AGA recommendation for colonoscopic postoperative evaluation of colorectal cancer we found an improved survival rate by detecting earlier a significant number of recurrences and synchronal/metachronal tumors.
Coffee ground vomit - Can we spot it?

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Introduction: It is assumed that healthcare professionals can identify coffee ground vomit as a sign of gastrointestinal (GI) bleeding. However, there is no published evidence to support this.

Methods: We aimed to investigate sensitivity and specificity of nurses’ and physicians’ assessment of coffee ground vomit. Photographs of nine samples of vomitus were obtained from medical inpatients. Two samples were classified as positive with signs of upper GI bleeding on endoscopy. Two negative samples were from patients suspected of bleeding with normal endoscopy. A further five negative samples were from patients suffering from other medical conditions with no clinical evidence of GI bleeding. 56 nurses and 45 doctors were asked to assess these pictures with the question: “Is this a coffee ground vomit from a significant GI bleed?”

Results: Samples with confirmed bleeding were correctly identified in 197 cases and missed in five cases. Pictures of non coffee ground vomit were identified correctly in 419 cases and interpreted false positively in 288 cases. This results in a sensitivity of 97.5%, specificity of 59.3%, a positive predictive value of 0.41 and a negative predictive value of 0.99.

Discussion/Conclusion: Coffee ground vomit is difficult to identify with certainty. High negative predictive value allows ruling out of a significant bleed. Low positive predictive value however does not allow the diagnosis of a GI bleed solely based on vomit appearance.

Presented as abstract at DDW 2006 Los Angeles.
Endoscopic evaluation of colopathy in patients with some chronic liver diseases (CLD)

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Introduction: The population of Egypt has a very heavy burden of CLD, which includes hepatosplenic schistosomiasis, post hepatic cirrhosis and hepatocellular carcinoma (HCC). The most common complication of CLD is portal hypertension. The term portal hypertensive colopathy has growing interest, little is known about this problem in Egypt.

Aim of the work: To evaluate colopathy in patients with some CLD.

Patients & Methods: Duplex Doppler study and ultrasound of portal flow, upper gastroduodenoscopy and full length colonscopy were done for 20 patients with hepatosplenic schistosomiasis, 20 patients with hepatic cirrhosis and 20 patients with HCC.

Results: Colopathy was present in 60% of schistosomal and hepatic cirrhosis and only on 40% in HCC. Colopathy was presented as red spots, colitis like, patchy hyperemia, telangiectasia, angiodysplasia, and granular mucosa. There was no significant correlation between (PVF) and colopathy. There was no significant correlation between colopathy or past history of sclerotherapy in all studied groups.

Recommendations: Full length colonscopic examination should be considered in schistosomal and cirrhotic patients with unexplained lower gastrointestinal bleeding even if hemorrhoids are present. Further researches on portal colopathy should be designed to evaluate the effect of drugs that decrease portal pressure on the presence and progress of colopathy.
Histopathological and immunohistochemical aspects in the differential diagnosis of acute peritonitis with gastrointestinal etiology

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Introduction: The study of histopathological and immunohistochemical aspects in acute peritonitis appeared at the patients with gastrointestinal disorders, correlate with clinical aspect and postoperative evolution for the etiological diagnosis.

Methods: We studied resection surgery pieces and peritoneal pieces fixed in formol, included to paraffin and colored HE and PAS. Sometimes, it was necessary immunohistochemical exam using monoclonal antibodies (CEA, CD 7, CD 20, CA 125).

Results: At the studied patients, peritonitis had neoplastic and inflammatory etiology: duodenal ulcers, gastric ulcers, Meckel’s diverticulum, appendicitis, colon cancer, gastric cancer, ovarian tumors, ovarian cancer and inflammatory bowel diseases.

Discussion/Conclusion: The etiology at the most secondary peritonitis was perforation of the duodenal ulcers. We correlated histopathological study of the peritoneal lesions with the primary disease. Immunohistochemical exam was very important in peritonitis metastases which proved the histogenesis of the tumor.

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Therapeutical aspects in duodenal postbulbar ulcers

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Introduction: The purpose of this study is to show the different therapeutical aspects in duodenal postbulbar ulcers. The therapeutic difficulties are the consequence of the duodeno-bilio-pancreatic morphologic modifications, clinic polymorphism, radiologic indirect signs and difficult endoscopic localization.

Methods: Our study was made on a lot of 329 operated patients with duodenal ulcers during 2000–2007 at our Clinic. However, the incidence of the postbulbar duodenal ulcer remained constant – 8.2% (27 cases). Definitive diagnosis was set only intraoperatively.

Results: There are 2 forms of postbulbar duodenal ulcers: proximal (D1 fixed) – 70.3% (19 cases) and distal (D2 above duodenal papilla) – 29.6% (8 cases). Associated bilio-digestive lesions were encountered in 5 cases (18.5%). Gastric 2/3 resection or troncular vagotomy with limited gastric resection were achieved in 85.1% of cases (23 patients). We prefered the Billroth II type anastomosis (62.96%) excluding the ulcerous lesion. Drainage of the duodenal stump was employed in 25.92% (7 cases) of cases.

Discussion/Conclusion: Specific postoperative morbidity of 14.8% (4 cases), an early re-operations rate of 7.4% (2 cases) and postoperative mortality of 3.7% versus 1.82% for the duodenal ulcers, emphasize the severity of postbulbar duodenal ulcers. Due to its aggressive, endocrine-type etiology and pathogeny, evolution to severe complications and resistance to modern medical therapy, the postbulbar duodenal ulcer should be of first surgical intent, considering a radical procedure whenever possible.

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Correlations between the degree of atrophic gastritis, Helicobacter pylori infection, anti-parietal cell antibodies and some cytokines

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Introduction: Anti-gastric parietal cell antibodies (AGPA) are commonly associated with pernicious anemia and chronic atrophic gastritis but markers for predicting the progression of atrophic gastritis remain unidentified. We investigated the correlations between the degree of atrophic gastritis and presence of Helicobacter pylori, AGPA and the profile of some cytokines (interleukin-6, interleukin-8).

Methods: This study enrolled 50 patients with atrophic gastritis and 20 consecutive healthy adults as controls. We assessed serum levels of IL-6, IL-8, anti-parietal cell antibody by ELISA. H. pylori infection was defined as positivity by urease test.

