Transdermal estrogen does not affect levels of cortisol in the blood or saliva

Most cortisol that circulates in the blood is bound to proteins such as cortisol-binding globulin (CBG). Direct measurement of the 'free' (biologically active) form in the serum is difficult, but salivary cortisol levels are relatively easy to determine and are a marker of blood free cortisol levels. Oral estrogen preparations are known to increase CBG levels, thereby increasing total blood cortisol levels. As well as the potential physiological consequences of this, the increased cortisol affects assessment of the hypothalamic–pituitary–adrenal (HPA) axis. This single-center cross-sectional study compared effects of transdermal ($n=8$) and oral ($n=14$) estrogen therapy on salivary cortisol levels, and serum total cortisol and CBG levels in women. Controls ($n=15$) were not taking estrogens.

Total serum cortisol and CBG levels were higher in subjects taking oral estrogens than in controls ($P<0.001$); however, levels in subjects taking transdermal estrogen were similar to controls. Salivary cortisol levels were similar in all three groups.

The authors conclude that oral estrogen administration markedly increases serum levels of total cortisol and CBG; however, salivary cortisol levels were not affected. Further work is needed to assess whether this reflects serum free cortisol levels. Because transdermal estrogen seems not to affect cortisol levels, there appears no need to discontinue therapy in the weeks before assessing the HPA axis, which is the procedure currently used for people taking oral estrogens.

Original article Qureshi AC *et al.* (2007) The influence of the route of oestrogen administration on serum levels of cortisol-binding globulin and total cortisol. *Clin Endocrinol (Oxf)* **66:** 632–635

Increased incidence and prevalence of adverse outcomes in elderly patients with diabetes

Although increased age is a risk factor for development of diabetes mellitus, the effects of this disorder in the elderly population, in terms of mortality and diabetes-related complications, have not been well characterized. Bethel and colleagues conducted a national, longitudinal study of adverse outcomes in 33,772 patients aged >65 years who were diagnosed with diabetes in 1994; these patients were compared with 25,563 age-matched and ethnicity-matched controls without diabetes during the 11-year observation period.

By the end of 2004, patients in the diabetes group had excess mortality of 9.2% relative to controls ($P<0.001$). The cumulative incidence of adverse events over this time was 91.8% in the diabetes group, compared with 72.0% in controls. The most common complications occurred in the lower extremities (prevalence 835 and 592 per 1,000 for the diabetes group and control group, respectively), with the most marked between-group differences observed for severe adverse events requiring surgery (e.g. gangrene, debridement and amputation). The incidence of most adverse outcomes was significantly higher in the diabetes group than the control group, including stroke (62% higher incidence, $P=0.003$) and congestive heart failure (65% higher incidence, $P<0.001$); however, the incidence of several events, such as stroke, heart failure and myocardial infarction, generally decreased in both groups over time.

The authors conclude that elderly people diagnosed with diabetes are at increased risk of adverse outcomes, which places a considerable burden on these patients and health care systems.

Original article Bethel MA *et al.* (2007) Longitudinal incidence and prevalence of adverse outcomes of diabetes mellitus in elderly patients. *Arch Intern Med* **167:** 921–927

Increased risk of atrial fibrillation in individuals with subclinical hyperthyroidism

Several studies have indicated that changes in thyroid function might be associated with a risk of atrial fibrillation (AF), itself an independent risk factor for cardiovascular events and stroke. Gammage and colleagues performed a population-based study that investigated the relationship between thyroid function and AF in elderly individuals (aged ≥65 years).

Those included (mean age 72 years) were not being treated for thyroid dysfunction and had no history of hyperthyroidism. Participants were assigned to five categories: first, hyperthyroid ($n=14$, 0.2%)—increased free T_4, serum TSH <0.4 mU/l; second, subclinical hyperthyroid ($n=126$, 2.2%)—normal free T_4, TSH <0.4 mU/l;