David Al Dulaimi

Department of Gastroenterology, Alexandra Hospital, Redditch, UK

Varshosaz J et al. ***Development and Evaluation of a Novel Pellet-Based Tablet System for Potential Colon Delivery of Budesonide.*** *Journal of Drug Delivery 2012;2012:1-7.*

Although budesonide is important for the localised treatment of inflammatory bowel disease, current oral formulations have a low efficacy against ulcerative colitis (UC) due to inadequate delivery at disease sites. In this study a pH- and time-controlled colon-targeted pellet based delivery system of budesonide was designed using an in vitro model of the gastrointestinal tract. An 18 h extended drug release formulation with 6 h delay in onset was assumed suitable for colon targeting. The most promising preparation of budesonide-loaded pellets were coated with 12% (w/w) xanthan gum, 30% (w/w) mixture of Eudragit NE: Eudragit L30D55 (7:3 ratio) and 25% (w/w) eudragit FS 30D. This preparation protected drug release in simulated stomach and small intestine and 83.35% ± 2.4% of budesonide was released at 24 h. Furthermore the drug release profile was maintained after three months storage under accelerated stability test conditions. Although the designed pellet offers exciting potential, the need for in vivo investigation is recognised, particularly since colonic pH and bowel transit time may vary in the presence of active UC.

Lee JH et al. ***Reflux Episode Reaching the Proximal Esophagus Are Associated with Chronic Cough.*** *Gut and Liver 2012;6:197-202.*

Multichannel intraluminal impedance combined with pH monitoring (MII/pH monitoring) is considered the current, most sensitive tool for diagnosis and characterisation of gastroesophageal reflux disease (GERD). This two year prospective study of 70 patients who were referred to a Korean hospital with suspected GERD evaluated the diagnostic usefulness of MII/pH monitoring over a 24 h period. Medications with effects on oesophageal motor function and gastric acid secretion were discontinued at least one week prior to monitoring. Forty-five patients (64.3%) were diagnosed with GERD of which 11 patients (15.7%) had pathologic acid reflux by pH data. The remaining 34 patients (48.6%) had pathologic bolus exposure by impedance which would have been overlooked had only conventional pH monitoring been used. This demonstrates the diagnostic usefulness of MII/pH monitoring in patients with suspected GERD.

There was no significant difference in MII/pH monitoring results between patients with/without typical gastroeosophageal reflux symptoms, non-cardiac chest pain or globus. Patients with chronic cough (n=30) had a greater DeMeester score (8.78 vs 6.66; p=0.009), % acid exposure time (2.53% vs 1.89%; p=0.007), % acid bolus exposure time (1.69% vs 0.93%; p=0.027), distal acid reflux episodes (34.0 vs 15.6; p=0.015) and proximal acid reflux episodes (16.9 vs 7.8; p=0.030) compared to patients without chronic cough. Although a strict temporal relationship linking reflux events documented by MII/pH monitoring and coughing episodes could not be identified, these results highlight an important association between chronic cough and reflux episodes at the proximal and distal oesophagus.

Haque S, Genta RM. **Lymphocytic oesophagitis: clinicopathological aspects of an emerging condition.** *Gut 2012;61:1108-1114.*

Lymphocytic oesophagitis (LyE) is a rare condition that to date has been poorly characterised. This single centre study of 129,252 patients who underwent oesophagogastroduodenoscopy with biopsy from July 2009 to December 2010 determined the prevalence of LyE and investigated associated demographic, endoscopic and clinical findings. Criteria for the histopathological diagnosis of LyE, established in a pilot study, included (1) dense lymphocytic infiltrates in the peripapillary oesophageal squamous mucosa; (2) peripapillary spongiosis involving the lower two thirds of the epithelium; and (3) absence of significant neutrophil or eosinophilic infiltrates.

The prevalence of histopathologically diagnosed LyE was 0.92 per 1000 patients. Endoscopically, appearances suggestive of eosinophilic oesophagitis (EoE) (33.6%), normal oesophageal appearances (22.6%) and oesophagitis (18.5%) were identified in patients with LyE. Compared to those with normal oesophageal biopsies, patients with LyE were older (median age 63 vs 55 y; p<0.001), presented more often with dysphagia (52.9% vs 33.0%; p<0.0001), less often with gastroesophageal reflux disease (GERD) (18.5% vs 37.4%; p<0.01) and were more frequently suspected of having EoE (31.1% vs 26.3%; p<0.01). There was no significant difference between the clinical presentation (dysphagia or GERD) of patients with LyE or EoE although LyE was more prevalent in older females compared to EoE which predominantly affected younger males (p<0.001). Although the clinical significance and aetiology of LyE remains uncertain, increased awareness and careful reporting of cases is important to reveal clinical and aetiological relationships.