Results: The prevalence of AGPA in patients with atrophic gastritis were much higher (50%) than those of controls (5%). In H. pylori-positive patients, the levels of AGPA were statistically higher in patients with severe atrophy than in those with mild atrophy. However, Helicobacter pylori infection did not affected the AGPA levels determined. No significant difference was found between patients with and without H. pylori. IL-6 levels of patients were significantly higher than in control group (25.6 ± 7.0 pg/ml vs. 10.3 ± 4.2 pg/ml). Plasma IL-8 had pathological values at 25% of patients. Our results suggest an important role of interleukin-8 (IL-8) in Helicobacter pylori infection associated chronic atrophic gastritis. In response to H. pylori, interleukin-8 (IL-8) is secreted from host cells to attract components of the innate and adaptive immune systems to the site of infection.

Discussion/Conclusion: Helicobacter pylori infection did not affect the AGPA levels. Helicobacter pylori plays an important role in induction and the progression of atrophic gastritis by stimulation of IL-6 and IL-8 production. We suspected a relation between the increased cytokines (IL-6 and IL-8) levels and a higher risk of atrophic gastritis to patients with H. pylori infection.

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Oblique anastomosis in soave endoanal pullthrough for Hirschsprung’s disease – A way of reducing strictures

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Background: Anastomotic stricture is a recognized complication of the Soave endoanal pullthrough for Hirschsprung’s disease. There are multiple risk factors for these strictures, circular anastomosis being one of them. There are techniques to decrease the incidence of strictures by doing non-circular anastomosis of the pulled through bowel. We describe a new technique of oblique anastomosis to lower the stricture rate.

Methods: The child is placed into lithotomy position. Mobilisation of aganglionic bowel commenced, either open or with laparoscopic assistance. The level of innervation is established utilising frozen section biopsies. The surgeon moves to the perineal field. The pulled through ganglionic bowel is anastomosed posteriorly 0.5 cm from the dentate line, and anteriorly 1.5 cm above this point. Also in the event a stricture occurs, Y-V anoplasty is simple to perform, as the previous anastomosis is very near the anocutaneous junction on the posterior aspect.

Results: We present our experience using this technique. Seventeen consecutive children underwent the procedure at our institution between 2003 and 2006. The mean age at operation was 3.3 months [range 1–7 months]. A total of 17 children were studied, 16 of which were boys. The median follow-up was 19 months [range 6–42 months]. A primary pullthrough was performed in 13 children (no prior colostomy) and of these 11 were laparoscopic assisted. Only 1 child developed an anastomotic stricture requiring anal dilatation.

Conclusion: An oblique anastomosis reduces the incidence of postoperative strictures. A long-term follow-up with larger number of patients is required.
Interobserver variability in the diagnosis of megarectum by pelvic ultrasound

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Aim of study: Recently published literature describes the use of pelvic ultrasound in the diagnosis of megarectum in children with chronic idiopathic constipation. However, there is no mention of interobserver variability. Thus the aim of this project was to study interobserver variability, an important pre-requisite before this data and the technique can be applied globally.

Methods: A pelvic ultrasound was carried out on 46 children (with a full or partially full bladder) with a history of chronic idiopathic constipation (CIC). Two different observers measured the rectal crescent seen behind the bladder on the same occasion in each child. The observers were blinded to each other's readings. All children also had documentation of their age, weight and height. Agreement between the two observers was measured using the Bland-Altman limits of agreement. We also calculated a spearman’s rank correlation.

Results: The mean age of the children was 8.1 years (SD 4.67). The mean rectal crescent was 3.10 cms (SD 1.58) with observer 1 and 3.06 cms (SD 1.59) with observer 2. The mean difference between the two observers was 0.039 cms (SD 0.15). The 95% limits of agreement with Bland-Altman were found to be -0.26 to +0.33 cm. In our analysis of the 46 children, 44 observations (95.7%) fell within the limits of this agreement, indicating statistically significant agreement between two observers. The spearman’s rank correlation between the two observers’ was 0.994, which is highly significant.

Conclusion: The interobserver variation with pelvic ultrasound is not statistically significant. Thus pelvic ultrasound can be done effectively with different operators.
Anorectal manometry: A comparison of sevoflurane general anesthesia with ketamine anesthesia

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**Purpose:** Ketamine anesthesia is commonly used in poorly compliant children undergoing anorectal manometry (ARM). Sevoflurane has a more favorable side effect profile than ketamine. The effects of sevoflurane on ARP are not known. This study was designed to assess the effect of sevoflurane compared to ketamine on ARP.

**Methods:** Ten children (age 2–11 years) received ketamine (ketamine (phase 1) followed by sevoflurane GA (phase 2). Although we had ethics approval to study 30 children, interim analysis of the first ten children showed a highly significant effect of sevoflurane GA on ARP, continued recruitment was therefore considered unethical.

Phase 1: Intravenous ketamine 2 mg x kg\(^{-1}\) induced anesthesia, which was maintained by increments of 0.5 mg x kg\(^{-1}\) if needed to enable stable measurement of ARP.

Phase 2: General anesthesia was induced with sevoflurane in oxygen and air and the dose increased to 1.5 MAC (Minimum Anesthetic Concentration) measured by end-tidal sevoflurane concentration.

ARP was measured at steady state during phase 1 and phase 2 using a solid-state catheter with four radial sensors (Gaeltec UK).

The data was analyzed using Wilcoxon Signed Rank test. P < 0.05 was accepted as significant.

**Results:** Ten children had ARP measured under ketamine and sevoflurane. The median ARP during ketamine sedation and 1.5 MAC sevoflurane was 57.5 cm H\(_2\)O (IQR 52.5–61) and 37.5 cm H\(_2\)O (IQR 32.75–55.5) respectively. The decrease in ARP is statistically significant at 1.5 MAC sevoflurane (sevoflurane (P < 0.05)

**Conclusion:** ARP measurements at 1.5 MAC sevoflurane anesthesia should not be used to inform management decisions.
Slow transit constipation – Diagnostic pitfalls

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Purpose: It is important to distinguish Slow Transit Constipation (STC) in children from Constipation due to Functional Fecal Retention (FFR); the latter is associated with outlet problems leading to Megarectum (MR) whereas former has normal rectal size. Current literature lacks any measured rectal dimensions differentiating normal from constipation children. We have recently described this using pelvic ultrasound. The purpose of this study was to re-evaluate the diagnosis of STC given by scintigraphic colonic transit studies alone to take account of the rectal size.

Methods: 10 Children with bowel problems underwent scintigraphic colonic transit studies. FFR was defined as retention of tracer in the recto sigmoid colon at 48 hours whereas STC was defined as retention of tracer proximal to the recto sigmoid at 48 hours. Ultrasound measurement of the rectal crescent posterior to the bladder greater than 3cms was taken as MR.

Results: Of the 10 children, 6 were identified as STC on the basis of transit studies. All these 6 children had megarectum median rectal crescent greater than 4.6 cms (range 3.1 to 7.2 cms). The remaining 4 of the 10 children were grouped as FFR on transit studies. All of these had MR on US median rectal crescent 5.0 cms (range 4.2 to 7.0 cms).

