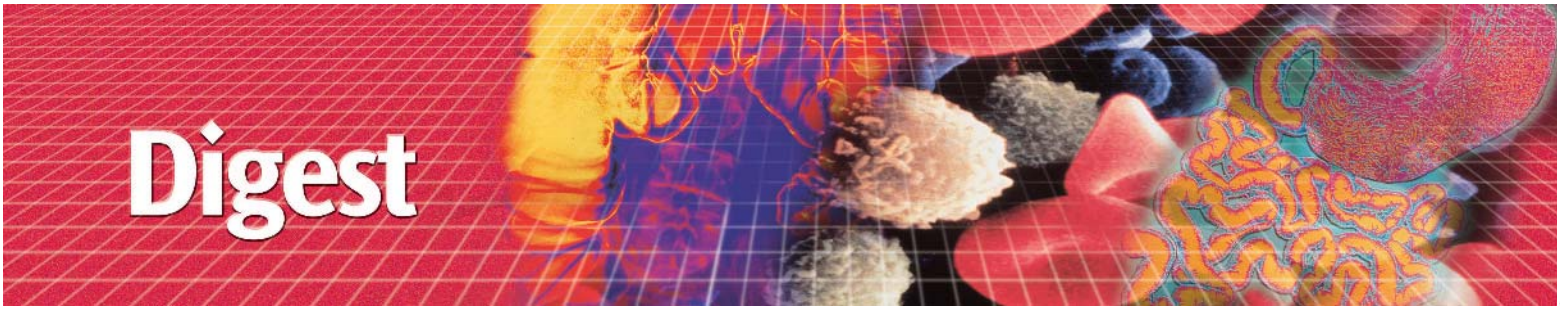
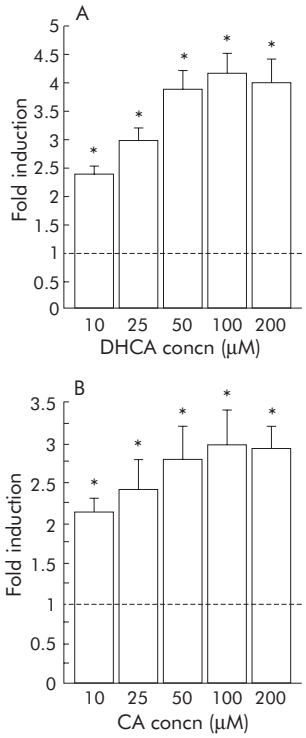


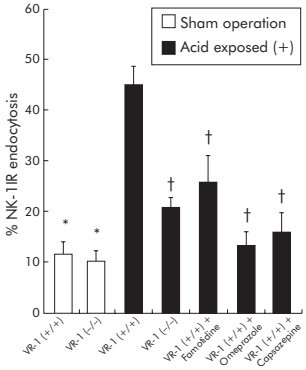
Robin Spiller and Alistair Watson, *Editor and Deputy Editor*



BILE SALTS IN GASTRO-OESOPHAGEAL REFLUXATE STIMULATES EXPRESSION OF CDX2 WHICH CHANGES SQUAMOUS EPITHELIUM INTO INTESTINAL COLUMNAR EPITHELIUM

Barrett's oesophagus is a condition in which the squamous epithelium of distal oesophagus is replaced by columnar epithelium more characteristic of the intestine. This phenomenon dramatically increases the risk of adenocarcinomas of the oesophagus and is largely caused by gastro-oesophageal reflux. Some investigators have noticed this change is reminiscent of the development of the gut in the embryo. Factors in the mesoderm cause the endoderm to differentiate into midgut and hindgut. The precursor of the stomach is seen as the "default" phenotype which must be actively converted to midgut or intestinal phenotype. Cdx2 is a transcription factor that causes activates a family of genes causing the stomach precursor to change into the intestine. It is therefore an interesting hypothesis that Cdx2 might be responsible for the conversion of squamous epithelium to columnar epithelium of the intestine. In this article the authors demonstrate that expression of Cdx2 is stimulated by cholic acid and dehydrocholic acid. These components of gastro-oesophageal refluxate stimulate the binding of NFκB to the promoter causing increased transcription of Cdx2 as shown in adjacent fig. Furthermore transfection of primary cultures of normal squamous oesophageal epithelial cells causes them to express MUC2, a protein characteristic of intestinal epithelium. This study gives important new insights into the pathogenesis of Barrett's oesophagus. It also highlights the importance of reduction of bile salt levels in gastro-oesophageal refluxate in the treatment of Barrett's oesophagus.

