preoperative TSH levels were significantly higher in the 241 patients with malignancy (2.5 ± 0.3 mIU/l) than in the 602 patients with benign disease (1.4 ± 0.1 mIU/l). The prevalence of malignancy was lowest in patients with TSH levels <0.06 mIU/l and highest in patients with TSH levels ≥5.0 mIU/l (17% versus 46%). The increased risk of DTC in patients with elevated preoperative TSH values persisted when levothyroxine-treated patients were removed from the analysis. An increased risk of DTC was also seen in patients whose TSH levels were within the normal range, but above the population mean. In addition, patients with advanced DTC had significantly higher mean TSH levels than those with low-grade tumors.

The authors conclude that high TSH levels are associated with increased incidence and with advanced stages of DTC, and suggest that TSH could have an important role in the development and progression of thyroid cancer.

Original article Haymart MR *et al.* (2008) Higher serum thyroid stimulating hormone level in thyroid nodule patients is associated with greater risks of differentiated thyroid cancer and advanced tumor stage. *J Clin Endocrinol Metab* **93:** 809–814

High IGF-I levels imply active acromegaly even when GH levels are 'normal'

Biochemical control of acromegaly in noncured patients is usually defined as serum growth hormone (GH) levels <2.0 μg/l, plus normal-for-age serum levels of insulin-like growth factor I (IGF-I). Alexopoulou *et al.*, however, have confirmed reports of discordant IGF-I and GH results in noncured patients with acromegaly: in over one-third of their cohort, one parameter was elevated despite the other being normal.

The Belgian Acromegaly Register provided data on 229 patients (mean age ± SD 54 ± 14 years; 124 men) with noncured acromegaly. Serum IGF-I and GH levels were measured by validated assays. In total, 81 patients had active disease (IGF-I and GH both high), 68 patients had biochemically controlled disease (IGF-I and GH both normal), and 80 patients had discordant results (25 had elevated GH only, and 55 had elevated IGF-I only). Notably, the high-GH phenotype was most frequent in young, nonirradiated, estrogen-sufficient women, which could indicate roles for age, sex and radiotherapy in IGF-I–GH discordance. The high-IGF-I phenotype was twice as common as the high-GH phenotype, and was associated with a notably poor metabolic profile; the authors concluded that high IGF-I might indicate persistently active disease even when mean GH values lie in the normal range.

The authors infer that constant peripheral exposure to even slightly elevated GH levels might be sufficient to raise IGF-I levels above normal, and suggest that different GH threshold values might be needed to monitor acromegaly in estrogen-exposed patients.

Original article Alexopoulou O *et al.* (2008) Divergence between growth hormone and insulin-like growth factor-1 concentration in the follow-up of acromegaly. *J Clin Endocrinol Metab* [doi:10.1210/jc.2007-2104]

DMPA use by young women decreases spine and hip BMD

Several studies have linked depot medroxyprogesterone acetate (DMPA) use with reduced BMD. Walsh and colleagues' case–control study assessed whether this BMD deficit is age-specific and/or site-specific, and examined the effects of DMPA on markers of bone turnover and hormone levels.

The study included 50 white women aged 18–25 years who began DMPA use before age 20 years (before peak bone mass was attained), and 50 white women aged 35–45 years who began DMPA use after age 34 years (after peak bone mass was attained). DMPA users were paired with controls matched for age, height, BMI and smoking status.

Compared with controls, BMD was decreased at the lumbar spine (–5.6%, $P<0.05$) and hip (–5.2%, $P<0.05$) in DMPA users aged 18–25 years only. There was no difference in forearm BMD between DMPA users and controls in either age-group. Regardless of age, serum levels of propeptide of type I procollagen and N-terminal telopeptide of type I collagen (markers of bone turnover) and insulin-like growth factor 1 were significantly higher in DMPA users than controls ($P<0.05$), whereas levels of estradiol were significantly lower in DMPA users than controls ($P<0.001$).

The authors conclude that DMPA is associated with a site-specific BMD deficit in users who have not attained their peak bone mass, and that estrogen deficiency is the main mechanism of increased bone turnover. Further

study is needed to determine whether the BMD deficit is reversible in young DMPA users.