Conclusion: Rectal dimension should be taken in account along with colonic transit studies before making a diagnosis of STC. We propose an algorithm where pelvic ultrasound is done first and only those children with normal rectal size are subjected to colonic transit studies.
Pelvic ultrasound for diagnosis of megarectum in constipation in children

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Purpose: Establishment of rectal size is essential to distinguish between slow transit constipation and constipation with megarectum. This has not been possible so far, as the existing medical literature lacks rectal dimensions for normal or children with chronic idiopathic constipation (CIC). We, for the first time, describe the use of pelvic ultrasound, to achieve this.

Methods: A pelvic ultrasound was carried out on full bladder on 82 children with no history of bowel problems and 95 children with CIC. Rectal crescent seen behind the bladder was measured. All children had documentation of height, weight.

Results: The median age, weight and height for the normal population is 5.5 yrs (range 0.30–15.30, IQR 3.75), 20.05 kgms (range 6.88–107.80, IQR 11.4) and 112 cms (range 65–165, IQR 25). In the children with constipation the median age is 6.5 yrs (range 0.40–16.40, IQR 5.8), weight 23.1 kgms (range 7.10–82.40, IQR 14.9) and height 116.90 cms (range 63.20–177.10, IQR 35.3). These values are comparable between two groups.

The mean rectal crescent diameter in children with constipation is 3.4 cms (range 2.10–7.0 IQR 1.0) as compared to 2.4 cms (range 1.3–4.2, IQR 0.72) in healthy children and this difference is statistically significant on multiple regression of logs, adjusted for height weight and age (p value < 0.05).

An ROC analysis indicated good discrimination between rectal diameters of normal children and children with CIC (AUC 0.847 95% CI: 0.791–0.904).

Conclusion: Pelvic US is a quick child friendly investigation to document megarectum.
Malignant tumors of the small intestine (a review of clinical cases)

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Introduction: The malignant tumors of the small intestine are rare – about 1% of all malignant tumors of the gastrointestinal tract.

Methods: duodenoscopy with biopsy, enteroclysis, CT of the GI tract with oral contrast media and abdominal ultrasound.

Results: For a ten years period (1997–2007), 26 cases (17 males and 9 females) of malignant tumors of the small intestine were diagnosed. Regarding the localization the cases were as follows: 5 carcinomas of the duodenum, 13 periampullary carcinomas (in pars desc. duodeni), 5 cases of carcinoma of the jejunum, 2 of the ileum and one of the appendix. Adenocarcinoma was the most frequent histological type – 21/26 (80.76%). Carcinoids were found in 4/26 cases (15.38%), two of which were hormonally active, one with liver metastases. Two non-Hodgkin’s lymphomas (extranodal localization in the small intestine) were also diagnosed. Adenocarcinomas of the small intestine mainly developed from malignized adenomas with villous components.

The leading symptom of the small intestine malignant tumors was the impaired intestinal passage. Second in frequency was the obstructive jaundice (in all cases of periampullary carcinomas). Recurrent bleeding from the GI tract and iron-deficiency anemia was also a frequent symptom.

Combined pathology was found in 6/26 cases – adenomatous polyposis of the stomach and the colon with malignant tumor of the small intestine; adenomatous polyposis of the small intestine and the colon with metachronous carcinoma of the colon and carcinoma of the small intestine.

Discussion/Conclusion: The clinical diagnosis of these tumors is difficult because of the impossibility to perform enteroscopy in the revised period. Capsule endoscopy and double balloon enteroscopy would improve the timely diagnosis.
Serum IL-13 concentration in patients with inflammatory bowel diseases

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Introduction: Interleukin-13 (IL-13) is an important cytokine involved in inflammatory processes. Lately it has been reported, that there is an increase of IL-13 concentration in colonic biopsies taken from patients with inflammatory bowel diseases (IBD), specially with ulcerative colitis (UC). The aim of the study was to assess the usefulness of the assessment of serum IL-13 concentration in IBD.

Methods: IL-13 concentration was assessed in sera of 39 patients with IBD (24 UC and 15 Crohn’s disease - CD) using ELISA immunoenzymatic method. There were blood tests performed – blood cell count, C-reactive protein (CRP) concentration, erythrocyte sedimentation rate (ESR), iron concentration and total iron binding capacity (TIBC) and additionally body mass index (BMI) was evaluated.

Results: IL-13 concentration was 27.4 ± 74.7 pg/ml (in 12 patients IL-13 was not detectable) and there was no important difference between UC and CD group. There was a statistically important negative correlation between IL-13 and BMI in whole group, and between IL-13 and platelet concentration among UC patients. Other correlations were not observed.

Discussion/Conclusion: The usefulness of the IL-13 assessment in serum in IBD seems to be poor in comparison with its evaluation in colonic biopsies. Possibly usage of more sensitive methods than performed ELISA test could improve accuracy of the IL-13 assessment and its clinical utility.
The importance of the vessels changes in the appearance of an ischemic colonic disease

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Introduction: The presence of the colonic disorders in elderly is due to the circulatory changes at this level.

Material and methods: The study, a meta-analysis, was carried out on a group of 36 patients, aged between 63–86 years (the mean age was 74.5 years), hospitalized in a 6 mounts period in the IV<sup>th</sup> Medical Clinic- the geriatric compartment. Those patients had complaints such as constipation or alternation of constipation and diarrhea.

Results: The study of the blood flow in the abdominal aorta and the mesenteric artery, performed with a color Doppler ultrasonograph, showed blood flow changes, followed by secondary ischemic changes. The most frequent symptoms in those patients were: postprandial abdominal pain in 70% of patients, postprandial bulging with flatulence in 75% of patients, changes of the heart rhythm and the blood pressure in 38% of patients, false diarrhea in 29% of patients.

Conclusions: The diagnosis of ischemic colitis in the elderly is underestimated, and it is necessary an complex analysis in all patients with coronarial and cerebral arteriosclerosis and severe dislipidemia, for the follow-up, the treatment and the prevention of severe complications such as an acute mesenteric infarct, in those patients.
Morphological evaluation of tumor stroma in colorectal carcinoma: Correlation with prognosis and survival

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Introduction: To establish the role of stromal reaction in the biological behavior of colorectal cancer and the patients survival.

Methods: The prospective study that lasted 5 years included 63 patients diagnosed with colorectal cancer between 1.01.2004 and 31.12.2005 at the County Hospital Timisoara. The patients were between 31 and 78 years of age (mean age 61.7 years), 31 men and 32 women being included in the study. We examined the reaction of the peritumoral stroma at the front of invasion, using HE, van Gieson and tricrom Gomori stains.