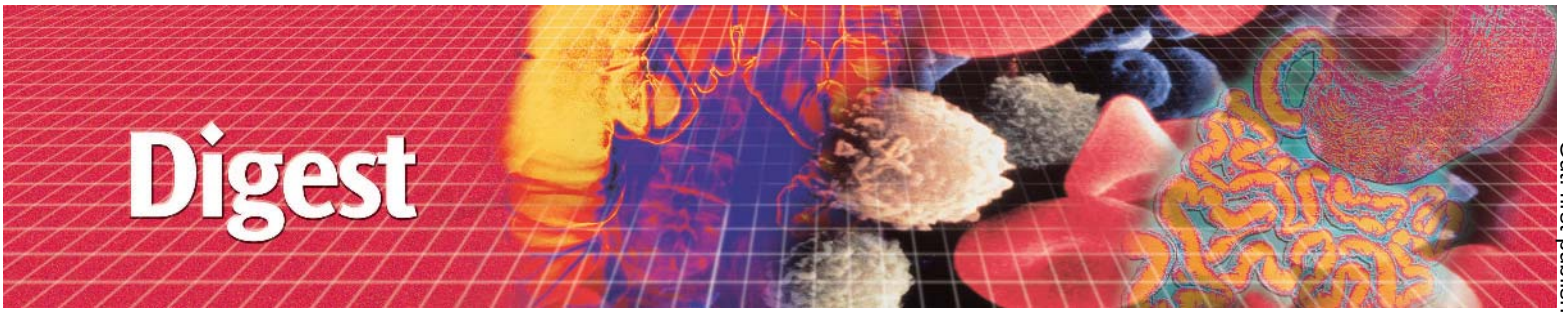
See p 16

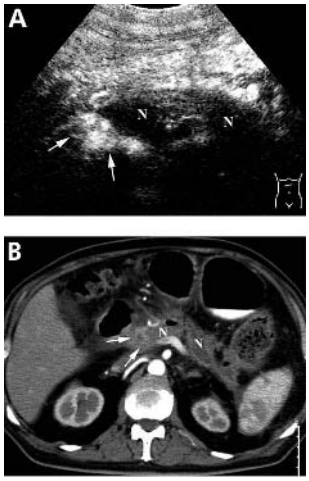


NEUROGENIC INFLAMMATION IN THE OESOPHAGUS

Neurogenic inflammation caused by the release of substance P (SP) from the terminals of primary sensory neurones is well recognised by dermatologists. This paper shows it may also be relevant to gastroenterologists. The gastro-oesophageal junction is particularly well supplied with SP containing neurones. Tissue injury releases SP from these afferent neurones by activating the vallinoid receptor subtype 1 (VR1) also known as TRPV1. This receptor is activated by heat, H+, and capsaicin, and is responsible for the burning sensation produced by tissue injury. The authors set out to test the hypothesise that activation of VR1 on mucosal sensory nerve terminals by refluxed gastric acid would increase SP release and thus cause neurogenic inflammation. They tested this by using mice lacking the VR1 receptor (VR1−/−). Acute reflux oesophagitis was induced under anaesthesia by ligating the stomach so that gastric acid refluxed into the lower oesophagus. The animals were sacrificed at 5 h and showed acute oesophagitis with ulceration and acute inflammation. Injury in VR1−/− mice was a half to third that of the wild type animals. Blocking VR1 with capsazepine reduced tissue injury with a benefit similar to that produced by a more conventional treatment, namely omeprazole. SP release causes receptor binding and internalisation of the neurokinin 1 receptor (NK-1R) so that receptor endocytosis can be used as a marker for SP release. There was a striking reduction of receptor endocytosis in the VR1−/− mice similar to that seen with acid suppression or the VR1 antagonists capsazepine (see fig). These studies strongly suggest that refluxed acid acts via the VR1 to induce neurogenic tissue injury and suggests alternative ways of treating this common condition.

See p34

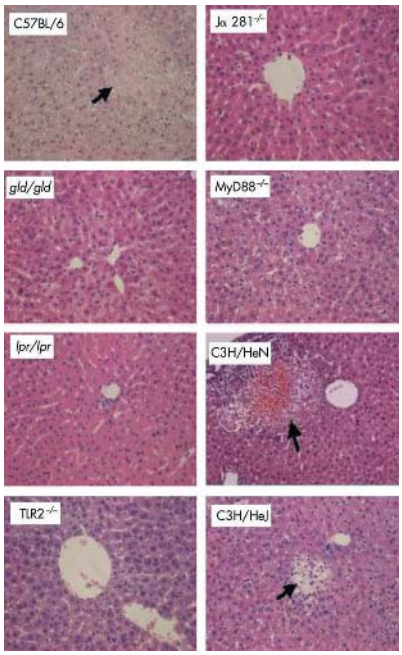




USE OF A NOVEL ULTRASOUND TECHNIQUE TO ASSESS SEVERE ACUTE PANCREATITIS

Early assessment of the presence of necrosis is important in assessing patients with acute pancreatitis since it allows clinicians to focus on the patients with the worse prognosis. Currently this is done by CT but this study suggests that a novel echo-enhancing technique allows ultrasound to compete favourably. Gas filled micro-bubbles are infused intravenously to generate bright images in the echo-enhanced ultrasound image. The current study compared this technique with CT, assessing its sensitivity in detecting necrosis and other features of severe pancreatitis at 72 h. Fig A shows the ultrasound image in a patient 20 h after admission with severe necrotising acute pancreatitis. There are several areas of necrosis (labelled N) in the body and tail while the head (arrows) shows a bright image indicating good perfusion. Fig B shows a CT scan performed immediately afterwards showing necrotic (N) and perfused areas (arrows). Ultrasound compared favourably, detecting all 8 out of 31 patients who had pancreatic necrosis at CT, with just 2 false positives. Ultrasound has some advantages over CT including both cost and the ability to assess blood flow by means of the Doppler technique. Another advantage is the ability to guide interventions including percutaneous drainage of abscesses. Current numbers are small and plainly greater experience is needed, but this looks a promising advance in management.

