POST INFLAMMATORY VISCERAL HYPERSENSITIVITY DEPENDS ON NERVE GROWTH FACTORS AND THE SENSORY NEUROPEPTIDE CGRP

Visceral hypersensitivity is a common feature of functional diseases, with a variable central and/or peripheral component. Colitis induced by the installation of trinitrobenzene sulfonic acid (TNBS) is a frequently used model of peripherally driven hypersensitivity. Antibodies to nerve growth factor are known to inhibit post inflammatory hypersensitivity in both visceral and somatic territories. Calcitonin gene related peptide (CGRP) is expressed in visceral afferents and increased in TNBS colitis. This study used antibodies to nerve growth factor (NGF), brain derived nerve growth factor (BDNF), and antagonists to CGRP to examine their role in visceral hypersensitivity. TNBS induced a visceral hypersensitivity which was blocked by BDNF antibodies and mimicked in a dose-dependent fashion by intraperitoneally injected BDNF. This hypersensitivity could be inhibited by a CGRP antagonist, leading the authors to conclude that both NGF and BDNF are key mediators of the hyperalgesic effect of inflammation and act through CGRP as a final common pathway.

See p 940

SUBCLINICAL INFLAMMATION MAY ACCOUNT FOR ABNORMAL MUCIN IN UNAFFECTED MONOZYGOTIC TWINS WITH IBD

Previous evidence of abnormal mucin in healthy monozygotic twin siblings of patients with ulcerative colitis (UC) suggested that genetically determined alterations in mucin might impair the mucosal barrier and be a risk factor for UC. The current study confirmed increased expression of the oncofetal Thomsen-Friedenreich (TF) carbohydrate antigen in mucins in 16 unaffected twins. However, the abnormal mucin was found to be localised to the surface epithelium and not in the crypt cells, suggesting that this was an acquired rather than genetic abnormality. Careful histological examination showed no increase in inflammatory cells in the uninfected twins, however, activated NF-kB was identified in all but one. Furthermore, there was a strong correlation between expression of TF and NFκB. This refutes the original idea but confirms other studies suggesting that unaffected relatives often show subclinical “pre-inflammatory” changes. Determining what prevents them from developing full blown clinical disease remains a key question for IBD researchers.

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WIRELESS CAPSULE ENDOSCOPY V ILEOCOLONOSCOPY FOR THE DETECTION OF RECURRENT CROHN’S DISEASE

Wireless capsule endoscopy (WCE) has the advantages over ileocolonoscopy that it visualises the entire small intestine, can detect small lesions, does not require sedation, and is well tolerated by patients. However, the role WCE plays in the detection of recurrence of Crohn’s disease following resection compared with ileocolonoscopy has not been evaluated. In this study WCE was compared with ileocolonoscopy in patients six months after small bowel resection for Crohn’s disease. The sensitivity for WCE was between 62% and 76% with a specificity between 90% and 100%. Lesions were detected outside the range of ileocolonoscopy in 66% of patients. The authors conclude that WCE is less sensitive than ileocolonoscopy, but recommend further study to determine the clinical value of detecting disease outside the range of ileocolonoscopy.

See p 978
CANCER RISK IN PATIENTS WITH MUTATIONS IN LKB1

Germline mutation of the tumour suppressor gene LKB1 (a serine/threonine kinase) causes Peutz-Jeghers syndrome. Patients have an increased risk of cancer, however, previous studies have been on patients recruited on the basis of a clinical diagnosis and not mutation of LKB1, leaving the possibility of misdiagnosis. In this study the cumulative risk of cancer was evaluated in 149 patients with the LKB1 mutation. There was an age-related increase risk of cancer of 6% at age 30, rising to 67% at age 60. Most cancers occur in patients with a mutation in exon 6. Most cancers occur in the gastrointestinal tract with breast and gynaecological cancers also being found.

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COMPARISON OF PET WITH CT SCANNING IN THE STAGING OF COLORECTAL CANCER

Fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) is the most sensitive imaging modality for the detection of recurrent or metastatic colorectal cancer. However, the efficacy of FDG-PET in the staging of primary colorectal cancer has not been evaluated. In the study the value of FDG-PET has been compared with whole body multidetector helical tomography (MDCT) has been compared using histopathological diagnosis as the gold standard. FDG-PET had an accuracy of 59% compared with 62% for MDCT. Of interest, macroscopic diagnosis at surgery was superior to both imaging techniques with an accuracy of 70%. It is concluded that for primary staging of colorectal cancer FDG-PET offers no advantage over MDCT. Moreover, MDCT can image the whole body much faster that FDG-PET.

See p 1007

HEPATIC VENOUS DYSREGULATION CONTRIBUTES TO BLOOD VOLUME POOLING IN CIRRHOTIC RATS

Peripheral arterial vasodilatation is often quoted as the explanation as to why patients with cirrhosis have an impaired response to infused fluid. However, most circulating blood lies in the venous system, particularly the splanchnic venous bed, hence the relevance of this study. The authors used a combination of methods including intravital microscopy to examine changes in hepatic presinusoidal and post sinusoidal venules in response to haemorrhage, mannitol infusion and vasoconstrictor and vasodilator drugs. Cirrhotic rats showed an increased diameter of presinusoidal and post post sinusoidal venules and an increased hepatic weight. By all these measures cirrhotic rats showed decreased responsiveness to the vasoconstrictor effect of norepinephrine and the β-adrenoreceptor agonist terbutaline. The vasoconstrictor response to haemorrhage was also impaired while the dilation in response to mannitol infusion was increased. Both these effects appear to be mediated by nitric oxide because they were impaired by blocking nitric oxide pathways with L-NAME (N-nitro-L-arginine methyl ester).

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