Results: In 65.1% of colorectal carcinomas we identified a rich stroma made up of thin mature collagen fibres (type I stroma). 23.8% of carcinomas showed thick keloid-like collagen strips between the malignant cells (type II stroma). In only 7 cases (11.1%), the tumor proliferation from the front of invasion is accompanied by a myxoid, edematous stroma (type III stroma). The 5-year survival had different values depending on the stromal response from the front of invasion. We noted survival rates of 63.4% in patients that presented carcinomas with type I stroma, 40% in patients with tumors that associated type II stroma and only 14.3% in the case of patients with tumors that had type III stroma.

Discussion/Conclusion: Our results support the assumption that the desmoplastic reaction limits the aggressiveness of the tumors, and they contradict the almost classical concept of tumors with stromal desmoplasia that evolve much more rapidly. The edematous and myxoid nature of the stroma facilitates tumor differentiation, resulting deep infiltrative carcinomas with high metastatic potential at the distance and in regional lymph nodes.
Eosinophils in inflammatory bowel disease correlated with disease activity

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Introduction: Neutrophils and monocytes are considered as responsible for the intestinal mucosal damage in inflammatory bowel disease (IBD). Increased numbers of normal and functionally activated eosinophils have also been shown in the colonic mucosa of patients with IBD. A pathogenic role for the eosinophils has not been fully established in IBD. We aimed to compare the degree of eosinophilic infiltration in colonic mucosa of patients with ulcerative colitis, Crohn's disease, amebiasis superimposing on ulcerative colitis and control patients with irritable bowel disease.

Methods: 79 IBD patients (44 ulcerative colitis, 23 Crohn's disease and 12 amebiasis with ulcerative colitis) were recruited and 44 irritable bowel syndrome (IBS) patients were included as a control group. Disease activity assessment on the basis of the Truelove & Witt's criteria in the ulcerative colitis and Crohn's disease Activity Index criteria in the Crohn's disease patients. Biopsy specimens were taken during the colonoscopy from involved and uninvolved colonic mucosa in all patients.

Results: Most of the IBD patients exhibited severe eosinophilic infiltration on the colonic mucosa (79.5% in ulcerative colitis, 78.3% in Crohn's disease, 58.5% in the amebiasis with ulcerative colitis and 4.5% in the IBS patients). The eosinophil infiltration was found as 25% in the IBS group however only were severe. The degree of eosinophilic cellular infiltration showed positive correlation with disease activity. The degrees of eosinophilic infiltration and the localization or the type of the diseases were not associated.

Discussion/Conclusion: Infiltrating eosinophils seem to accelerate the severity of the IBD activity, unrelated with the amebiasis infestation.
Peroxide-enhanced endoanal, endovaginal and transperineal sonography in perianal fistulas

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Introduction: The use of hydrogen peroxide improves the depiction of perianal fistulas during subsequent combined endoanal (or endovaginal) and transperineal ultrasonography.

Material and methods: Fourteen patients (9 male and 5 female) with perianal fistulas were tested. Four women had active Crohn’s disease. After conventional transperineal and endoanal sonography, 1–2 ml of 3% hydrogen peroxide was insufflated in the external openings of the fistulas. The exams were repeated by simultaneous endovaginal and transperineal approaches in females. In men endoanal and transperineal sonography were performed likewise.

Results: All fistulas were identified by contrast-free endoanal sonography. The fistulas were distributed as follows: superficial – 2 patients, intrasphincteric – 7, transsphincteric – 4 and suprasphincteric – 1 patient. There were 3 cases of complex fistulas with one or two secondary tracks, identified only by contrast-enhanced approach. By means of Doppler investigation hypervasularisation of the fistula wall was detected in 5 patients: arterial blood flow was registered in 2 cases and venous blood flow in 4 patients (1 patient with arterial and venous flow).

Conclusion: Peroxide-enhanced combined endoanal (or endovaginal) and transperineal sonography is a well tolerated method, offering detailed depiction of the fistula tracks. The Doppler technique further allows a characterization of their blood supply.

Key words: perianal fistulas, endoanal sonography, transperineal sonography, endovaginal sonography, hydrogen peroxide
Diagnosis and follow-up of celiac disease using small intestinal contrast ultrasonography

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Background and aim: Small intestinal ultrasonography with anechoic contrast agents (SICUS) has been shown to have a diagnostic accuracy on small bowel morphology similar to X-ray barium follow-through. We want to assess SICUS characteristics of celiac disease patients

Patients and methods: SICUS was performed using PEG 4000 as contrast agent. Forty-three patients with celiac disease at the first diagnosis were enrolled and 30 healthy volunteers, matched for sex and age, were selected as control group. Celiac disease diagnosis was based on anti-endomysium and anti-transglutaminase positivity as well as jejunal histology. We considered following echographic parameters: liquid endoluminal content before contrast, loop diameter, Kerckring's folds, peristaltic waves, ileal jejunalization, mesenteric lymphadenomegaly and Doppler resistance index (RI) of mesenteric superior artery. Statistical analysis was performed by Student's t test for unpaired data; one-way analysis of variance was used to correlate echographic and histologic pictures.

Results: Loop diameter, Kerckring's fold number, peristaltic waves, and Doppler RI appeared to be significantly different between celiac disease patients and controls. Liquid content, ileal jejunalization and mesenteric lymphadenomegaly were present only in the celiacs (52.1%, 47.7%, and 95.6% respectively), but not in controls. Only Doppler RI values significantly correlated with the histologic degree of damage.

Conclusions: SICUS could be a reliable and non-invasive technique to confirm a diagnosis and to follow up of celiac disease performed using conventional investigations.
Transcutaneous sonographically guided 18-gauge-needle biopsy of gastrointestinal tract wall lesions

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Background and aim: Ultrasound-guided fine needle biopsy (USFNB) is a widely accepted procedure for diagnosis of abdominal and retroperitoneal space-occupying lesions. Gastrointestinal tract lesions, both inflammatory and/or neoplastic, may be accurately visualized by US; although the diagnosis of such lesions is conventionally obtained with endoscopic biopsy, the possibility to accurately obtain the diagnosis of gastrointestinal neoplasia by using a USFNB with 18 or usually 20–22-gauge has been reported. In this study we aimed to evaluate the safety and accuracy of USFNB using a 18-gauge aspiration needle (BIOMOL) in the diagnosis of gastrointestinal tract lesions.

