The authors believe that diurnal variation seen in serum bile-acid levels could be a hormonal signal reflecting food intake, and conclude that postprandial bile-acid levels should be sufficient to trigger cyclic AMP production and increase D2 activity. These findings further the understanding of energy homeostasis, and could also have implications for treating obesity.

Chrissie Giles

Original article Watanabe M *et al.* (2006) Bile acids induce energy expenditure by promoting intracellular thyroid hormone activation. *Nature* **439:** 484–489

Denosumab improves low BMD in postmenopausal women

Denosumab is a fully human monoclonal antibody that targets RANKL (the receptor activator of nuclear factor κB ligand)—a protein that acts as the primary mediator of osteoclast differentiation, activity, and lifespan. In a phase II, randomized, placebo-controlled study, McClung *et al*. evaluated the efficacy of denosumab in postmenopausal women younger than 80 years who had a low BMD.

In total, 369 women from 29 study centers in the US completed this 12-month study. Participants were randomly assigned to receive subcutaneous denosumab, either every 3 months (6, 14, or 30 mg) or every 6 months (4, 60, 100, or 210 mg), open-label 70 mg alendronate per week, or placebo. At 12 months, women who received denosumab had a mean increase in BMD of 3.0–6.7% at the lumbar spine, compared with a 4.6% increase and a 0.8% decrease in women who received alendronate and placebo, respectively. Women who received denosumab also had a greater increase in total hip BMD and BMD in the distal third of the radius compared with the alendronate and placebo groups. Levels of serum C-TELOPEPTIDE decreased as early as 3 days in women who received denosumab. A dose of 30 mg denosumab every 3 months, or 60 mg every 6 months seemed to be the most effective regimens. Adverse events were not significantly different among the three treatment arms.

The authors conclude that denosumab administered subcutaneously to postmenopausal women causes a decrease in bone turnover and an increase in BMD. Denosumab might, therefore, be an effective treatment for osteoporosis.

Marie Lofthouse

Original article McClung MR *et al.* (2006) Denosumab in postmenopausal women with low bone mineral density. *N Engl J Med* **354:** 821–831

Hypogonadism might cause insulin resistance in prostate cancer

Men with prostate cancer often receive androgen-deprivation therapy (ADT), which renders them hypogonadal. Basaria *et al.* performed a cross-sectional study to see if the insulin-resistant profile associated with ADT is caused by an increased BMI— a side effect of hypogonadism—or by hypogonadism directly.

The authors compared two groups with prostate cancer: 18 hypogonadal men who had received ADT for at least 12 months and 17 men who had undergone nonchemotherapeutic treatment but not ADT. Also included were 18 age-matched controls with normal serum PSA levels. Most participants were white and none had diabetes mellitus.

The highest LEPTIN levels and BMI were seen in hypogonadal men. After adjustment for age and BMI, these men still had the highest fasting blood levels of insulin and glucose. They were more insulin-resistant than eugonadal men, and 44% had fasting glucose levels sufficient for a clinical diagnosis of diabetes mellitus. Combining all groups' data, there was a substantial negative correlation of testosterone with the metabolic parameters measured.

Insulin resistance is a risk factor for cardiovascular disease, and the authors suggest that leptin could promote the growth and survival of prostate-cancer cells. So, although ADT might be beneficial initially, its effects on insulin and leptin levels could cause the high cardiovascular mortality of patients with prostate cancer, and enhance recurrence and metastasis of the disease itself. The authors recommend hyperglycemic screening of patients on ADT and investigation into the use of insulin-sensitizing agents.

Chrissie Giles

Original article Basaria S *et al.* (2006) Hyperglycemia and insulin resistance in men with prostate carcinoma who receive androgen-deprivation therapy. *Cancer* **106:** 581–588

GLOSSARY

C-TELOPEPTIDE
Type I collagen breakdown product that is used as a marker of bone resorption

LEPTIN
A hormone released by adipose cells in concentrations proportional to body fat levels