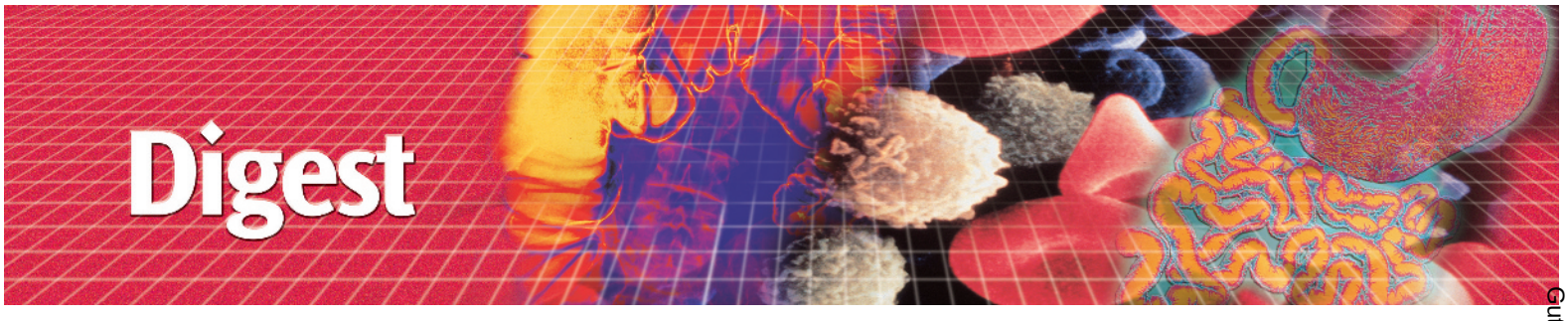

Emad El-Omar, *Deputy Editor*

Multivariate analyses for new-onset dyspepsia at 10 years using the British Society of Gastroenterolgy definition.

Variable	Adjusted OR (99% CI)	p Value
Body mass index at 10-years	1.05 (1.02 to 1.08)	<0.001
Quality of life		
High	1.0	
Medium	1.6 (1.1 to 2.2)	0.001
Low	2.6 (1.9 to 3.71)	<0.001
Irritable bowel syndrome at baseline		
No	1.0	
Yes	3.1 (1.5 to 6.4)	<0.001

INITIAL POOR QUALITY OF LIFE PREDICTS THE NEW ONSET OF DYSPEPSIA: RESULTS FROM A LONGITUDINAL, 10-YEAR, FOLLOW-UP STUDY

Does quality of life influence development of dyspepsia? Ford *et al* attempted to answer this important question by conducting a 10-year, longitudinal, follow-up study of subjects who were screened for *Helicobacter pylori* infection. Using a validated postal dyspepsia questionnaire, they contacted 8407 individuals. Of these, 3912 (46.5%) provided symptom data at baseline and at 10-year follow up. Two thirds of these individuals (2550) were asymptomatic at entry and one third (717) had developed new-onset dyspepsia at the10-year follow up, giving an incidence of 2.8%. After multivariate logistic regression, lower quality of life at study entry, higher body mass index, presence of irritable bowel syndrome at study entry and use of non-steroidal anti-inflammatory drugs and/or aspirin were significant risk factors for new-onset dyspepsia (see table). Low quality of life at baseline exerted a strong effect on the likelihood of developing dyspepsia at 10 years. This has implications for treatment trials of patients with dyspepsia, as these data predict that curing dyspepsia symptoms will not necessarily improve all patients' quality of life as dramatically as might be suggested by cross-sectional surveys.

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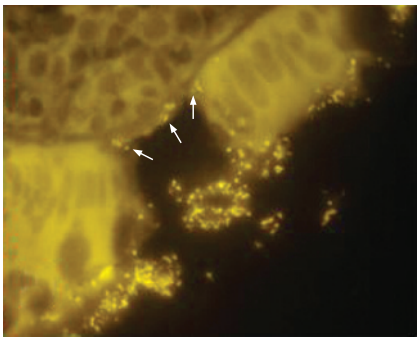
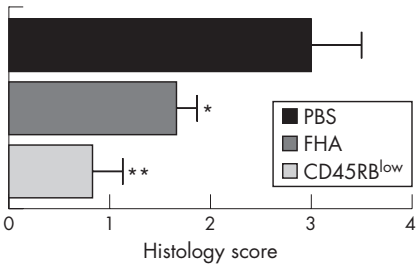


Denuded submucosa with directly attached bacteria (arrows) in a patient with active ulcerative colitis.



