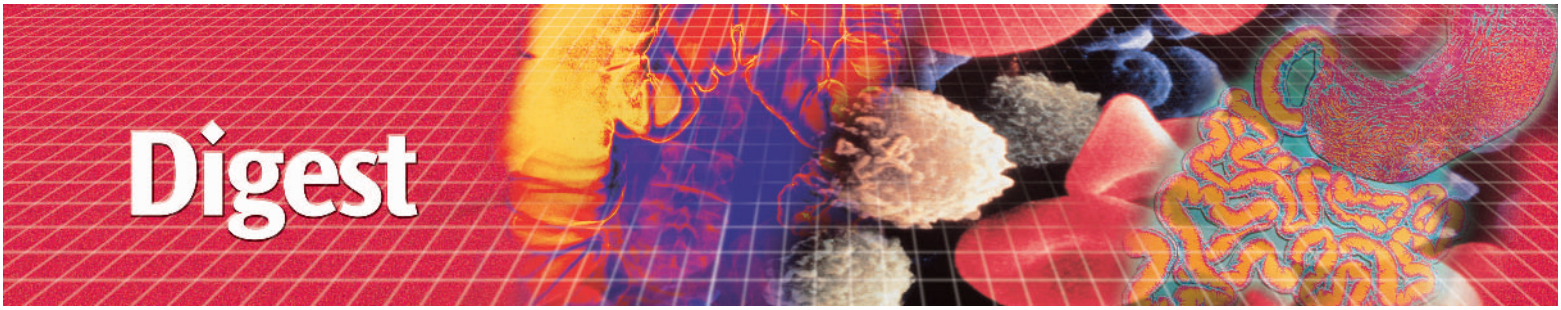

Robin Spiller, *Editor*

GRHELIN, *H PYLORI* AND OBESITY – THE PLOT THICKENS

The hormone ghrelin is released from the gastric fundus during fasting and stimulates food intake and gastric acid production. We have recently published a report that serum levels increase after *H pylori* eradication, raising the possibility that ghrelin suppression by *H pylori* might contribute to thin stature and avoidance of obesity-associated diseases. However, the present study shows that the situation in gerbils (which have proved a good model for aspects of *H pylori* associated pathogenesis) is not so simple. Chronically infected gerbils exhibited reduced gastric ghrelin concentrations, but because the inflamed stomach was enlarged total gastric ghrelin was unaffected. Gerbil weight was unchanged, and unexpectedly serum ghrelin levels were increased. Further studies are now needed in human adults and children – both observational and following *H pylori* eradication long term. Whether *H pylori* affect ghrelin dynamics in the longer term, and if this is important or not for avoidance of obesity and its associated diseases remains an important question to be answered.

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DEFINING HOW NITRIC OXIDE IMPAIRS BARRIER FUNCTION IN RADIATION ENTERITIS

GI toxicity is one of the limiting factors in successful cancer cure by external beam irradiation. It is known that radiation impairs barrier function, allowing bacterial translocation and subsequent inflammation. This is due, at least in part, to the impairment of chloride secretion which is part of normal intestinal defence mechanisms. The present study demonstrates that the reduction in chloride secretion in response to forskolin (a adenyl cyclase activator) by nitric oxide is secondary to inhibition of the specific adenyl cyclase (AC) isoforms, AC5 and AC6. They also show that these isoforms are expressed in both human and mouse colon. This opens the door to the design of specific molecules to counteract these adverse effects of radiotherapy.

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HOW PROTEASES EXCITE THE COLON

The effect of inflammation on gut motility is varied with both stimulation and inhibition in different models, no doubt reflecting the wide range of mediators released. Proteases released from either mast cells (tryptase) neutrophils (cathepsin G) or generated by activation of coagulation pathways (thrombin) by tissue injury, are now recognised to act on a range of protease activated receptors (PAR_{1-4}). These receptors are activated in a unique fashion. The proteases cleave the extracellular N-terminal domain of the receptor, unmasking a sequence that acts as a tethered receptor-activating ligand. The study from Palermo shows that the rat colon expresses the PAR_4 receptor and the immunohistochemical staining suggests that the receptor is in the sub-mucosal nerves. They also show that activating these receptors causes contractions of colonic longitudinal muscle. Pharmacological blocking experiments indicate that this effect is mediating via the release of acetylcholine or tachykinins. The effect is inhibited by capsaicin, possibly because it depletes tachykinins from sensory fibres and so prevents augmentation of the inflammatory response by axon reflexes. NK_2 antagonists appear to inhibit the PAR_4 induced contractile effects. This adds to or understanding of how inflammation alters motility and suggests new ways of manipulating this phenomena.

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HOW SYNBIOTIC (PREBIOTICS PLUS PROBIOTICS) THERAPY WORKS?

Although there are several recent studies reporting that synbiotics can reduce the incidence of sepsis in patients undergoing major surgery, the mechanisms are far from clear. The present study set out to painstakingly examine whether synbiotic therapy could reduce bacterial translocation, which the same authors have previously shown to be associated with post-operative sepsis. Patients about to undergo elective surgery were randomised to receive either 16g of oligofructose b.d and a probiotic (a mixture of lactobacilli, bifidobacterium and streptococci) t.d.s or placebo capsules t.d.s plus sucrose 16g b.d. for 14 days prior to surgery. Mesenteric lymph nodes and serosal scrapings obtained during laparotomy were examined and positive cultures were detected in 9% from the placebo group and 5% in the synbiotic group (difference not significant). Though negative, this is an important study, since it suggests the need to rethink our ideas. It is possible that probiotics may act more widely by altering the systemic immune response rather than just acting locally at the level of the mucosa as has previously been thought.

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HIP FRACTURES IN IBD – HOW IMPORTANT ARE STEROIDS?

When a condition is as rare as 12 per 10,000 patient years, as hip fracture is in IBD, a very large number of patients need to be studied to give accurate estimates of risk. The UK General Practice Research Database (GPRD) which is the world's largest primary care database has provided such a number. Card and colleagues used the GPRD to study 61,130 years of patient follow up in an inflammatory bowel disease (IBD) cohort and identify 72 hip fractures. The corresponding crude hip fracture rate, 11.8 per 10,000 patient years for IBD patients compared with 7.3 per 10,000 patient years for controls. Multi-variate analysis showed that having IBD increased the risk significantly and in Crohn's disease by over 60%, while taking 16-25 courses of steroids doubled the risk compared to Crohn's patients who never took steroids. Thus while we should aim to minimise steroid use in our IBD patients, if we are forced to prescribe, we can now put a figure on the absolute increase in risk of fracture to the individual patient.

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