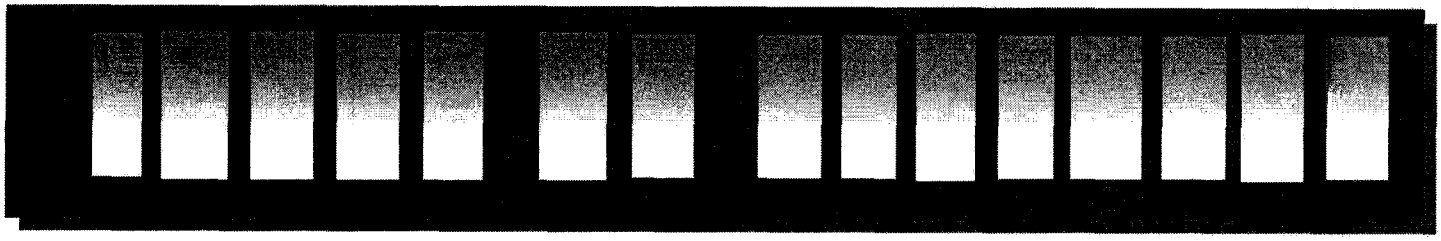
Scottish Executive Health Department Chief Scientist Office



Levels of neonatal thyroid hormones in preterm infants and neurodevelopmental outcome at 5 ½ years

Researchers
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Aim
To determine whether transient hypothyroxinaemia, low levels of thyroxine (T4), in infants born ≤34 weeks gestation is associated with compromised developmental outcome measured at age 5.5 years.

Project Outline/Methodology
This project is a follow-up of a cohort of preterm and term infants who were recruited between 1st November 1999 and 31st August 2001 as part of the Millennium Study, which measured thyroid hormone levels and recorded details of maternal and infant health during pregnancy, delivery and postnatally.

Children were assessed, by trained psychologists, at the age of five years 6 months ±2 months. Information on a range of factors that may influence neurodevelopment was collected at birth and also postnatally. The main outcome measures were the scores on the McCarthy Scales, which give an indication of general cognitive and motor function.

Transient hypothyroxinaemia was defined as a level of T4 (the thyroid hormone required for normal brain development) below the 10th percentile on postnatal day 7, 14 or 28 adjusted for gestational age.

Key Results
We followed up 442 infants ≤34 weeks gestation and 100 term infants. Twenty percent (88/442) of infants ≤34 weeks gestation were hypothyroxinaemic.

Infants classified as transiently hypothyroxinaemic had a mean general cognitive score of 95, those classified as euthyroid (normal thyroid levels) a mean score of 105, and term infants a mean score of 109. Mothers with infants classified as transiently hypothyroxinaemic were significantly more likely to report that their children had difficulties with hearing, speech, and hand or leg co-ordination.

Following adjustment for a range of factors that might influence general cognitive outcome, transient hypothyroxinaemia remained a significant factor, reducing the score by 6 points. The association of transient hypothyroxinaemia with the other major components of the McCarthy scales (motor and quantitative scores) although non-significant were -2.5 and -1.0 point respectively.

Conclusions
Our findings do not support the view that hypothyroxinaemia in preterm infants is harmless.

What does this study add to the field?
Our study is the first to investigate the relationship between transient hypothyroxinaemia and cognitive and motor development adjusted for an extensive number of confounders of neurodevelopment. That this relationship is maintained after adjustment suggests that the cognitive loss associated with transient hypothyroxinaemia is not simply an epiphenomenon of premature birth and postnatal illness.

Implications for Practice or Policy
Data from the Millennium study enables the definition of hypothyroxinaemia relative to gestational age of birth, allowing clinicians to quantify objectively and monitor transient hypothyroxinaemia. Thyroxine substitution for transient hypothyroxinaemia is not recommended routinely as the necessary randomised trials have not yet been designed to evaluate the most effective treatment doses and duration.

Where to next?
Premature infants fed on parenteral nutirtion can quickly become iodine deficient. Iodine deficiency is one of the modifiable causes of transient hypothyroxinaemia. In 2009 we start a trial of iodine supplementation of 1500 preature infants. The results of this trial should allow us to test the efficacy of iodine supplementation in reducing the severity of transient hypothyroxinaemia.

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