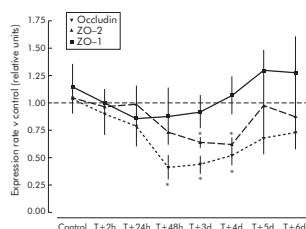


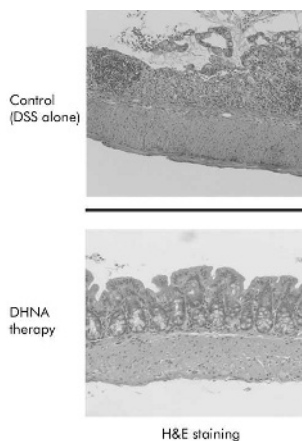
Table 3 Characteristics of the patients in the polyethylene glycol (PEG) and placebo groups at the end of the treatment period

Characteristic	PEG	placebo	P Value
Caecal diameter (cm)	3.4 (0.2)	5.6 (0.8)	0.017
Ascending colon diameter (cm)	3.1 (0.1)	4.6 (0.5)	0.018
Transverse colon diameter (cm)	3.0 (0.06)	4.2 (0.4)	0.014
Abdominal circumference (cm)	92.2 (1.1)	101.3 (2.9)	0.008
Stool evacuations (n/day)	1.4 (0.1)	0.6 (0.1)	0.001
Flatus evacuations (n/day)	2.4 (0.1)	1.5 (0.3)	0.032
Relapse (n)	0	5	0.04

Values are mean (SEM).



Time related changes in mRNA expression of ZO-1, ZO-2, and occluding after acute stress in mice. Values are mean (SEM) and expressed as arbitrary units (normally expression is 1 arbitrary unit relative to glyceraldehyde-3-phosphate dehydrogenase (GAPDH) gene expression). * $p < 0.05$ compared with GAPDH mRNA expression; $n = 8$ per group. T = time after single stress session.



H&E staining

POLYETHYLENE GLYCOL REDUCES RELAPSE OF ACUTE COLONIC PSEUDO-OBSTRUCTION

Acute colonic pseudo-obstruction is a rare condition on which there are few randomised control trials. Although neostigmine has been shown to be effective acutely, the condition recurs in around a fifth of patients. The present study evaluated 32 patients with acute colonic pseudo-obstruction. Thirty were successfully treated with neostigmine or endoscopic decompression and randomly allocated to receive either polyethylene glycol (PEG) solution or placebo. Compared with placebo, over the 7 day study period PEG reduced colonic diameter, increased the number of bowel movements and flatus evacuations per day, and reduced the relapse rate, which was 0/15 on PEG v 5/15 on placebo (see table). There were no serious adverse events, although a few patients receiving PEG developed nausea and mild colicky abdominal pain. Although this is the first trial, the results are convincing and neostigmine followed by PEG should probably be the first line of management for such patients.

See p 638

STRESS DECREASES COLONIC EXPRESSION OF TIGHT JUNCTION PROTEINS AND INCREASES PERMEABILITY

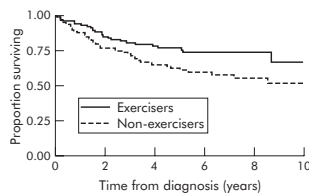
Stress activates mast cells and increases gut permeability, an effect that occurs after 72 h of chronic stress via an interferon γ (IFN- γ) dependant pathway. In this study, mice were subjected to either restraint or acoustic stress and permeability measured by instilling ^{51}Cr -EDTA into the colon and assessing the amount remaining after 2 h. RT-PCR showed a time dependant decline in tight junction protein mRNA (see figure) with occludin and zona occluding-2 (ZO-2) levels falling to a nadir on day 3, when colonic permeability and mucosal IFN- γ peaked. Electron microscopy showed dilated intracellular spaces and opening of the tight junctions. Alkaline phosphates, a marker of colonocyte differentiation, were also reduced at this time. Similar effects at day 3 were seen with a mast cell degranulating agent. Thus, acute stress has a delayed effect on colonic permeability acting via mast cell activation and IFN- γ production to alter tight junction expression and colonocyte differentiation. This study throws new lights on the mechanisms whereby stress exacerbates inflammatory bowel disease and may also be relevant to functional bowel disorders.