A blinded pathologist assessed different inflammatory characteristics to determine the degree of colitis using a score from 0 to 4. Significant differences compared with phosphate-buffered saline(PBS)-treated mice: *p<0.05 and **p<0.01.

COMPARATIVE STUDY OF THE INTESTINAL MUCOUS BARRIER IN NORMAL AND INFLAMED COLON

It is widely believed that humans happily co-exist with their "normal" colonic microbiota because of "immune tolerance". Swidsinski *et al* present data that challenge this paradigm. They studied the characteristics of the barrier for intestinal bacteria within the mucus layer, under normal as well as pathological conditions. Biopsies from purged colon were compared with biopsies from colon pretreated by enemas (left colon) and with material of whole appendices (right colon) removed by appendectomy without pretreatment. Swidsinki *et al* found a complete separation of bacteria from mucosa in practically all normal controls, regardless of the method used for preparation of the patients for endoscopy. By contrast, none of the samples from patients with colonic inflammation (inflamed appendices, ulcerative colitis or infective colitis) showed an intact mucus barrier (see fig). The thickness of the mucus layer and its spread decreased with increasing severity of the inflammation and the concentration of bacteria within mucus was inversely correlated to the numbers of leucocytes. The authors conclude that restitution of the intact mucus barrier is the optimal means of stopping inflammation and restoring immunological equilibrium and intestinal health.

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PREVENTION OF EXPERIMENTAL COLITIS BY PARENTERAL ADMINISTRATION OF A PATHOGEN-DERIVED IMMUNOMODULATORY MOLECULE

Filamentous haemagglutinin (FHA) is a major virulence factor of *Bordetella pertussis*. It subverts host immune responses by inhibiting interleukin (IL) 12 and enhancing IL10 production by macrophages and dendritic cells, and promoting the induction of regulatory T cells. Braat *et al* hypothesise that FHA would ameliorate disease in a T cell-dependent model of colitis by this mechanism. They induced colitis by injection of CD4CD45RB^{high} naive T cells into severe combined immunodeficient (SCID) mice. Compared with phosphate-buffered saline (PBS)-treated mice, FHA-treated SCID mice had significantly ($p<0.01$) less weight loss, lower colon weight, less colon shrinkage and reduced inflammatory lesions (see fig). The therapeutic effect of FHA was associated with enhanced IL10 and reduced type 1 and type 2 T helper cytokine production by spleen cells. As FHA is a component of pertussis vaccine used widely in children, the authors suggest that it could be considered as a potential tool for inducing remission in patients with Crohn's disease.

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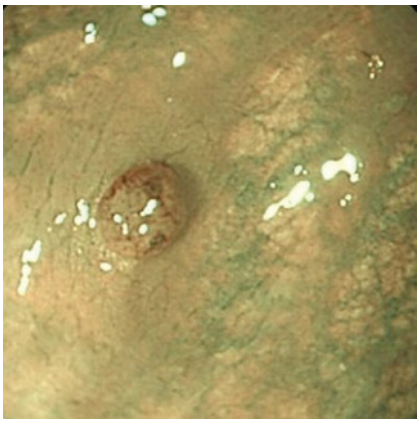
Digest



Low-magnification narrow-band imaging (NBI) showing an adenoma as a characteristic brown blob.

