Reply

John H. Lazarus^a Jonathan P. Bestwick^b Nicholas J. Wald^b

^aCentre for Endocrine and Diabetes Sciences, Cardiff School of Medicine, Cardiff, and

^bWolfson Institute of Preventive Medicine, Barts and The London School of Medicine and Dentistry, London, UK

We thank Dr. Negro for his letter on our study and would like to comment on the five points he makes.

(1) If maternal TSH and FT4 levels were unrelated to childhood IQ in our population, the conclusion against screening in pregnancy would still hold, as Negro says, because the problem would not be present rather than the preventive treatment not working.

(2) The power of the trial was adequate. In the study of Haddow et al. [1] the hypothyroid group had TSH ≥ 98 th (mostly above 99.7th) centile and there was about a fourfold increase in the number of children with IQ < 85 born to mothers in this group compared with the control group. Our trial was adequately powered to detect a threefold difference between the treated and control group in women with TSH ≥ 97.5 th centile ($> 90\%$ power at the 5% significance level). In the subset of women with TSH ≥ 99.7 th centile, 6/30 (20%) chil-

dren of control group mothers and 4/23 (17%) children of screen group mothers had an IQ < 85 , a result that was not statistically significant ($p = 0.81$). For both subgroups (high TSH and low FT4) the power was $> 90\%$.

(3) We mentioned the possibility that thyroxine therapy was started too late in pregnancy, but a trend analysis on starting thyroxine treatment from 8 to 15 weeks of pregnancy showed no great effect at the earlier gestation.

(4) The TSH levels in Haddow et al. [1] may have been higher than in the women with high TSH levels in our study, but we identified the women with TSH levels in the highest 2.5% of values and it would be surprising if pregnant women in the USA were much more hypothyroid than in Western Europe. The 99.7th centile of TSH in the study by Haddow and colleagues was about 9 mU/l, whereas in our study it was 7 mU/l in the UK and 5.7 mU/l in Ita-

ly. Systematic differences in mU/l measurements between laboratories preclude any direct assessment of this.

(5) There is no indication that FT4 assays materially distort the ranking of pregnancies according to FT4 and so bias is unlikely to have occurred.

Considering these points there is no reason to change our conclusion that our trial results do not support screening for childhood detected disability by antenatal TSH or FT4 measurement.

Reference

- 1 Haddow JE, Palomaki GE, Allan WC, et al: Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *N Engl J Med* 1999; 341:549–555.