Original article Walsh JS *et al.* (2008) Effects of depot medroxyprogesterone acetate on bone density and bone metabolism before and after peak bone mass: a case–control study. *J Clin Endocrinol Metab* [doi:10.1210/jc.2007-2201]

Clinical features of PCOS linked to increased risk of cardiovascular events

Women with polycystic ovary syndrome (PCOS) have several cardiovascular risk factors, including excess androgens, although studies have failed to demonstrate a definitive association between PCOS and risk of cardiovascular disease. Shaw and colleagues investigated this relationship in a group of postmenopausal women enrolled in the Women's Ischemia Syndrome Evaluation (WISE) study.

The authors identified 390 postmenopausal women who were not receiving hormone therapy or using oral contraceptives. Of these, 102 women had clinical features of PCOS, including hyperandrogenemia and a history of irregular menses. The primary end point was time to cardiovascular events.

Women with PCOS were more likely to have diabetes ($P = 0.022$), the metabolic syndrome ($P = 0.001$), increased angiographic coronary artery disease ($P = 0.044$) and obesity ($P = 0.006$) than women without PCOS. During 6 years' follow-up, a total of 55 cardiovascular events (25 cardiovascular-related deaths and 30 nonfatal myocardial infarctions) were reported. Compared with women without clinical features of PCOS, women with PCOS had a significantly raised risk of cardiovascular events (hazard ratio 3.3, 95% CI 1.8–5.9, $P < 0.0001$) and their 5-year cardiovascular-event-free survival was significantly reduced (78.9% versus 88.7%, $P = 0.006$).

The authors conclude that treatment targeted at improving coronary risk factors in postmenopausal women with clinical features of PCOS might help to reduce the incidence of cardiovascular events.

Original article Shaw LJ *et al.* (2008) Post-menopausal women with a history of irregular menses and elevated androgen measurements at high risk for worsening cardiovascular event-free survival: results from the National Institutes of Health–National Heart, Lung, and Blood Institute (NHLBI)-sponsored Women's Ischemia Syndrome Evaluation (WISE). *J Clin Endocrinol Metab* [doi:10.1210/jc.2007-0425]

Diabetes-associated retinopathy increases risk of CVD events

Previous studies suggested that diabetes-associated retinopathy increases the risk of cardiovascular disease (CVD) events, but cohorts were generally small and the findings were conflicting, particularly for possible sex-specific effects. Targher and colleagues examined the association between retinopathy and incident CVD events in a large population of men and women with type 2 diabetes and without a diagnosis of CVD at baseline.

The authors included 2,103 outpatients (1,302 men, 801 women) with type 2 diabetes enrolled in a prospective, observational study during 2000. Patients were grouped according to their retinopathy status at baseline (no retinopathy, $n = 1{,}116$; nonproliferative retinopathy, $n = 798$; proliferative or laser-treated retinopathy, $n = 189$). CVD events included cardiovascular death and nonfatal ischemic stroke or coronary heart disease.

During ~7 years of follow-up, 406 patients experienced CVD events. After adjustment (for age, BMI, waist circumference, smoking status, lipid level, glycated hemoglobin level, diabetes duration and medication use), the risk of incident CVD events was significantly greater in patients with nonproliferative (hazard ratio [male versus female] 1.61 versus 1.67) and proliferative or laser-treated retinopathy (hazard ratio [male versus female] 3.75 versus 3.81) than in patients with no retinopathy (each comparison $P < 0.001$). After further adjustment for hypertension and advanced nephropathy, the risk of incident CVD events remained significantly increased only in patients with proliferative retinopathy.

The authors conclude that retinopathy, particularly at advanced stages, is an independent risk factor for incident CVD events in both men and women with type 2 diabetes.

Original article Targher G *et al.* (2008) Diabetic retinopathy is associated with an increased incidence of cardiovascular events in type 2 diabetic patients. *Diabet Med* **25:** 45–50

Weight loss >10% is required to improve inflammatory marker levels in the obese

Long-term metabolic complications of obesity include low-grade inflammation, characterized by decreased levels of the anti-inflammatory