Gut Digest

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ENDOGENOUS PROSTAGLANDINS SENSITISE THE "NEURAL EMERGENCY SYSTEM" IN THE STOMACH

The afferent neurones of the gastric mucosa are known to respond to noxious chemicals such as ethanol in a protective way and form the "neural emergency system". The release of the vasodilatory peptide calcitonin gene related peptide (CGRP) from these nerves ameliorates the impairment of mucosal blood flow that alcohol and other noxious agents induce. The paper by Arai *et al* in this issue using a range of pharmacological manipulations in wild type and prostaglandin I_2 (prostacyclin) receptor knock-out animals now add to our knowledge by showing that endogenous prostaglandin enhance this neural emergency system. Furthermore it seems that prostaglandin I_2 is the most important of the prostaglandins since prostaglandin I receptor knock-out mice do not demonstrate the protective action of capsaicin.

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HOW *H PYLORI* INTERACTS WITH EPITHELIAL CELLS TO MODULATE THE IMMUNE RESPONSE

The control of T cell proliferation and activity in *Helicobacter pylori* induced gastritis is poorly characterised. The paper by Futagami *et al* demonstrates in vitro that *H pylori* extracts stimulate gastric epithelial cells to express cytokines, and that these activate T cells. Furthermore, different aspects of the epithelial cytokine response stimulated Th1 or Th2-like activation. The effect on T cells was partly dependent on T cell cyclo-oxygenase 2 activity and could be blocked by a COX-2 inhibitor.

Observational studies in human gastric biopsies were consistent with these mechanisms also operating in vivo. This work paves the way for further dissection of the interaction of the innate and acquired immune response in the stomach. It also supports the interesting concept that cyclo-oxygenase 2 expression in T cells may be important in their immunomodulatory response.

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ANTI-INFLAMMATORY PROPERTIES OF CARBON MONOXIDE

Carbon monoxide (CO) is known to be toxic at high concentrations due to its ability to interfere with oxygen delivery. Recent studies have shown that CO is also a gaseous second messenger produced in the body during the oxidative catabolism of heme by the heme oxygenase (HO) enzymes. The inducible isoform of heme oxygenase, HO-1, is induced in response to a diversity of injurious stimuli. In animal models of heart transplantation and ischemia/reperfusion injury of the lung, a number of anti-inflammatory and cytoprotective properties have been attributed to CO at low concentrations, concentrations that are well below those that would otherwise create toxic effects. Bauer *et al* used a model of syngeneic intestinal transplantation in the rat to study the effects of low doses of inhaled CO on post-transplantation inflammation and motor function. They observed that transplantation induced inflammatory cytokines and HO-1 in the small bowel, accompanied by a delay in transit. CO inhalation significantly decreased the expression of inflammatory mediators and improved post-transplantation motor function. These findings not only confirm the anti-inflammatory properties of CO in the gastrointestinal tract, they also suggest that CO inhalation could potentially be a therapeutic adjunct for clinical small bowel transplantation.

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TELOMERE SHORTENING AND THE ADENOMA CARCINOMA SEQUENCE

It is now realised that chromosomes in the majority of colorectal neoplasms accumulate errors far more rapidly than in normal tissue. This chromosomal instability causes multiple copies of abnormal chromosomes to be synthesised during cell division and occurs very early in carcinogenesis. A major question in cancer biology is how this chromosomal instability is initiated. One current hypothesis is that loss of telomere function triggers the chromosomal instability and initiates cancer. Support for this hypothesis has come from studies in ageing telomerase-deficient mice, which have an increased incidence of spontaneous malignancy. Furthermore, mice deficient in both telomerase and p53 develop colon cancer. These observations are given relevance to colorectal cancer in man by the article by Plentz and colleagues. The authors demonstrate that cells with high grade dysplasia but minimal invasive growth in colonic adenomas have telomeres that are significantly shorter than those of neighbouring connective tissue cells. This is an important observation, which suggests that telomere shortening is an initiating event in colorectal cancer. Further studies are required to put this observation in context with other more established initiating events such as mutation of APC.

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HEPATITIS C RISK FOR SURGEONS

While protection against hepatitis B by vaccination is routine for all medical personnel no such protection is available for hepatitis C, which as we have recently become aware carries the risk of serious morbidly and mortality. The paper by Thorburn *et al* therefore makes important reading for anyone carrying out exposure prone procedures on patients potentially infected with HCV. They show that surgeons, particularly general surgeons, are exposed to annual risk which they calculate to vary from 0.4 to 3.2 per 100 000. The authors calculated risk of a surgeon becoming infected with HCV in a high prevalence area such as Glasgow and conclude that the risk is low over the surgeon's lifetime (maximum estimate being 0.05–1.1%). Given that prompt treatment of acute hepatitis C infection can be 90% successful, this article should encourage surgeons to be aware of their occupational risk and promptly report needle stick injuries which occur during surgery. The study is of particular importance in the UK given the recent guidelines from the UK Departments of Health requiring exclusion of HCV-infected health care workers from exposure-prone procedures until eradication of the virus.

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