Patients and methods: 81 patients (M/F 48/33, median age 68 yrs, range 45–80) underwent in the last 15 years a percutaneous USFNB with a convex transducer (3.5–5 MHz) provided with a biopsy device. All patients were fasting from 8 hours and signed a written informed consent; no bowel preparation or antibiotic prophylaxis was used. The procedure was usually performed without local anesthesia. Contraindications were only severe coagulation impairment (platelet count ≤ 40,000/mm³; prothrombine time ≤ 40%), and presence of distended bowel loops.

Results: The intestinal USFNB represented the 3.1% (81/2676) of all abdominal USFNB performed over a 15 years period; 27 were made on gastric wall, and 54 on gut wall (30 at colon-sigma, and 24 at the small bowel). The indications to the procedure were impossibility to perform endoscopy in 20 cases, non-diagnostic endoscopic biopsies in 47 cases, and endoscopically inaccessible lesion in 14 cases, respectively. The gold standard of comparisons were surgery or II level technique imaging. Sensitivity, specificity, diagnostic accuracy, predictive positive and negative values were 90%, 100%, 90%, 100%, and 87%, respectively. The procedure was well tolerated; no mortality has been reported although four serious complications were recorded: one case of small hemoperitoneum non requiring further treatment, one case of sepsis, one of small parietal hematoma and one self-controlled bile peritonitis.

Conclusion: Our study demonstrates that 18-G USFNB of gut wall is a simple, relatively safe, and accurate approach to obtain histologic sampling of gastrointestinal wall lesions, in case of endoscopic failure. By using a larger size needle an higher accuracy has been achieved at the expenses of some self-limiting complications.
Granular cell tumor of the esophagus and EMR procedure (Duette): A case report

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Case: A 31-year-old woman was admitted to our outpatient clinic with a history of epigastric discomfort and epigastric pain of 1 year which was unresponsive to PPI therapy. Upper gastrointestinal endoscopy revealed a sessile polypoid tumor at the esophagus, at 27 cm distance from the incisor teeth. The tumor was of firm consistency when touched with the biopsy forceps, measured about 10 mm in diameter, and was covered with and surrounded by normal looking mucosa. The histological findings were consistent with GCT. Magnetic resonance (MR) scan of his chest revealed no additional pathology in the esophagus. The patient subsequently underwent an endoscopic mucosal resection (EMR). EMR procedure was carried out by Duette Multiband Mucosectomy Kit. The lesion was completely removed as one piece by a single intervention of Duette, and no major complications, early or late, were observed. Microscopical examination of EMR specimens were consistent with GCT, showing a diffuse thickening of the mucosa and growth of large cells with fine eosinophilic granules in the cytoplasm. Immunohistochemistry showed, S-100 protein present nearly in all cells within the tumor mass. Microscopically, the surgical margin was free of tumor cells.

Conclusion: Granular cell tumors are uncommon tumors of the GI tract and are very rare at the esophagus. Although the natural history of the tumor is unknown, most esophageal GCTs have a benign clinical course. EMR which is recently considered of a choice of treatment of the esophageal tumors is generally safe and successful procedure and the complications rate is low.
Leptomeningeal carcinomatosis associated with colorectal carcinoma – A case report

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Leptomeningeal carcinomatosis is an extremely rare site of colorectal cancer dissemination. We present a 61-year-old woman presented to the infectious diseases ward with a one-month history of fatigue, fever, strong headache and photophobia. Additionally, the patient alleged a one year history of convergent strabismus of the right eye and substantial weight loss of 12 kg in several months period. Adenocarcinoma cells were found in the cerebrospinal fluid (CSF). CT scans of the brain were negative but the abdominal CT scans revealed ascendant colon tumor mass. The patient were referred to the gastroenterology department. The diagnosis of ascendant colon adenocarcinoma was confirmed as well as adenocarcinoma cells in the CSF. In this case, the leptomeninges are found to be the only dissemination site of the colorectal cancer at the time of diagnosis. Surgery was not performed and the patient was referred to the oncologist.
Colonic diverticulitis in the elderly

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Introduction: The most common complication of diverticulosis is diverticulitis, whose frequency is given at about 20%. Diverticulosis in patients over 80 years may be as high as 60%.

Objectives: This study reports on the management of acute diverticulitis with reference to the severity and outcome of the disease with respect to age.

Methods: Between 2000 and 2007, 112 patients were treated for the acute left colonic diverticulitis. Patients were divided in two groups: those older than 64 (group 1: 78 patients) and those aged 64 years or less (group 2: 34 patients). The diagnosis was confirmed by CT, barium enema or by endoscopy in some cases.

Results: Patients in group 1 had successful conservative treatment in 61.5%, while 38.5% needed emergency surgery. In both groups antibiotic therapy (rifaximin, metronidazole, piperacillin, and cefotaxim) was administrated. The recurrence rate was 23.07% in elderly patients and 26.4% in group 2. The type of surgical procedure and incidence of peritonitis in emergency patients was similar in the two groups. The mortality rate was similar in patients with conservative therapy (in both groups), but it was higher in elderly patients who underwent emergency surgery (36.4% vs. 2.9%).

Discussion/Conclusion: Diverticulitis in elderly patients doesn’t have a particularly aggressive course, except the cases who developed peritonitis. The mortality may be higher in the last group related also to the associated diseases at this age (cardiovascular and respiratory pathology).
The activity of serum beta-galactosidase in colon cancer patients with history of alcohol abuse

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Introduction: Beta-galactosidase is a lysosomal exoglycosidase involved in the catabolism of glycoconjugates through the sequential degradation of beta-linked terminal galactosyl residues. Enhanced serum activity of beta-galactosidase in invasive colon tumors has been reported earlier. It has been also noted that alcohol abuse increases activity of some of the serum exoglycosidases. Malignant tumors produce various hydrolases, including beta-galactosidase, which degrade pericancerous matrix, favoring tumor growth, invasion and metastatic propagation. The proteolysis of matrix glycoproteins depends on initial removal of the carbohydrate sidechains. Since the stimulation of glycosidases and other degradative enzyme activities have been associated with the tumor development and with the alcohol abuse, the activity of beta-galactosidase in colon cancer patients with history of alcohol abuse might be higher than in patients without such a history.

Methods: Material was serum of 16 colon cancer patients and 15 healthy volunteers. Six of colon cancer patients met alcohol abuse criteria. The activity of beta-galactosidase (pKat/ml) was determined by the colorimetric method described by Marciniak et al (2006). The results were processed with Statistica 6.0, p < 0.05 was considered statistically significant.

Results: The activity of serum beta-galactosidase was significantly higher in colon cancer patients with history of alcohol abuse than without alcohol abuse (p < 0.01). The activity of serum beta-galactosidase in colon cancer patients without a history of alcohol abuse had tendency to be higher than the activity in healthy volunteers.

