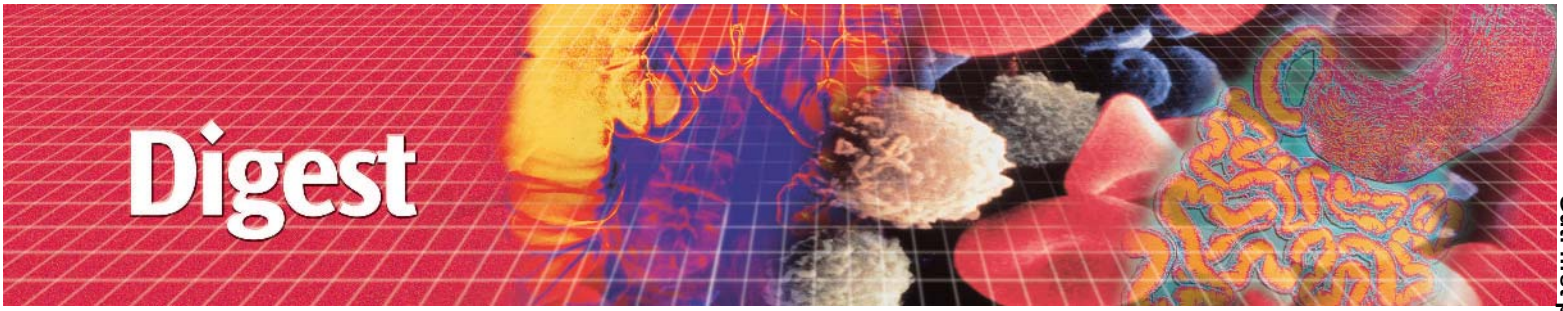

Robin Spiller, *Editor*

REDUCED ASCORBIC ACID TO NITRITE RATIO IN BARRETT'S OESOPHAGUS

Although the recent rise in oesophagus adenocarcinoma has been linked to the increasing incidence of reflux, the active ingredient of the refluxate is unclear. The current study focuses on the possible role of dietary nitrate, which is excreted in saliva, metabolised in the mouth to nitrite, and, on contact with gastric acid, converted to nitrous acid and reactive nitrozating species which produce potential carcinogenic N-nitrozo compounds. Studies in normal subjects without reflux have demonstrated that the lowest vitamin C to nitrite ratio, which predisposes to the generation of N-nitroso compounds, occurs in the gastric cardia. The current study of patients with Barrett's oesophagus with reflux shows that the site where this ratio is lowest has migrated proximally and lies in the squamous oesophagus and the Barrett's segment. By directly studying the generation of nitric oxide they were also able to show in three patients that reflux of acid into a Barrett's oesophagus produces a substantial local increase in nitric oxide concentration. Whether this could be modified by altering dietary nitrate intake and/or it's conversion to nitrite by buccal organisms remains to be seen.

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LONG TERM BENEFITS OF CURING HELICOBACTER PYLORI INFECTION

The progressive atrophy and later intestinal metaplasia that develops after many years of *H pylori* infection might at first be thought to be an irreversible process. Several small and rather short term studies have been inconclusive so the current substantial study of 795 adults with preneoplastic gastric lesions followed for up to 12 years is to be welcomed. The study, a randomised, placebo-controlled trial, included both *H pylori* eradication as well as β-carotene and ascorbic acid treatment arms. The anti-oxidant treatment had no effect, whereas *H pylori* eradication therapy significantly improved histology at 12 years. This improvement was proportional to the square of the duration of time that the patient was free from *H pylori* infection, hence the need for the prolonged study of up to 12 years. They conclude that prevention of gastric cancer by eradiation of *H pylori* is a viable option but that very prolonged studies are needed to clearly show the benefit. The message is clear that patients with pre-neoplastic gastric lesions should be treated and cured of their *H pylori* infection.

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REDUCED RISK OF COLORECTAL CANCER IN IBD IN REGULAR USERS OF AMINOSALICYLATES

There is much evidence from both clinical and basic science to suggest that chronic inflammation increases the risk of cancer. It would seem plausible therefore that the long term use of 5-aminosalicylates (5-ASA) to suppress colonic inflammation in ulcerative colitis would reduce the risk of colorectal cancer. However, previous case control studies have failed to confirm this presumption. The current study, which utilises the very large UK General Practice Database, overcomes the weakness of previous studies by substantially increasing the number of cases of colorectal cancer. The study population included nearly 19 000 IBD patients, 100 of whom developed colorectal cancer while taking 5-ASA preparations. Those who took 6 or more 5-ASA prescriptions in the previous 12 months had a 40% reduction of risk of colorectal cancer compared with those who took <6 prescriptions. Even with this substantial study size, confidence intervals are wide, which explains why previous studies using half the number of patients have been negative. One problem with case control studies is the possibility of confounding with compliance, because patients who regularly take medication are also more likely to visit doctors and take other advice, which might reduce their cancer risk. The authors attempted to overcome this by only considering patients who had taken at least some 5-ASA. They found no evidence of increased barium or colonoscopies in regular compared with irregular users and it seems likely that the finding is a genuine one. This study should encourage clinicians to convince the patients of the benefit of long term 5-ASA usage.

See p 1573

GENETIC INFLUENCES ON BONE MINERAL DENSITY IN CROHN'S DISEASE

Iatrogenic osteoporosis is a constant concern to clinicians looking after patients with Crohn's disease. Although there are many prophylactic treatments to prevent osteoporosis, Crohn's patients are often already burdened with numerous medications. A genetic marker of susceptibility to this complication would be very helpful in selective targeting of treatment to those who really need it. The current study examined a range of genes likely to be important in influencing the risk of developing osteoporosis. These include the vitamin D receptor (VDR), the pro-inflammatory cytokine interleukin 6 (IL-6), and collagen Type 1α1 (COL1A1). A large, well characterised cohort of 245 patients with Crohn's disease had assessments of both bone mineral density (BMD) and genotype. Patients with the IL-6 GG genotype had significantly lower BMD in both lumbar spine and the hip compared with the CC genotype. Those with either the GG or the TT COL1A1 genotype had a significantly lower BMD than the GT heterozygotes. Surprisingly there was no effect of VDR nor CARD 15 genotypes. Putting this in perspective steroid use accounted for 5% of the variation in BMD, similar to the effect of either IL-6 GG (5.3%) or COL1A1 GT genotype (5.8%). Plainly, there is still a lot to learn about osteoporosis in IBD.

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