A total of 55 patients with severe, adult-onset GHD of at least 2 years' duration underwent consecutive 9-month periods of treatment with recombinant human GH therapy (Genotropin®, Pfizer, New York, NY, USA) and placebo. There was a 4-month washout period in between treatments. The dose of GH therapy given to each patient was individually titrated to maintain levels of serum insulin-like growth factor 1 to within the normal range. Women were given a 50% higher mean dose of GH therapy than men, such that similar levels of serum insulin-like growth factor 1 were reached in both sexes. GH therapy decreased serum C-reactive protein levels by 41% and improved levels of apolipoprotein B cholesterol compared with placebo. There was no effect on levels of apolipoprotein A-I and interleukin 6 in patients throughout the study period.

The authors conclude that, in treatment-naive patients with adult-onset GHD, GH-replacement therapy has a positive effect on cardiovascular risk, mediated by decreased levels of both apolipoprotein B and C-reactive protein. These factors are markers of atherogenesis and subclinical inflammation, respectively.

Original article Bollerslev J *et al.* (2006) Positive effects of a physiological dose of GH on markers of atherogenesis: a placebo-controlled study in patients with adult-onset GH deficiency. *Eur J Endocrinol* **154:** 537–543

Prolonging survival of patients with medullary thyroid carcinoma

At present, there is no effective therapy for the treatment of metastatic medullary thyroid carcinoma (MTC). In two previous studies, pretargeted radioimmunotherapy—in which a bispecific antibody that localizes to carcinoembryonic-antigen-expressing carcinoma tissue, then binds a ^{131}I-labeled bivalent hapten that is administered later—resulted in disease stabilization in ~50% of treated patients who were followed up for up to 6 years after treatment. Chatal *et al.* compared the overall survival of 29 of these treated patients with that of 39 untreated patients with MTC.

A trend was noted for prolonged survival in treated patients, but did not reach statistical significance ($P = 0.059$). Among high-risk patients (patients with a serum calcitonin doubling time <2 years), however, treated patients survived significantly longer than untreated patients (median survival 110 months versus 61 months, $P < 0.03$). Biologic response to treatment, defined as a >100% increase in pretherapy calcitonin doubling time, was also associated with longer survival. The mean survival of patients who responded ($n = 9$) was 159 months, compared with 109 months for those who did not respond ($n = 10$) and 64 months for untreated patients ($P = 0.035$ and $P = 0.01$, respectively). Unexpectedly, treatment resulted in high-grade hematologic toxicity in several patients.

These results indicate that pretargeted radioimmunotherapy is a promising treatment for high-risk patients with metastatic MTC.

Original article Chatal J-F *et al.* (2006) Survival improvement in patients with medullary thyroid carcinoma who undergo pretargeted anti-carcinoembryonic-antigen radioimmunotherapy: a collaborative study with the French Endocrine Tumor Group. *J Clin Oncol* **24:** 1705–1711

Animal study points the way for future obesity treatments

Obesity has become an important worldwide health problem, not least because it is associated with a host of related conditions, including diabetes. Preclinical studies have shown that the hypothalamic metabolism of fatty acids affects appetite and glucose metabolism in normal animals. American and Italian researchers hypothesized that a defect in hypothalamic lipid sensing might contribute to the insulin resistance seen in a rat model of diet-induced obesity and insulin resistance. Specifically, they investigated whether inhibition of lipid oxidation in the hypothalamus would restore lipid sensing.

Sprague-Dawley rats were fed a standard diet or one supplemented with 10% lard. Within 3 days, the overfed rats had doubled their daily caloric intake and developed severe insulin resistance. *In vivo* studies demonstrated that the overfed rats had impaired lipid sensing: an exogenous increase in the level of circulating lipids failed to increase hypothalamic levels of fatty acids in these animals. Moreover, Pocai *et al.* found that inhibiting lipid oxidation in the hypothalami of overfed rats restored normal lipid sensing, and normalized food intake and glucose homeostasis.