Discussion/Conclusion: The higher activity of beta-galactosidase might contribute to increased cancer cell invasion and metastasis when alcohol abuse coincides with colon cancer.
Lactase activity in children with IgE-dependent food allergy

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Introduction: The decrease in lactase activity being a result of damaging influence of food allergen on the small intestine mucosa is described in literature, however, there are no data concerning the frequency of its occurrence.

The aim of the study was evaluation of incidence of decreased lactase activity in children with IgE-dependent food allergy and evaluation of the correlation between the incidence of decreased lactase activity and age, sex, the degree of body mass deficiency and atrophic changes within the small intestine mucosa.

Materials and methods: The examined group included 61 children with diagnosed IgE-dependent food allergy. Moreover, lactase activity was determined in 40 children, in whom we excluded organic diseases of the alimentary tract and in 16 children with total or subtotal atrophy of villi in the small intestine mucosa. In all the patients we determined lactase activity in the biopsy specimens from the small intestine mucosa taken during endoscopy using Dahlquist’s method in Dyduch’s modification.

Results: In the group of patients with IgE-dependent food allergy decreased lactase activity was observed in 11.5%. The mean values of lactase in the group of patients with IgE-dependent food allergy were lower than in the reference group without organic diseases of the alimentary tract and they were respectively: 5.39 vs. 8.64 U/1g of tissue. The lowest values were in the group of patients with diagnosed atrophy of villi -1.88 U/1g of tissue. The differences were statistically significant. We did not find a correlation between lactase activity and the incidence of abnormalities concerning its concentration related to sex and the degree of the nutritional status. In the patients with diagnosed partial atrophy of the small intestine villi in the course of food allergy, the mean values of lactase activity were only slightly different from the values in the subgroup with the normal structure of mucosa, however, lactase deficiency was observed more frequently in patients with atrophy of villi.

Discussion/Conclusion: In children with IgE-dependent food allergy decreased activity of lactase occurred more rarely than in the population group, however, the mean values of lactase activity were twice lower.
P53 expression fails to associate with Bax and gets correlated with Bcl-xL in colorectal cancer

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Introduction: P53 mediates apoptosis with engagement of Bax protein and it usually causes opposite effects to Bcl-xL action in irreversibly injured cells. However, majority of colorectal cancers over-express P53, probably due to mutation of the p53 gene. In consequence relations between P53 and apoptosis regulators could be altered. The aim of our study was to compare expressions of P53 with Bcl-xL and Bax in 96 human colorectal cancers.

Methods: P53, Bcl-xL and Bax were detected with immunohistochemistry. Their expressions were scored and statistically analyzed with Spearman rank correlation test in all colorectal cancer patients and groups of clinical and pathological variables.

Results: P53 was expressed in nuclei in dense granular fashion, while Bax and Bcl-xL gave finely granular staining pattern in cytoplasm of colorectal cancer cells. To our surprise P53 failed to correlate with its downstream protein Bax in all of colorectal cancers and in detailed analysis in different groups of clinical and pathological variables. On the contrary to Bax, P53 correlated with Bcl-xL in all of cases (p = 0.042, r = 0.208), cancers without nodal involvement (N0) (p = 0.014, r = 0.361) and deeply invading cancers (pT3 + pT4) (p = 0.048, r = 0.212) that penetrated through muscularis propria and invaded other organs or structures.

Discussion/Conclusion: Lack of association between P53 and Bax could contribute to impairment of apoptosis in colorectal cancer cells. On the other hand, survival of colorectal cancer cells might be promoted and surprisingly it could be associated with overexpression of P53 due to positive correlations between P53 and Bcl-xL in colorectal cancers.
Epidemiology and clinical characteristic of Crohn’s disease in Polish population – Preliminary data

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Introduction: We analyzed several aspects of the epidemiology and clinical characteristic of Crohn’s disease in Polish population over 16 years using data from National Registry of Inflammatory Bowel Disease.

Methods: 1681 patients from 65 centres have been registered from September 2005. We have analyzed sex, domicile, education, family history, age, phenotype, coexistence of the other diseases, extraintestinal manifestations, smoking, medical treatment and surgical interventions.

Results: Disease tends to occur with higher frequency in urban areas among groups with secondary or higher education. There was no significant gender difference (males/females: 847/834, ratio 1.015). Family history was positive in 4.46%. With respect to age of diagnosis 7.0% were under 16, 66.5% between 17 and 40, 26.5% over 40. Disease location was as follows: terminal ileum 28.6%, colon 22.7%, ileocolon 20.1%, upper gastrointestinal 9.6%, 18.9% had upper gastrointestinal disease coexisting with other location. The predominant disease behavior among women was non-structuring and non-penetrating (40.6%) whereas among men penetrating disease predominated (37.9%). Rheumatoid arthritis and ankylosing spondylitis were the most prevalent coexisting diseases. Extraintestinal manifestations were present in 5.89%. Men more often than women had undergone at least one surgical intervention under the age of 40 (29.2% vs. 20.74% p < 0.001). There were more smokers among men than women (23.5% vs. 15.8% p < 0.001).

Discussion/Conclusion: In terms of age at onset and gender Polish data appear similar to other European countries. The predominant disease location is terminal ileum. Almost half of patients had undergone at least one surgical intervention.
Fecal calprotectin in children with autistic spectrum disorders

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Introduction: Autistic children often have gastroenterological disturbances and complains. Micro and macroscopic lesions in gut mucosa called “colitis autistica” are observed during endoscopy. Fecal calprotectin is a marker of inflammation and it is useful tool in distinguishing between organic abdominal disorders and functional disturbances of digestive system.

Aim of the study: The aim of the study was the assessment of fecal calprotectin concentration in children with autistic spectrum disorders (ASD) and with abdominal complains.

Methods: Fecal calprotectin concentration was measured in 26 children: mean age: 7.5 yr (3–17 yr): 9 (35%) girls and 17 (65%) boys. Fecal calprotectin concentration was measured in stool samples by ELISA using PhiCal Test by Calpro.

Results: 24 children had normal level of FC (1.9–44.99 mg/kg), 2 of children had insignificantly elevated FC levels (59.72 and 189.6 mg/kg). Normal value 0–50 mg/kg.