See p74



TOLL-LIKE RECEPTORS 2 AND 4 AND FAS INDUCED APOPTOSIS ARE INVOLVED IN THE PATHOGENESIS OF SEPSIS FOLLOWING BILE DUCT LIGATION

Extrahepatic cholestasis is often accompanied by severe sepsis caused by the translocation of bacteria from the gut lumen to the portal and systemic circulation. Factors causing bacterial translocation include diminished bile salt secretion lowering mucosal integrity and impaired phagocytes function. Diminished host defence exacerbates sepsis further. Mammalian toll homologues are expressed in monocytes, macrophages, and epithelial cells. They recognise bacterial and viral components and activate are host innate immune responses. Recent studies have suggested that signalling from toll-like receptors (TLRs) can also in some circumstances contribute to liver injury. In the present study the authors used a variety of mouse strains with abnormalities of TLRs and Fas signalling pathways to dissect their contribution to hepatic injury and host defence after bile duct ligation. They found that B cells are rapidly depleted from Peyer's patches following bile duct ligation. This is due to apoptosis of B cells mediated by MyD88 dependent TLR 4 and Fas signalling. By contrast hepatocyte death is mediated by TLR2, TLR4, and Fas signalling as shown in the adjacent fig, which shows necroinflammatory foci (arrows) in the liver of various genetically modified mice. Necrosis was not seen in those with defects in TLR2 (TLR−/−), TLR-4 (MyD88−/−), and Fas signalling pathways (gld/gld, lpr/lpr) nor in those deficient in NKT cells (Jalpha281−/−). These studies point to the complex mechanisms involved in sepsis and suggest therapeutic targets for future therapy.

See p105

might make the handbook marginally more user friendly. It would be easy to recommend this handbook to those wanting a quick entry into the world of meta-analysis. The outputs produced would not be wrong in statistical terms. But unless one wanted to make use of the less conventional outputs (and this would generally only apply to experienced reviewers and analysts anyway), it would make much better long term sense to become familiar with the Cochrane software and the entire systematic review package.

D Forman

NOTICE

Joint Meeting: International Association of Pancreatology and American Pancreatic Association

This meeting will be held on 1–4 November 2006 and the CME sponsor is American College of Surgeons. The meeting will be heald at Westin Chicago River North Hotel, Chicago, Illinois, USA. For more information please contact APA Headquarters, 45 High Valley Drive, Chesterfield, MO 63017; http://www.american-pancreatic-association.org/; email: American-pancreatic-association@lettuceplanet.com; tel: +1 314 210 2904; fax: +1 314 754 9515.

CORRECTION

doi: 10.1136/gut.2005.08195corr2

In the March supplement to *Gut* (*Gut* 2006;**55**(suppl 1)) the affiliation of the author Dr V Villanacci was provided incorrectly. His correct address is: 2nd Department of Surgical Pathology, Spedali Civilli, Brescia, Italy.

EDITOR'S QUIZ: GI SNAPSHOT

Answer

From question on page 742

A differential included hydatid cyst and cystic tumour metastasis. The cyst was aspirated under computerised tomography (CT) guidance which showed endometrial glandular and stromal elements confirming a diagnosis of endometrial cyst.

Clinical features are non-specific. Theories behind the pathogenesis include coelomic metaplasia and lymphovascular dissemination. Imagings show a 12 cm loculated cystic lesion with irregular outline in the posterior aspect of the right lobe of the liver. Ultrasound and CT findings in endometrial liver cysts are non-specific and may include cystic and solid components, septations, loculations, and calcifications. On magnetic resonance imaging, endometrial implants usually demonstrate signal intensity similar to normal endometrium on T1 and T2 weighted images. A CT scan repeated during the menses is valuable in suspected pulmonary endometriosis.[1] It is unknown if the same approach would benefit diagnosis in suspected hepatic endometrial cysts. Although there is no literature to support or refute, we wonder if repeating a CT scan coincident with menses might help in the diagnosis of a suspected hepatic endometrial cyst. Although surgery is the treatment of choice, gonadotrophin releasing hormone analogues have been used for treating pulmonary endometriosis and may prove beneficial in hepatic endometrial cyst.

Teaching point: This differential should be kept in mind when dealing with a hepatic cyst of unknown origin in a female, especially with history of endometriosis or pelvic surgery.

doi: 10.1136/gut.2005.066498

REFERENCE

1 **Terada Y**, Chen F, Shoji T, *et al*. A case of endobronchial endometriosis treated by subsegmentectomy. *Chest* 1999;**115**:1475–8.