See p 655

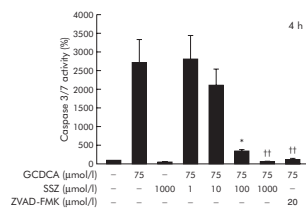
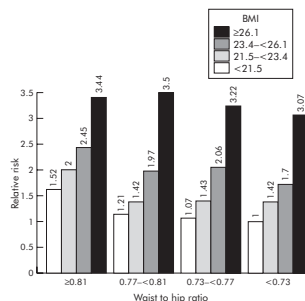
A PRODUCT OF *PROPIONIBACTERIUM FREUDENREICHII* IMPROVES A MOUSE MODEL OF COLITIS

There is a great interest in the role of bacteria and bacterial products in the pathogenesis of colitis. There is accumulating evidence that an inappropriate inflammatory response to some luminal bacteria cause colitis. There is also evidence that *Bifidobacterium* and *Lactobacillus* improve colitis. 1,4-Dihydroxy-2-naphthoic acid (DHNA), a product from *Propionibacterium freudenreichii*, stimulates the growth of *Bifidobacterium*. The authors of the present article report that oral administration of DHNA reduces colonic inflammation in the well known dextran sodium sulphate mouse model of colitis. Alterations in balance of different bacterial flora species were corrected by DHNA. Lymphocyte infiltration was also reduced by reduction in the expression of mucosal addressin cell adhesion molecule 1. The therapeutic potential of DHNA needs to be investigated further.

See p 681



Kaplan-Meier curve for colorectal cancer specific survival for cases with IGFBP-3 levels above the medium by exercise group.



Glycochenodeoxycholic acid (GCDCA) induces apoptosis in the liver. This is inhibited by sulphasalazine (SSZ).

EXERCISE IMPROVES SURVIVAL FROM COLORECTAL CANCER

It is well established that exercise reduces the risk of developing a number of cancers including colorectal cancers. It has recently been reported that exercise also prolongs the survival of patients with colorectal cancer. But how does this occur? One idea is that exercise might be reducing hyperinsulinaemia and/or by acting on the insulin-like growth factor axis. The authors of the present paper show that elevated plasma concentration of insulin-like growth factor binding protein 3 (IGFBP-3) is associated with a 48% reduction in cancer specific death. Levels of IGF-1 are not related to survival. Of interest, IGFBP-3 had no effect on cancer survival in patients who do not exercise.

See p 689

CENTRAL ADIPOSITY INCREASES THE RISK OF CHOLECYSTECTOMY

Fair, fat, and fertile was said to describe those with gallstones, but exactly how adiposity contributes is controversial. Visceral fat is metabolically very active, increasing the exposure of the liver to free fatty acids and reducing insulin sensitivity. The resulting hyperinsulinaemia is known to increase hepatic cholesterol secretion. This study examined the waist circumference, corrected for height, and waist to hip ratio in the Nurses Health Study, which collects biennial data from 121 700 female nurses in the USA. Measurements in 1986 were related to the risk of cholecystectomy by 2000. The figure shows that both high body mass index (BMI) and a large waist independently increase the relative risk for cholecystectomy. The risk for someone with a waist >33 inches and BMI >26 was 3.6 times the risk of someone with a waist <28 inches and BMI <21.5. Waist captures important additional information about the distribution of fat compared with just BMI alone. It appears that central fat, as with other diseases, is the more dangerous when it comes to gallstones.

See p 708

SULPHASALAZINE REDUCES BILE ACID INDUCED APOPTOSIS

The induction of apoptosis by bile salts is an important mechanism of liver injury in many cholestatic diseases. This is thought to occur through a number of mechanisms including the oligomerisation of the death receptor Fas and the generation of reactive oxygen species. The transcription factor NF-κB inhibits apoptosis in many contexts and is a potential target for antiapoptotic therapy. The experiments reported in this paper show that sulphasalazine inhibits apoptosis of hepatocytes induced by glycochenodeoxycholic acid in vitro and in vivo. The sulphasalazine metabolites 5-aminosalicylic acid and sulfapyridine have no effect. This study suggests that patients with ulcerative colitis and sclerosing cholangitis should be treated with sulphasalazine and not 5ASA preparations. This hypothesis should be tested by clinical trial.

See p 719