Serum total bilirubin level, prevalent stroke and stroke outcomes

Bilirubin inhibits experimental atherosclerosis, is inversely associated with carotid plaque burden and confers neuroprotection in experimental stroke. Clinical data addressing the association of bilirubin with stroke are not available. In this study, the group hypothesized that higher bilirubin levels would be associated with reduced stroke prevalence and improved stroke outcomes.

The group used the National Health and Nutrition Examination Survey 1999 to 2004, a nationally representative cross-sectional examination of the United States civilian population, to examine the association of bilirubin with stroke. Of 13 214 adult participants with data on stroke history, serum total bilirubin level and stroke risk factors, 453 reported a history of stroke. Of these, 138 participants reported an adverse stroke outcome, defined as a long-term health problem or disability resulting from stroke. Multivariable logistic regression was performed to estimate odds ratios and 95% confidence intervals with adjustment for demographic characteristics and stroke risk factors.

It was found that a higher serum total bilirubin level is associated with reduced stroke prevalence and improved stroke outcomes. These findings support the hypothesis that bilirubin may protect from stroke events and from neurological damage in stroke.

Perlstein T, Pande R, Creager M, Weuve J, Beckman J (2008) Serum total bilirubin level, prevalent stroke, and stroke outcomes. *Am J Med* **121:** 781–8

Reducing uric acid levels in adolescents with newly diagnosed essential hypertension

Hyperuricaemia is a predictor for the development of hypertension and is commonly present in new-onset essential hypertension. Experimentally increasing uric acid levels using a uricase inhibitor causes systemic hypertension in animal models. The objective of this study was to determine whether lowering uric acid lowers blood pressure in hyperuricaemic adolescents with newly diagnosed hypertension.

A randomized, double-blind, placebo-controlled, crossover trial was carried out involving 30 adolescents who had newly diagnosed, never-treated stage 1 essential hypertension. Patients were excluded if they had stage 2 hypertension or known renal, cardiovascular, gastrointestinal tract, hepatic or endocrine disease. The intervention was allopurinol, twice daily for 4 weeks, or placebo, twice daily for 4 weeks, with a 2-week washout between treatments. The order of treatments was randomized, and the main outcome measure was a change in casual and ambulatory blood pressure.

It was concluded that in this short-term, crossover study of adolescents with newly diagnosed hypertension, treatment with allopurinol reduced blood pressure. The results represent a new potential therapeutic approach, although this is not a fully developed therapeutic strategy because of potential adverse effects.

Feig D, Soletsky B, Johnson R (2008) Effect of allopurinol on blood pressure of adolescents with newly diagnosed essential hypertension. *JAMA* **300:** 924–32

Distinct gene expression-defined classes of gastrointestinal stromal tumour

The majority of gastrointestinal tumours can be cured by surgery alone but relapse occurs in 20–40% of cases. Gastrointestinal tumours are considered to invariably arise through gain of function KIT or PDGFA mutation of the interstitial cells of Cajal. However, the genetic basis of the malignant progression of gastrointestinal tumours is poorly understood.

In this study, the expression levels of 54613 probe sets in 32 surgical samples of untreated gastrointestinal tumours of the stomach and small intestine were analysed with oligonucleotide microarrays. The representative GeneChip data were validated by real-time reverse transcriptase polymerase chain reaction and immunohistochemistry.

The group concluded that CD26 appears to be a reliable biomarker of malignant gastrointestinal tumours of the stomach. The postoperative recurrence rate of CD26-negative cases was as low as 2%. Therefore, postoperative follow up of such patients might be less intensive. CD26 may play an important role in the malignant progression of gastric gastrointestinal tumours and serve as a therapeutic target.

Yamaguchi U, Nakayama R, Honda K et al (2008) Distinct gene expression-defined classes of gastrointestinal stromal tumour. *J Clin Oncol* **26:** 4100–8

New regimen for initial treatment of multiple myeloma

The standard treatment for patients with multiple myeloma who are not candidates for high-dose therapy is melphalan and prednisone. This study compared the use of melphalan and prednisone with or without bortezomib in previously untreated patients with multiple myeloma who were ineligible for high-dose therapy.

The study group randomly assigned 682 patients to receive nine 6-week cycles of melphalan and prednisone on days 1–4, either alone or with bortezomib on days 1, 4, 8, 11, 22, 25, 29 and 32 during cycles 1–4 and on days 1, 8, 22 and 29 during cycles 5–9. The primary end point was the time to disease progression.

The time to progression among patients receiving bortezomib plus melphalan and prednisone was 24 months, compared with 16.6 months among those receiving melphalan and prednisone alone (hazard ratio for the bortezomib group, 0.48; $P<0.001$). The proportions of patients with a partial response or better were 71% in the bortezomib group and 35% in the control group; complete response rates were 30% and 4% respectively ($P<0.001$). The group concluded that bortezomib plus melphalan and prednisone was superior to melphalan and prednisone alone in patients with newly diagnosed myeloma who were ineligible for high-dose therapy.

San Miguel J, Schlag R, Khuageva N et al (2008) Bortezomib plus melphalan and prednisone for initial treatment of multiple myeloma. *N Engl J Med* **359:** 906–17