Discussion/Conclusion: Fecal calprotectin concentration is not increased in children with autistic spectrum disorders what could indicate there is no inflammation in gut mucosa. To find out the reason of complains from digestive system we need further examinations like motility examinations and/or hormonal tests.
Peutz-Jeghers syndrome (PJS) is an unusual hamartomatous polyposis of the gastrointestinal (GI) tract, with pigmentation around lips and macules on the buccal mucosa. The case of a 18-year-old man who presented with intussusception is reported. A polyp was found to be the cause of an invagination. Histologically it was a hamartoma. PJS is a rare syndrome inherited in an autosomal dominant pattern. Most patients have recurrent episodes of polyp induced bowel intussusception which requires repeated laparotomies. In addition, these patients have an increased risk of malignant disease in gastrointestinal and also non-gastrointestinal sites. To prevent cancer and short bowel syndrome, aggressive screening is recommended. Upper and lower endoscopy should be performed every two years from 10 years of age. Extraintestinal surveillance for cancers, including abdominal and pelvic ultrasound, as well as testicular and breast examinations once yearly should be introduced in the second decade of life.

Introduction: Peutz-Jeghers Syndrome (PJS) was discovered in 1921 by J.L.A. Peutz and later more fully described by H. Jeghers in 1944 (1, 2). It is a rare disease affecting about 1 in 25,000 individuals. Familial cases are genetically transmitted through families, and sporadic cases of PJS are diagnosed when there is no family history of the disease. In the familial cases of PJS, there is a 50% risk of genetic transmission of the carrier to his or her offspring (3). The disease risk is fairly distributed between the males and females, and there is no ethnic or racial predisposition to the disease (4). For those who are diagnosed with PJS, there is great variability in the symptoms of the disease. Some patients experience symptoms requiring minor clinical treatment while others undergo numerous hospitalizations. In addition, PJS patients are at increased risk for tumors of the colon, rectum, stomach, ovaries, and pancreas (5).

Case report: A 18-year-old man with no significant past medical history presented to the emergency department with a 3-day history of progressively worsening abdominal pain, nausea, emesis, and obstipation. On physical examination in the emergency department; his abdomen was tender and evidence of peritonitis. Family history was significant for “intestinal problems” in 2 uncles. There was obviously found the brown to black, freckle-like hyperpigmented macules on the buccal mucosa, nose, lips, and skin of the perioral area (figure1-2-3). Results of laboratory tests were within normal limits, except for an amylase level of 254 U/L (reference range, 25–115 U/l), and a mildly elevated white blood cell count of 13 000/µL (reference range, 4000–11,000/µl). Multiple hydroaeric fluid was seen in Plain X-Ray. The patient was taken to the operating room for abdominal exploration. Surgical intervention consisted of partial jejunectomy with primary anastomosis after failed attempts at reduction; enterotomy removed the remaining palpable masses from the small intestine. Pathologic inspection of the ischemic segment of resected jejunum revealed 5 cerebriform-like polyps ranging from 0.5 to 4.5 cm (figure 4, 5), the largest of which served as the lead point of intussusception. Enterotomy produced 4 additional cerebriform-like polyps ranging from 0.5 to 2.5 cm; 3 of these polyps were near the ligament of Treitz, and 1 was in the distal ileum.
Discussion: Peutz-Jeghers syndrome is a rare, autosomal dominant inherited trait characterized by the presence of gastrointestinal hamartomatous polyps and mucocutaneous pigmentation. Intussusception, intestinal obstruction and bleeding frequently occur in patients with this syndrome and may lead to multiple laparotomies. In addition, these patients are at risk of gastrointestinal and extraintestinal malignancies (6). Accurate preoperative diagnosis, intraoperative endoscopic polypectomy and careful postoperative surveillance will reduce the number of laparotomies, complications and benefit these patients (7). We herein report a case of jejunojejunal intussusception induced by a Peutz-Jeghers polyp. The management and literature are reviewed.

Peutz-Jeghers Syndrome (PJS) is an autosomal dominant heritable polyposis syndrome characterized by a triad of findings, including multiple large hamartomatous polyps of the gastrointestinal tract, mucocutaneous melanocytic macules, and an increased incidence of neoplastic disease, both within and outside the gastrointestinal tract.

In 1998, the PJS gene was localized to chromosome 19p13.3 by linkage analysis performed by Jenne, et al. Recently, the PJS gene at this locus was identified by Mehenni, et al, as LKB1, a ubiquitously-expressed serine-threonine kinase. The latter research group identified more than seven novel mutations in the LKB1 gene that caused loss of kinase function. It is likely that this kinase defect underlies the increased incidence of benign and malignant neoplasms seen in PJS patients (8).

Key words: intussusception, Peutz-Jeghers syndrome.

References:

A very rare cause of chronic constipation in an adult patient

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Introduction: Hirschsprung’s disease (HD) is characterized by aganglionosis, which mainly occurs in rectum and distal sigmoid colon. Typical HD is diagnosed seldom in adulthood and segmental involvement is very rare.

Case report: 37-year-old man suffered from refractory constipation for twenty years. He had no response to laxative treatment. He could defecate only once a week and frequently needed enema for defecation. He had undergone laparotomy due to intestinal obstruction in the childhood, but no specific pathology had been found. On admission, physical examination was normal. Routine laboratory evaluation, including complete blood cell count, urine analysis, biochemical tests and thyroid tests, was normal. Barium enema showed an annular stenotic segment of the rectosigmoid colon 8 cm in length, which was starting 10 cm above anal circulation and showing dilated colon above the stenotic segment. Distal rectum was normal (Figure 1). On colonoscopy, stenotic segment had no haustratum pattern and lumen of the proximal colon was dilated; mucosa of the whole colon including stenotic area was normal. Biopsy specimen from stenotic zone showed no pathologic findings. Rectoanal manometric examination was also in normal limits. The narrowed segment of the rectum was resected. In one year follow-up period, the patient had normal defecation without need of laxatives.

Discussion: Most of the HD patients are detected before the age of 5 years. Some patients have not been diagnosed until adulthood due to the relatively short segment of involved colon. The diagnosis of HD is rarely considered in adults but could represent 2% of chronic refractory constipation. Segmental involvement occur less than 10% of the all patients with HD and segmental involvement of HD may occur in any part of bowel. Once the diagnosis is confirmed, the basic treatment is to remove the poorly functioning aganglionic bowel and create an anastomosis to the distal rectum with the healthy innervated bowel. Segmental HD is a very rare clinical entity which should be kept in mind among the differential diagnosis of constipation even in adults.
An unusual complication of colonoscopy

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Introduction: Ischemic colitis is a characteristic disease of the large intestine caused by varying degrees of anatomic or functional vascular insufficiency. Colonoscopy is the gold standard for identification of colonic ischemia. However, very rarely colonoscopy itself may induce ischemic colitis under certain condition.