A PROSPECTIVE, COMPARATIVE STUDY OF NARROW-BAND IMAGING, CHROMOENDOSCOPY, AND CONVENTIONAL COLONOSCOPY IN THE DIAGNOSIS OF COLORECTAL NEOPLASIA

Early detection and removal of colorectal adenomas is the primary aim of colorectal cancer screening programmes. Conventional videoendoscopy often fails to differentiate between neoplastic and non neoplastic lesions and several new endoscopic techniques have been developed to provide more precise diagnosis (see fig). Chiu *et al* compared the diagnostic efficacy of narrow-band imaging (NBI) with that of conventional colonoscopy and chromoendoscopy. Their prospective study examined 180 colorectal lesions from 133 patients with conventional colonoscopy, and under low-magnification and high-magnification NBI and chromoendoscopy. Lesions were resected for histopathological analysis. NBI and chromoendoscopy scored better under high magnification than under low magnification in comparison with conventional colonoscopy. Both low-magnification and high-magnification NBI were capable of distinguishing neoplastic from non-neoplastic colorectal lesions: the diagnostic accuracy of NBI was better than that of conventional colonoscopy and equivalent to that of chromoendoscopy. NBI promises to be a very useful tool in screening for colorectal neoplasia and clinical trials are now warranted.

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Factors associated with moderate or severe fibrosis (multivariate analysis; n = 205)

	Modality	OR (95% CI)	p Value
Menopause	Yes	3.73 (1.7–7.8)	0.0004
	No	1	
Hormone replacement therapy	Yes	0.35 (0.1–0.8)	0.0119
	No	1	

LIVER FIBROSIS IN WOMEN WITH CHRONIC HEPATITIS C: EVIDENCE FOR THE NEGATIVE ROLE OF MENOPAUSE AND STEATOSIS AND THE POTENTIAL BENEFIT OF HORMONE REPLACEMENT THERAPY

Cirrhosis is largely a disease of men and postmenopausal women. The severity of fibrosis in chronic hepatitis C is significantly different between males and females. In females, acceleration seems to occur at approximately 60 years and an antifibrogenic effect of oestrogen has been suggested, possibly via inhibition of stellate cells. Codes *et al* prospectively studied 251 women with chronic hepatitis C using a questionnaire and blood sample on the day of liver biopsy. Of the women studied, 122 (52%) were menopausal and 65 were receiving hormone replacement therapy (HRT). They identified characteristics associated with moderate/severe fibrosis using univariate and multivariate analysis. The severity of fibrosis was associated with a longer duration of infection (>15 years), a higher body mass index, advanced steatosis and the menopause. Menopausal women receiving HRT presented with a lower stage fibrosis (see table). The findings reinforce the hypothesis of a protective role of oestrogens in the progression of fibrosis. Codes *et al* recommend fibrosis evaluation should be carried out more frequently in menopausal women (every 3 years) and HRT should be discussed.

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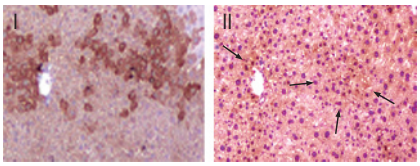

Predominant periportal engraftment of human bone marrow-derived mesenchymal stem cells detected immunohistochemically by the expression of hepatocyte-specific HepPar1 (I). The expression of phosphoenolpyruvate carboxykinase was detected in a serial section to identify periportal regions of the liver (II, arrows) (magnification x100).

FUNCTIONAL INTEGRATION OF HUMAN MESENCHYMAL STEM CELL-DERIVED HEPATOCYTES INTO MOUSE LIVERS

Hepatocyte transplantation is a potential alternative to whole liver transplantation but is limited by availability of suitable donor organs and a poor proliferative rate that is insufficient to effectively repopulate the host liver. Thus, novel sources for transplantable cells are urgently needed. Mesenchymal stem cells (MSCs) from human bone marrow may have the potential to differentiate into hepatocytes in vitro and in vivo. Aurich et al isolated human bone marrow-derived MSCs from bone marrow aspirates of voluntary donors. These cells were then differentiated in the presence of human hepatocyte growth medium and transplanted into immunodeficient Pfp/Rag2 mice. In vitro, the human MSCs gained the characteristic morphology and function of hepatocytes in response to specified growth factors. The preconditioned MSCs stored glycogen, synthesised urea and expressed the active hepatocyte-specific gene promoter of phosphoenolpyruvate carboxykinase. After transplantation into the livers of immunodeficient mice, the preconditioned MSCs engrafted predominantly in the periportal portion of the liver lobule (see fig). The transplanted cells retained prominent qualities of hepatocytes after their regional integration. These exciting studies suggest that bone marrow-derived MSCs may serve as a novel source for the propagation of hepatocyte-like cells suitable for cell therapy in liver diseases.

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