Early insulin therapy does not improve survival in babies with very low birth weight

Hyperglycemia is common in babies who weigh <1.5 kg at birth and is associated with morbidity and mortality. Beardsall *et al.* investigated whether early insulin treatment improves glycemic control and survival in babies with very low birth weight.

This international, multicenter study enrolled 389 newborn babies younger than 24 h with a birth weight <1.5 kg. Babies randomly assigned to the treatment group received a fixed-dose, continuous infusion of insulin (0.05 (U/kg)/h) for 7 days. Babies randomly allocated to the control group received standard intensive care, and dextrose and insulin as needed.

The mean daily glucose level of the treatment group was significantly lower than that of the control group, and the mean daily energy intake was significantly higher in insulin-treated babies ($P = 0.007$ and $P < 0.001$, respectively). The incidence of hypoglycemia among babies with a birth weight >1 kg, however, was higher in the insulin group than in the control group ($P < 0.001$). No difference was observed between the groups in adjusted mortality before the expected date of delivery, but the rate of death before 28 days after birth was marginally higher in the insulin group (adjusted $P = 0.02$). The study was terminated early by the Trial Steering Committee on the grounds of futility for the primary outcome.

The authors conclude that elective use of early insulin therapy in newborn babies who weigh <1.5 kg does not improve survival, and is associated with an increased risk of hypoglycemia in those <1 kg in weight.

Original article Beardsall K *et al.* (2008) Early insulin therapy in very-low-birth-weight infants. *N Engl J Med* **359:** 1873–1884

High levels of C-reactive protein do not increase the risk of ischemic vascular disease

Elevated levels of C-reactive protein (CRP) are associated with an increased risk of ischemic vascular disease, but whether this association is causal has not been determined. Study of genetic variants provides a relatively unbiased analysis of association, because gene assortment occurs randomly. Thus, Zacho *et al.* examined whether genetic variants that elevate levels of CRP throughout life increase the risk of ischemic cerebrovascular disease and ischemic heart disease. The analysis involved four large, independent cohorts, and included >50,000 Danish people in total.

First, in a multivariate analysis, the researchers showed that the risk of ischemic cerebrovascular disease was increased by a factor of 1.3 and that of ischemic heart disease was increased by a factor of 1.6 in people who had a CRP level >28.6 nmol/l, compared with those who had levels <9.5 nmol/l. The researchers next showed that genotype combinations involving four different CRP polymorphisms were associated with increases of up to 64% in lifelong CRP levels, which would theoretically predict an increased risk of up to 25% and up to 32% for ischemic cerebrovascular disease and ischemic heart disease, respectively. Nevertheless, CRP genotypes were not associated with increases in the risks of either ischemic cerebrovascular disease or ischemic heart disease.

The researchers conclude that CRP level is a marker for an increased risk of ischemic vascular disease, but is not causally related to the increased risk.

Original article Zacho J *et al.* (2008) Genetically elevated C-reactive protein and ischemic vascular disease. *N Engl J Med* **359:** 1897–1908

LHRH agonists could benefit premenopausal women with early-stage breast cancer

As over half of all early-stage breast cancers remain estrogen-receptor-positive, the goal of adjuvant hormone therapy is to reduce the local concentrations of estrogen. Sharma and colleagues present the findings of a systematic review, in which they evaluated adjuvant, luteinizing hormone-releasing hormone (LHRH) therapy in premenopausal women with early-stage estrogen-receptor-positive breast cancer.

The authors searched the Cochrane Breast Cancer Group register for randomized clinical trials that assessed any of four interventions: LHRH agonist versus LHRH agonist plus tamoxifen; LHRH agonist versus chemotherapy; LHRH agonist versus ovarian ablation; and