relative adrenal failure resulted in a dramatic increase in total and free cortisol levels.

The authors conclude that the decrease in serum cortisol levels explained part of the improved outcome achieved by intensive insulin therapy in critically ill patients. They also suggest that hydrocortisone doses currently used for relative adrenal insufficiency might be too high, and should be re-evaluated.

Original article Vanhorebeek I *et al.* (2006) Cortisol response to critical illness: effect of intensive insulin therapy. *J Clin Endocrinol Metab* **91:** 3803–3813

Intensive insulin therapy improves survival of patients in critical care

Compared with conventional insulin therapy, intensive insulin therapy (IIT) improves the outcomes of critically ill patients, but concerns remained that IIT might be less beneficial for medical than surgical cases, and might have reduced efficacy in some subgroups of patients. Van den Berghe and colleagues, therefore, pooled datasets from two similar randomized, controlled trials of IIT in 1,200 medical and 1,548 surgical patients in critical care, respectively.

Overall mortality was lower in IIT-treated than conventionally treated patients (20.5% versus 23.6%). IIT had the greatest benefit in patients treated for ≥3 days in the critical-care unit (37.9% mortality with conventional therapy, versus 30.1% with IIT). IIT did not improve the survival of patients who remained <3 days in the critical-care unit, but caused no harm.

Maintenance of blood-glucose levels <150 mg/dl was crucial to reduce mortality, but the greatest benefit was obtained by blood-glucose levels <110 mg/dl, especially over several days. IIT strictly maintained blood glucose within 80–110 mg/dl from admission onwards, which protected the kidneys and peripheral nervous system, albeit with an increased risk of hypoglycemia that caused only transient morbidity (although the authors conceded that the survival benefit of IIT might be reduced). Only patients with diabetes experienced no survival benefit with IIT, and showed a trend towards increased mortality risk at blood-glucose levels <110 mg/dl. The authors postulate that diabetic patients might have adaptations to chronic hyperglycemia that render normalization of blood glucose potentially harmful; they suggest that diabetic patients' IIT blood-glucose targets should be based on the patient's usual values.

Original article Van den Berghe G *et al.* (2006) Intensive insulin therapy in mixed medical/surgical intensive care units. *Diabetes* **55:** 3151–3159

Testosterone gel and progestin show promise as a male hormonal contraceptive

Administration of exogenous androgens and progestins suppress pituitary secretion of sex hormones and inhibit spermatogenesis, but only injectable or implantable testosterone had previously shown efficacy. Page and colleagues have now demonstrated that transdermal testosterone gel plus depomedroxyprogesterone acetate (DMPA, a progestin) induced severe oligospermia in 80–90% of treated men; they also confirmed that acyline (a gonadotropin-releasing-hormone antagonist that directly suppresses pituitary sex hormones) did not improve the efficacy or rapidity of spermatogenesis suppression achieved by testosterone gel plus DMPA.

Their open-label study involved 44 men aged 18–55 years with normal spermatogenesis, who were randomly allocated to 24 weeks of treatment (100 mg of 1% testosterone gel self-applied daily, plus 300 mg intramuscular DMPA once every 3 months, with or without 12 weeks of 300 μg/kg subcutaneous acyline once every 2 weeks). Patients were evaluated at monthly intervals. The protocol was completed by 17/22 acyline-treated and 21/22 non-acyline-treated men. Sperm count declined to ≤1 million/ml after a mean of 7–9 weeks in both groups, and had normalized by a mean of 11–15 weeks after treatment ceased. There were no serious adverse events, and changes in body weight, serum lipids and PSA were minimal and reversible.

The authors conclude that transdermal testosterone gel plus DMPA is well tolerated and effective; they call for extended-duration studies to determine the dose of testosterone gel required to optimize spermatogenesis suppression.

Original article Page ST *et al.* (2006) Testosterone gel combined with depomedroxyprogesterone acetate is an effective male hormonal contraceptive regimen and is not enhanced by the addition of a GnRH antagonist. *J Clin Endocrinol Metab* [doi:10.1210/jc.2006-1411]