CORRESPONDENCE

To the Editor:

We read with interest an article by Dr I.J. Chopra in the April 2004 issue describing the measurement of 3.3′-diiodothyronine sulfate (T_2S) in thyroidal and nonthyroidal disease, pregnancy, and fetal/neonatal life.[1] In the article, the author describes development of a sensitive and specific radioimmunoassay for T_2S, and reports a 5-fold increase in serum levels in pregnant women and a 20-fold increase in cord serum levels in neonates as compared to "normal" euthyroid values. A significant portion of the data was presented at the Annual Meeting of the American Thyroid Association in San Diego in 1996 (Thyroid 6:S23). The number of patients studied does not appear to have increased in the intervening years.

It has been a decade since we reported detecting a T_2S cross-reactive material in pregnant and cord sera (compound W).[2] We observed that the majority of T_2S-reacting material was not T_2S per se; it could be separated from T_2S on high-performance liquid chromatography, and was acid stable as compared to T_2S, which is readily hydrolyzed by 0.5 N HCl at 80°C.[2,3] Although Chopra included our paper in his references, he failed to use these criteria to separate T_2S from compound W in the sera of pregnant women or the cord sera in his study.

Further, it seems likely that the reported values for T_2S in nonpregnant individuals are too high. T_2S, a hydrophilic derivative of T_2, is readily cleared by the kidney. In addition, it is rapidly degraded by the type 1 deiodinase with a V_{max}/K_m ratio of 1,040,[4] compared with a V_{max}/K_m of 21 for T_2, and is poorly bound to TBG. Chopra reported the serum level of T_2S (51 ng/dL) in nonpregnant euthyroid individuals was 10 times that of T_2 (~5 ng/dL).[5] Even if one assumes that T_2S has a metabolic clearance rate similar to T_2 (~700 L/d), the production rate of T_2 would be nearly 350 μg/d (10 times that of T_2),[5] a rate 2 to 3 times that of T_4. Thus, available information would suggest that the material measured by Chopra is not totally attributable to T_2S and the cross-reacting material(s) in his T_2S radioimmunoassay remains to be identified. Incidentally, our values for normal women, about 10 ng/dL, were reported not only for 14 patients in reference 2, but also more in recent publications that reported similar results in additional 27 more nonpregnant women.[6,7]

Finally, the article states that T_2S assays in maternal serum are a poor indicator of fetal thyroid function. We have never claimed that authentic T_2S is such an indicator. Rather, we have presented extensive evidence that compound W, a compound that is cross-reactive with T_2S in our immunoassays, is an indicator of fetal thyroid function, and rises throughout pregnancy to reach values 15 to 20 times normal in the third trimester.[2,3] Compound W assays have proven useful in identifying fetal hypothyroidism,[8,9] and in monitoring fetal thyroid function in women treated with antithyroid drugs.[8-10]

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