COLONIC CRYPTS: SIZE MATTERS
The sequential molecular changes that lead to colon cancer are being unravelled. The sequence of related histological changes is less well understood. Wong and colleagues have used microdissection techniques to isolate individual crypts from normal and neoplastic colonic mucosa. The authors (who include two Wongs and a Wright) have shown that, unlike normal mucosa, adenomas and hyperplastic polyps grow by crypt fission and their crypts are larger than normal. Furthermore, adenomas show cell proliferation up to the crypt surface indicating loss of control of the cell cycle. Interesting, but histologists still seem to have some catching up to do in order to match the progress of molecular geneticists.

See page 212

INFLIXIMAB: WHERE DOES THE MAGIC BULLET STRIKE?
Most clinical gastroenterologists will by now have some personal experience of using the TNF-α antibody, infliximab, in the treatment of steroid refractory Crohn’s disease. The drug acts rapidly and will produce a remission in three quarters of such patients. Although it acts to neutralise soluble TNF-α, ten Hove and colleagues speculated that it may also have an effect on mucosal lymphocytes. Their study suggests that infliximab induces apoptosis of T lymphocytes in lamina propria and they suggest this as a mechanism for its rapid and sustained (at least in the medium term) therapeutic effect.

See page 206

A NOT SO PLEASANT MEAL FOR REFLUXERS
The role of gastric motor function in gastro-oesophageal reflux has received insufficient attention not least because of technical difficulties in its measurement. Tefera and colleagues wanted to study the distribution of a meal within the stomach and recognised that a 3D ultrasound technique might give more precise information about volume than could be obtained from barostat or radionuclide scanning. In contrast with normal subjects, patients with reflux showed abnormal pooling of a liquid meal in the proximal stomach. The implication of this abnormality in contributing to reflux symptoms did not escape the authors’ attention.

See page 153

VITAMIN C AND GASTRIC CANCER: BEARING FRUIT
Many claims have been made for the importance of vitamin C in human disease. Yet few have stood up to scientific rigour. Recent attention has focused on vitamin C and, in particular, whether it may have a role in reducing gastric cancer risk. Zhang and co-workers studied the effect of physiological concentrations of vitamin C on gastric cancer cell lines. Although vitamin C did inhibit cell growth in a dose-dependent manner, this inhibitory effect was lost at the low ascorbic acid concentrations found in patients infected with H pylori. Clearly a fruitful area for further research.

See page 165

THE SMALL BOWEL IS NOT THE LARGE BOWEL
Bearing in mind its relative inaccessibility, it is fortunate that small bowel cancer is rare. Although the small intestine accounts for 90% of the mucosal surface of the GI tract, large bowel cancer is 50 times commoner. Wheeler and colleagues were stimulated by progress in the molecular genetics of large bowel cancers and they chose to explore what changes could be seen in small bowel tumours. Quite unlike colorectal cancer, there were no APC gene mutations in small intestinal cancers, which clearly suggests cancer in the two sites has a very different genetic pathology. Now it really would be fascinating to find out quite how the small intestine is so relatively well protected against cancer.

See page 218

HOW THE LIVER MIGHT BE “UN-FIBROSED”
The search is on for treatments that will halt or reverse fibrosis in the liver. Animal models in which liver fibrosis resembles that seen in humans can be useful in studying potentially anti-fibrotic drugs. Pentoxifylline is both theoretically useful as well as having anti-fibrogenic effects in vitro. Raetsch and colleagues studied whether the drug could inhibit fibrosis and its mediators in bile duct ligated rats. They found that pentoxifylline powerfully down regulated procollagen I mRNA but caused a two-fold upregulation of metalloproteinase inhibitor—resulting in only a moderate therapeutic effort on liver fibrosis. They speculate that more specific targeting to the fibrogenic cells might lead the drug to be useful in man.

See page 241