Case report: A 34-year-old woman who had iron deficiency anemia was admitted to our Gastroenterology Department for colonoscopic examination. Colonoscopy was completely normal. The duration of procedure took a long time because of desire to achieve of terminal ileum examination. Seven hours after the colonoscopy, she developed bloody diarrhea and mild abdominal pain. She had readmitted to hospital. Abdominal examination was normal other than lower abdominal tenderness. Hemoglobin didn't decrease. Stool microscopy showed erythrocytes, and culture revealed normal flora. A plain abdominal radiography and an abdominal ultrasonography were normal. Colonoscopy promptly was performed showing patchy hemorrhagic, edematous, and thickened mucosa, with superficial ulceration extending from proximal rectum to the splenic flexure. Histological analysis of lesion biopsy was compatible with ischemic colitis. Tests for anti-nuclear Antibodies, anti-DNA antibodies and anti-mitochondrial antibodies were negative. The patient was followed as out-patient since she refused hospitalization. Abdominal pain and bloody stool improved gradually in two days. At the five day, colonoscopy was repeated demonstrating normal colon mucosa. She was free of complaint at the follow-up four months.

Discussion/Conclusion: We conceived three mechanisms for colonoscopy-induced ischemic colitis in the present case. First, overdistention of large bowel with air might reduce colonic blood flow and thus, caused a shunting of blood from the mucosa to the serosa, consequently producing colon ischemia. Second, mechanical effect of colonoscope body on colon wall may lead to diminished mucosal blood flow, particularly when procedure duration is long. Third, transient tortion of colon vascular system resulting from exaggerated pulling back and shortening might reduce blood flow.

Prognosis in the colonoscopy induced ischemic colitis has been usually reported as well. Nevertheless, ischemia with necrosis may extend into deep layers of the bowel wall and impair colonic barrier against microorganisms. Thereby it may be the cause of mortality and morbidity, particularly in patients with co-morbid diseases, immunodepressive disorders or companseted mesenteric ischemia. In those patients, colonoscopy should be carefully achieved, with giving small amount of air as far as possible, shortening the procedure time and finally with avoiding from exaggerated pull forces and shortening of colonoscope. Additionally, hypotensive effects of sedative drugs and bowel preparation agents should be kept in mind.
Collagenous gastritis: A rare cause of abdominal pain (case report)

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Case: A 38-year-old woman complained of recurrent abdominal pain 18 years duration. She had a history of epigastric pain 16 years ago and was diagnosed as chronic atrophic gastritis by endoscopic examination. She had undergone many courses of empirical therapy with omeprazole, sucralfate and corticosteroids. A thorough physical examination, complete blood count and routine serum chemistries were normal. Upper gastrointestinal endoscopy showed diffuse nodularity (diffuse cobblestone appearance) erythema and exudates of the gastric mucosa at the antrum and pyloric channel but no abnormalities in the esophagus or duodenum. We reviewed the endoscopic report and biopsy of 16 years previously and they suggested that there was already mucosal nodularity in the gastric body and antrum at that time. The first biopsy in 1991 revealed that collagenous gastritis at the antrum mucosa. There were dense lymphocytic infiltration and the findings of reactive gastropathy. Helicobacter pylori was not detected. In the last gastric biopsy, collagenous gastritis was still persisting. The other histological finding were similar with the findings of the first biopsy. Biopsies of the duodenum were normal, with no collagenous deposit.

Conclusion: Collagenous gastritis is a rare condition of unknown etiology, pathogenesis and long-term prognosis. Gastroenterologists need to be aware of this condition when evaluating a patient with epigastric pain, anemia or chronic diarrhea particularly when endoscopy reveals nodularity of gastric mucosa. Dramatically thickened gastric subepithelial collagen is the distinct histological feature. The identification, reporting and long-term follow-up results of cases will shed more light on this puzzling condition.
Sonographic asseessment of functional digestive disorders

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Functional gastrointestinal complains are common with prevalence rates ranging from 20–40% of population. Picture of disease often is atypical. Sonography as non-invasive, simple method usually precedes others clinical examinations. To exclude of organic changes in abdominal organs, is the strong diagnostic suggestion for suspicion of functional cause of complains.

We examined 50 patients suffering from advanced functional digestive disorders (long lasting anamnesis, negative physical and clinical observation). USG study included: morning fasting examination, assessment of visceral vessels flow and postprandial re-examination. Before usg examination patients did not take medicaments. Usg symptoms were compared to groups of 40 healthy patients and to 40 non-functional digestive diseases patients.

Results: 34 patients of functional group had not abnormality in usg examination. USG symptoms of 16 patients classified as abnormal or atypical. There were: enlargement of gallbladder, weak or lack gallbladder contraction, excessive hypertonic postprandial gallbladder reaction, incomplete urinary bladder evacuation.

Comments: Hypotonic or lack gallbladder postprandial reaction has significance for gall stone formation. Some gastrologists points importance of bile sludge presence inside lumen in usg diagnostic analysis for gallbladder dysfunction. Incomplete urinary evacuation favors urinary infections.

Conclusions: The majority of functional digestive disorders patients has not pathological symptoms possible for detect by usg methods. Abnormal gallbladder and urinary bladder reactions sometimes accompanies different forms of functional gastrointestinal diseases. USG abnormality met in functional gastrointestinal diseases has importance for treatment and grade of disease.
Treatment difficulties in extensive Crohn’s disease with pancolic, esophageal, buccal and anal affliction

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Introduction: Upper gastrointestinal tract involvement is a rare condition associated with inflammatory bowel disease. It is characterized by a male predominance, young age at diagnosis, and usually with a protracted courses, with many treatment difficulties.

Methods: We present a case of a 33-year-old woman, diagnosed with IBD first interpreted as ulcerative colitis with pancolic affliction and bleeding diarrhea as major sign. 5-ASA and corticoid treatment was not effective the patient undergoing coloproctectomy for toxic megacolon. The evolution knew 2 years of well being marked by a pouchitis episode and an anal polyp endoscopically removed. The Crohn’s diseases diagnose was established by two ano-vaginal fistulas closed after 3 gluing sessions. The disease progressed, gastric and perianal lesions appeared, followed by esophageal, buccal and perioral lesions, producing dysphagia and weights lose.

Results: Many therapeutic options were applied, the 5-ASA and corticoids weren’t effective. Immunomodulator and immunosupressor treatment followed: Azathioprine produced pancreatitis, anti-TNFα agents obtained an initial response to Infliximab but relapse after 12 cures, Adalimumab and hydrocortisone association were unsuccessfully, cyclosporine, leflunomide, cyclophosphamide two 750 mg pulses spaced by 4 weeks without response. Next options were two hemapheresis sessions. Having no clinical evidence of amelioration the next proposition was the bone marrow autographt preceded by stimulation in order to harvest stem cells.

Discussion/Conclusion: Particularities: Initial confusion with ulcerative colitis, locations of Crohn’s lesions, the numerous therapeutic measures and the adverse effects to consider including sterility risk in young female without children.
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