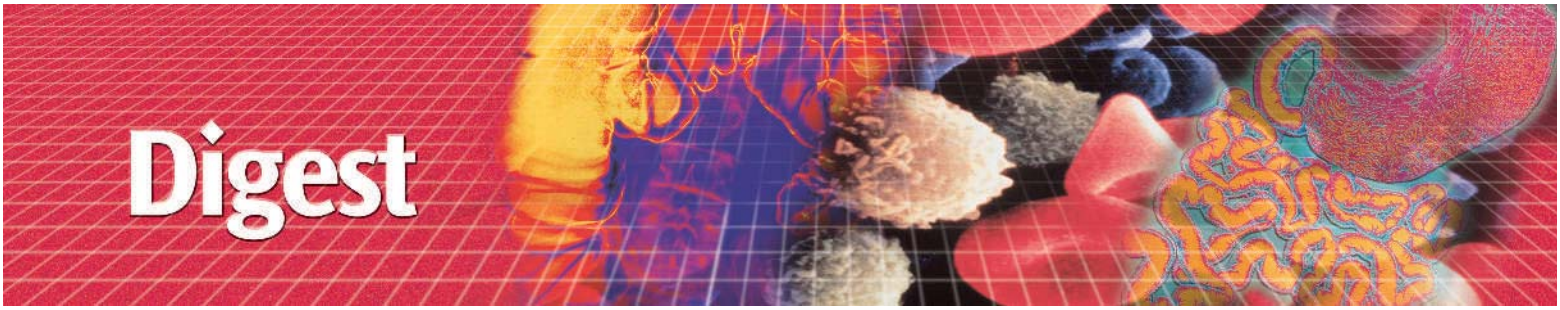

Robin Spiller, *Editor*

PRE-OPERATIVE CHEMO/RADIOTHERAPY FOR OESOPHAGEAL CANCER: SHORT TERM COST VERSUS LONG TERM BENEFIT

Oesophageal cancer continues to have an awful prognosis with a five year survival of only 10%. Attempts to improve the results of surgery by pre-operative chemotherapy or radiotherapy on their own has proved largely unsuccessful and trials of combined chemo/radiotherapy (CRT) have yielded conflicting results. This month we publish a meta-analysis of six randomised controlled trials **[see page 925]** which include data from 764 patients and show that pre-operative CRT improved survival at three years with an Odds Ratio of 0.5 (0.31 – 0.93). Part of the benefit relates to a down staging effect which is achieved by CRT with an odds ratio of 0.43 (0.26 – 0.72). Post operative adverse events were frequent with both CRT and surgery alone (39% versus 34%). However, the risk of dying within 90 days of surgery was increase by pre-operative CRT with an odds ratio of 2.1 (1.18 – 3.7). While demonstrating the benefit of CRT this meta-analysis also forces us to define in more detail the nature of the adverse effects on 90 day mortality and how these can be reduced.

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ROLE OF SEROTONIN AND VIP IN ROTAVIRUS DIARRHOEA AND ITS RELATION TO POSSIBLE NEW THERAPIES

Rotavirus gastroenteritis causes 600 000 deaths worldwide per annum, mostly in infants. Animal studies have shown that neural reflexes are important in mediating the associated profuse diarrhoea and vomiting, since these can be blocked by lidocaine and tetrodotoxin. Serotonin (5HT) may well be a key mediator since the diarrhoea in Rotavirus-infected mice can be significantly attenuated by both a $5HT_3$ antagonist (granisetron) and a vasoactive polypeptide (VIP) receptor antagonist **[see page 952]**. 5HT probably acts by activating intrinsic primary afferent neurones and inter-neurones, the final pathway being the VIPergic secretory neurones. Both the $5HT_3$ antagonists and the VIP receptor antagonists partially block secretion, effects which were not additive implying they act at different stages along the same pathway. These studies suggest novel ways of treating this potentially devastating disease.

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ASSOCIATION BETWEEN INFLAMMATORY BOWEL DISEASE AND A DEFECTIVE TOLL-LIKE RECEPTOR-4

The mucosal immune response to bacterial lipopolysaccharide (LPS) or peptidoglycan (PG) is mediated through pattern recognition receptors (PRRs). Best of known of these are the NOD cytosolic PRRs, polymorphisms of which are associated with defective NFκB response to peptidoglycans and are increased in Crohn's disease. LPS signals via a different receptor, the Toll-like receptor (TLR)-4, which binds the lipid A portion of LPS and is found on enterocytes, macrophages and dendritic cells. Recently a polymorphism, Asp299Gly, has been associated with decreased responsiveness to LPS and increased susceptibility to Gram-negative bacterial infection in man. The study **[see page 987]** by the group from the Erasme University Hospital in Brussels found the allele frequency of this polymorphism to be increased in both Crohn's disease (11%) and ulcerative colitis (10%) compared with controls (5%). Unlike the NOD2 polymorphisms both UC and Crohns were equally likely to have the Asp299Gly polymorphism. This association was supported by family studies showing that this polymorphism was more likely than chance to be transmitted to the affected child. This novel finding was not predictable from previous genome wide linkage studies and indicates that the genetic basis for IBD is likely to become increasingly complex, though the theme of abnormal responsiveness to luminal bacteria is further emphasised.

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DEFINING HOW TISSUE-TYPE PLASMINOGEN ACTIVATOR (TPA) BINDS TO PANCREATIC CANCER CELLS AND PROMOTES THEIR SPREAD

Previous studies have indicated that overexpression of t-PA in pancreatic cancer cells potentiates invasiveness. Annexin II is known to be overexpressed in pancreatic cancer and to bind tPA in endothelial cells. The study reported on page 993 used pancreatic cancer cell lines to study the binding of tPA. By using a specific peptide competitor for the binding site (LCKSL), the authors confirmed that tPA binds to pancreatic cell lines via Annexin II. They then studied a range of other cell lines and showed that expression of t-PA correlated well with their in vitro invasiveness and that this was blocked by the blocking peptide LCKSL. Chemotherapy for pancreatic cancer remains a dismal prospect so this study could be important as it suggests new ways to block pancreatic cancer spread.

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ROLE OF INTRA-LUMINAL IMPEDANCE MONITORING IN ASSESSING NON ACIDIC REFLUX

Most hospitals currently rely on a 24 hour pH recording to document the severity of reflux. However, not all the reflux is acid, particularly after a meal when gastric contents are often greater than 4 for several hours. Intra-luminal impedance monitoring measures the conductivity of oesophageal content which rises markedly when fluid gastric contents reflux into the lumen. It falls to very low levels when gastric gas is vented, thus the impedance record allows a very precise description of reflux events both acidic and non acidic, fluid and gaseous. While pH recording is familiar and in most cases adequate, intraluminal impedance monitoring would be helpful in those with apparently unremarkable pH records who continue to complain of severe symptoms. However its main role at present in research, is where it adds considerably to our ability to describe and understand the workings of the lower oesophageal sphincter.

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