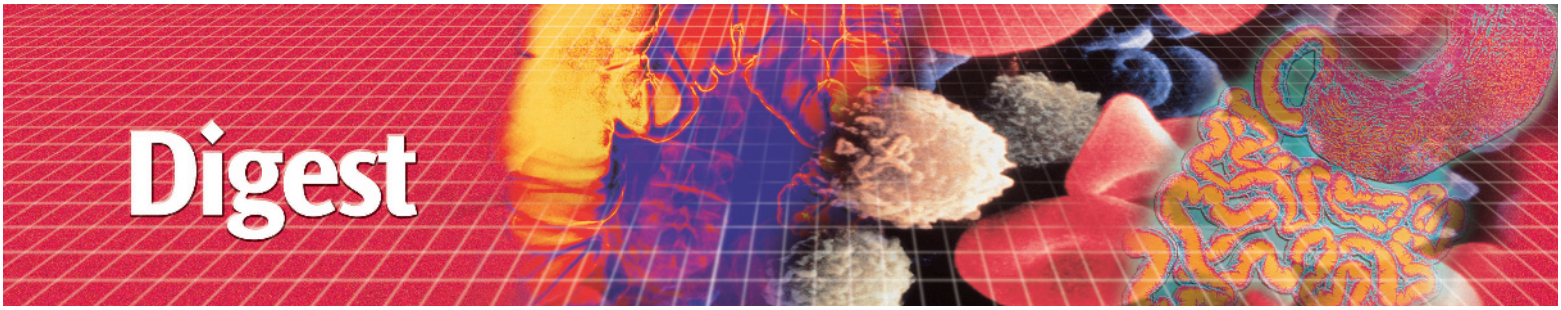

Robin Spiller, *Editor*

Nitric oxide generated at the oesophago-gastric junction causes nitrosation stress in gastric mucosa

Over the past two years *Gut* has published several studies showing that the oesophago-gastric junction is exposed to high concentrations of luminal nitric oxide (NO), which is generated when salivary nitrate meets gastric acid; but how this affects tissue levels was unknown. The current study addresses this important question in an animal model by infusing nitrate into the distal oesophagus and hydrochloric acid and ascorbic acid into the stomach. Peaks of NO were observed to rapidly appear in the gastric lumen, as boluses of nitrate solution, mimicking swallowed saliva, were perfused. Tissue samples were exposed to an iron-complex that traps NO and the resulting adducts were detected using electron paramagnetic resonance spectroscopy. This showed that tissue NO concentration was maximal at the gastro-oesophageal junction and this region also showed a reduction in reduced glutathione. This is important because glutathione is known to act as an anti-oxidant and protect against oxidant induced cell damage. This study provides an important mechanistic link between dietary nitrate, reflux, and oesophageal carcinogenesis.

See p 1072

Non-invasive demonstration of the gastrokinetic effects of ghrelin agonists in mice

As has been recently reported in *Gut*, ghrelin is an important regulator of energy balance stimulating both food intake and fat deposition. The current study is remarkable for two reasons. First, it demonstrates the feasibility of non-destructive assessment of gastric emptying in mice using the C14 octanoic breath test, something which should substantially reduce the numbers of animals used to assess gastrokinetic compounds. Second, it shows the acceleration of gastric emptying by both ghrelin and a non-peptide ghrelin agonist capromorelin. In vitro studies on gastric muscle show that these agents probably act by enhancing acetylcholine release when enteric nerves are stimulated. The non-peptide ghrelin analogues may well become useful therapeutic agents in the near future.

See p 1078

Sympathetic nerve regulation of colonic macrophage TNF and IL-6 secretion: impact of anti-TNF antibodies

Defense against infection in the gastrointestinal tract involves closely linked immune activation and profuse intestinal secretion together with propulsive motor patterns designed to expel infecting organisms. Sympathetic nerves normally inhibit secretion. Inflammatory cytokines (interleukin (IL) -1β, IL-6, and tumour necrosis factor α (TNFα)) remove this natural brake on secretion by inhibiting norepinephrine release from sympathetic nerves. The current study examined the control of IL-6 secretion in normal and inflamed colonic tissue. Immunohistochemical stains showed that most of the IL-6 came from macrophages and that the sympathetic nerves were largely destroyed in colitis induced by feeding dextran sodium sulphate. Norepinephrine dose dependently inhibited IL-6 secretion in uninflamed colons. Studies with anti-TNF antibodies showed a complex system of feedback loops in the uninflamed state, with TNF inhibiting its own and IL-6 release via sympathetic nerve stimulation. Colitis disrupts these controls, presumably by damaging the sympathetic nerves. Anti-TNF antibodies disturbed the control system and increased IL-6 secretion in normal but not inflamed tissue. This study is of relevance to all anti-TNF strategies and shows that such strategies interfere with a complex control system and may have both pro- and anti-inflammatory effects.

See p 1098

Significance of the collagen band in collagenous colitis

Investigators have pondered for many years on the role of the collagen band in this condition. The current case report shows clearly that the inflammation and increased gut permeability can be corrected by diversion of the faecal stream. This leads to disappearance of the collagen band. Reversing the surgical diversion caused a relapse of symptoms and an increase in permeability before the collagen reappears. It seems likely from this report that the collagen band is a result rather than the cause of increased gut permeability.

See p 1126

Increased genetic component in early onset colon cancer

Because colorectal cancer is the end product of an interaction between inherited and somatic genetic changes and environmental influences it is not surprising that in the elderly, the inherited component is relatively hard to detect, with abnormalities being found in only a small minority. Cancer appearing at an early age is likely to have a much stronger genetic predisposition, as was found in this unique series of 16 colorectal cancers diagnosed in patients aged $\leqslant$24 years. Seventy three per cent had demonstrated micro-satellite instability in their tumours and germline mutations in the mismatch repair genes were identified in 6 out of 12. Seven out of 16 (44%) developed additional malignancies, eight gastrointestinal and four extra intestinal tumours. The authors conclude that germline mutations of mismatched repaired genes are significantly common in this unique patient population that they should be sought for in all, even though the family history may not satisfy the strict Amsterdam criteria.

See p 1146