

Short term benefit but long term failure after endoscopic gastroplication

The idea of endoscopic surgery to cure gastro-oesophageal reflux has tremendous appeal and initial data looked very promising, with two thirds of patients off all medication soon after the procedure. However, reflux is a long term condition and as the current study of 70 patients from the University of Leipzig shows, the initial benefit receded rapidly. By 18 months 80% were considered failures and most were back on medication. Objective measures at 12 months showed no reduction in distal oesophageal acid exposure or lower oesophageal sphincter pressure. Disappointingly, at this time no suture remained in 26% of patients and two out of the three sutures had disappeared in 43%, suggesting that suture loss is an important reason for this poor result. Whether improved suturing techniques will solve this problem remains to be determined.

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Interval faecal occult blood testing improves detection rates in colonoscopy screening programmes

As many countries start to grapple with the problems of national colorectal cancer screening programmes, defining the optional combination of invasive and non-invasive procedures becomes vital. Interleaving interval faecal occult blood test (FOBT) with colonoscopy may permit more effective use of this expensive resource by allowing longer periods between colonoscopies. This current study offered interval FOBT to patients undergoing 3–5 yearly colonoscopy screening. Patients were put in a high risk group if they had either a personal history of previous cancer or a positive family history. Disappointingly, although the acceptance of the colonoscopy programme was 87%, only 48% of those offered the FOBT accepted. The yield of significant positives was 1.8%, with 0.8% having cancer. The difference

in compliance rate is interesting and may have been influenced by the telephone call which preceded colonoscopy but not FOBT. This suggests a potential valuable addition to any future studies of interval FOB screening that looks promising as a way of reducing costs without loss of effectiveness.

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Novel ways of preventing liver ischemia/reperfusion injury

Various surgical manoeuvres during liver surgery may result in temporary warm ischemia. The injury that develops on reperfusion is believed to involve reactive oxygen species (ROS) inducing NFκB activation. This transcription factor translocates to the nucleus and activates many proinflammatory genes, a process that is normal controlled by a natural inhibitor, IκB. Overexpressing an inhibitor of NFκB by administering an adenovirus containing IκBα super repressor (Ad5IκB) markedly reduced the liver injury induced by ischemic reperfusion in a rat model. Immunohistochemistry showed that the expected nuclear translocation of NFκB was prevented by Ad5IκB and this was accompanied by a fall in the mRNA of inflammatory mediators TNF-α and iNOS. It also reduced the appearance of nitrotyrosine (a marker of NO production in sinusoidal cells). However, because NFκB may be important for preventing hepatocyte apoptosis, the authors speculate that a more selective block of NFκB in non-parenchymal cells might be a safer way of applying this technology in clinical practice.

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α-Fetoprotein (AFP) expression and prognosis in hepatoma: is ephrin-A1 the link?

Although AFP has been used as a marker for hepatocellular carcinoma (HCC) for decades, why this particular protein should be linked to poor prognosis is unknown. Previous genetic studies in hepatoma cell lines have suggested that cells producing AFP also produce ephrin-A1. This is a ligand for the Eph receptor tyrosine kinase, which enhances cell growth, angiogenesis, and metastasis in melanoma cells. The current study examines its role in HCC and shows a good correlation between ephrin-A1 mRNA and AFP expression in 20 HCCs. The authors also demonstrate, using a range of elegant studies of cells both over- and underexpressing ephrin-A1, that this stimulates AFP and matrix metalloproteinase 2 (MMP2) while inhibiting cell proliferation inhibitors such as p21 and the tumour angiogenesis inhibitor TSP-1. Microarray studies showed that ephrin-A1 increased a range of cell cycle related and angiogenesis genes while decreasing angiogenesis inhibitors. These cell line studies were strongly supported by studies in HCC, which showed increased expression of ephrin-A1 and its receptor ephrin A1 and decreased TSP-1 and P21. Thus, the simple AFP test proves to be a marker for the activation of a range of tumour growth promoting factors, which may well explain its prognostic value in clinical practice.

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Changing hepatitis C virus (HCV) genotypes in Italian children

This study of 522 children showed important changes in subtype distribution between those born before or after 1990. Universal screening of blood transfusions appears to have produced a rapid drop in the number of children infected with 1a, the main genotype transmitted in the past by blood transfusions; improving social and economic circumstances have reduced the incidence of 1b and 2. The study found most childhood infection now results from vertical transmission from mothers who have genotype 3, usually obtained via intravenous drug misuse, and genotype 4, which is found mainly in Africa and in the Middle East. Somewhat encouragingly, around a third of type 3 showed spontaneous viral clearance within three years and genotype 3 appears to respond better to treatment. These findings have important implications for the future healthcare burden that these patients represent.

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