Farahmand F et al. **Prevalence of Occult Celiac Disease in Healthy Iranian School Age Children.** *Archives of Iranian Medicine 2012;15(6):342-345.*

This cross-sectional study, performed from June 2006 to August 2008, screened 634 randomly selected, healthy, school children from Tehran (50% males, mean age: 12.8 years, range: 7 to 18 years) for celiac disease using serum IgA and IgA anti-tissue transglutaminase antibody (tTG) levels. Children with positive tTG results underwent endoscopic duodenal biopsy to confirm a diagnosis of celiac disease. There were no children with IgA deficiency. The prevalence of celiac disease in healthy Iranian school age children was 0.5% (female to male ratio 2:1) compared to a background population prevalence of 0.6% reported in healthy blood donors in Iran. All children with celiac disease were asymptomatic however were treated with a gluten-free diet. The authors suggest that screening for celiac disease in healthy Iranian school age children may be justifiable by reducing the risk of disease complications by early initiation of a gluten-free diet.

Mahmodlou R, Mohammadi P, Sepehrvand N. **Colorectal Cancer in Northwestern Iran.** *ISRN Gastroenterology 2012;2012:1-4.*

This cross-sectional study determined the clinicopathological features of 546 patients from the West Azerbaijan province of Iran with pathological diagnosis of colorectal cancer (CRC) made between 2001 and 2008. The mean age at CRC diagnosis was 55.2 ± 11.5 years with 23% of patients aged under 40 years old. Rectal bleeding (26%), abdominal pain (25%) and large bowel obstruction (23%) were the most common initial presenting symptoms. 26% of CRC patients presented with an 'acute abdomen' secondary to bowel perforation or obstruction. The tumour was

located in the rectum in 44.5% of cases. Histologically, adenocarcinoma and lymphoma were diagnosed in 95% and 4% of cases respectively. Regarding the TNM (tumour, lymph nodes, metastasis) stage of CRC at presentation, 6% of patients were in stage I, 37% in stage II, 33% in stage III and 24% in stage IV.

Compared to patients from more developed countries, patients from the West Azerbaijan province presented with CRC at a younger age and with more advanced TNM stage. This may reflect specific hereditary characteristics of patients from this region and requires future investigation. In addition to alerting physicians to many of the clinicopathological features, particularly the young age, that CRC can present with, the useful findings of this study may aid development of a national CRC screening programme in Iran.

Kisseleva T et al. **Myofibroblasts revert to an inactive phenotype during regression of liver fibrosis**. PNAS 2012;109:9448-9453.

Myofibroblasts are rapidly generated from activated hepatic stellate cells (HSCs) to produce fibrous scar in hepatotoxic liver fibrosis. In the absence of fibrotic stimulus, regression of fibrosis is associated with complete disappearance of myofibroblasts although their exact fate is poorly understood. This study characterised myofibroblasts and HSCs during recovery from carbon tetrachloride (CCl_4)- and alcohol-induced liver fibrosis in a mice model using Cre-LoxP-based genetic labelling of myofibroblasts.

The authors demonstrated that during recovery from CCl_4- and alcohol-induced liver fibrosis, activated HSCs/myofibroblasts are cleared by two mechanisms: (1) cell death by apoptosis; and (2) down-regulation of fibrogenic genes to acquire an inactive phenotype similar to, but distinct from, original quiescent HSCs. These inactivated HSCs, which constituted ~50% of total HSCs in the liver one month after reversal of liver fibrosis, more rapidly reactivate into myofibroblasts with further fibrogenic stimuli compared to quiescent HSCs. In support of this a previously injured and recovered liver develops more fibrosis compared to a naive liver. Although the factors influencing whether activated HSCs undergo apoptosis or inactivation remain unclear, this study found that transient increased expression of anti-apoptotic heat shock proteins 1a/b may promote survival of inactivated HSCs during recovery from fibrosis.

Keshavarzi B, Moore F, Najmeddin A, Rahmani F. ***The role of selenium and selected trace elements in the etiology of esophageal cancer in high risk Golestan province of Iran****. Sci Total Environ 2012;433c:89-97.*

This study investigated the relationship between the concentration of several trace elements in cultivated soils, sediments, loess deposits and grain and the incidence of esophageal cancer in 45 villages in the Golestan province of Iran. Villages were classified into two groups based on esophageal cancer incidence in their local population. Increased concentrations of selenium, antimony and strontium and decreased concentrations of zinc in soils, sediments, loess deposits and grain were associated with villages classified as having a high incidence of esophageal cancer.

Papers were prepared by:

Drs Luke Materacki and **Ishfaq Ahmad,** Department of Gastroenterology, Alexandra Hospital, Worcestershire, UK