INVITED COMMENTARY

Adequate iodine intake – the good far outweighs the bad

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In this current issue of the *European Journal of Endocrinology*, Reinhardt and his colleagues report that the administration of 250 µg potassium iodide daily for an average of 4 months (range 2–13 months) in mildly iodine-deficient Germany induced subclinical hypothyroidism in some patients (1). As mentioned in that report, when Dr Reinhardt was a postdoctoral fellow in this laboratory in the 1980s, he carried out a similar but much smaller and briefer study on the effects of 1500 µg iodide daily on thyroid function in euthyroid patients with Hashimoto's thyroiditis and normal subjects residing in Massachusetts with a sufficient ambient iodine intake of approximately 200 µg daily (2). Although those results were never published as a full paper, review of the data revealed that when the iodine-treated patients with Hashimoto's thyroiditis were treated with iodine for 14 days, serum thyrotropin (TSH) concentrations increased to slightly above normal in some patients compared with normal subjects, but when iodine administration was continued for a total of 12 weeks, serum TSH values in both groups of subjects increased only slightly. This suggests that the longer period of a mild increase in iodine intake in euthyroid patients with Hashimoto's thyroiditis and a normal ambient iodine intake was associated with at least a partial adaptation to the excess iodine and escape from the acute Wolff–Chaikoff effect. In the present report of Reinhardt *et al.* (1), only a few patients with Hashimoto's thyroiditis developed subclinical hypothyroidism in the absence of an increase in thyroid peroxidase (TPO) antibodies or change in thyroid volume. Those patients with initial TSH values near the upper normal range appeared to be at greater risk of developing subclinical hypothyroidism, a not unexpected finding. It would have been of interest to have concomitantly studied the effects of 250 µg potassium iodide daily in euthyroid patients without Hashimoto's thyroiditis to be sure that the occurrence of subclinical hypothyroidism was unique to the Hashimoto's patients and would not have developed in normal subjects without a defect in the intrathyroidal organification of iodide. However, as the authors correctly point out, all previously published reports of iodine-induced hypothyroidism in patients with Hashimoto's thyroiditis employed very large doses of iodine. Whether supplementation of iodine to the level achieved in the present study in areas of mild iodine deficiency would increase the prevalence of subclinical hypothyroidism remains unknown. However,

relief of iodine deficiency, even of a mild degree, is certainly warranted.

Fortunately, only 2 of 40 patients developed mild hyperthyroidism, but this does raise a warning flag as to the optimum iodine supplementation in iodine-deficient regions. Over the past few years, small outbreaks of thyrotoxicosis in adults have been reported following iodine prophylaxis with iodized oil or iodized salt in severely iodine-deficient regions, probably due to excess iodination of these severely iodine-deficient populations (3–6). However, it must be emphasized that the eradication of iodine deficiency far outweighs this minor risk, which is almost always self-limited and disappears over many years as the iodine-deficient population achieves iodine repletion. Prevention of iodine-deficiency goiter, mental and growth retardation, poor productivity, and cretinism must be achieved through joint efforts of international, national, and local agencies. Great strides have been made. Careful monitoring of populations given iodine supplementation is essential to be sure that adequate but not excessive iodine intake is being maintained.

No change in TPO antibody concentrations was observed in the present study of Reinhardt *et al.* (1) during the administration of small supplementary doses of iodine. As the authors note, an increase in iodine intake has been reported to increase the prevalence of thyroiditis. Most of these studies were based upon iodine supplementation of patients residing in iodine-deficient areas. The use of small doses of iodine in the present study in a mildly iodine-deficient area did not increase TPO antibody levels. Perhaps a longer period of iodine administration would have aggravated the underlying thyroiditis. Certainly, the administration of large doses of iodine to susceptible animal models such as the BB/Wor rat (7), the obese strain chicken (8), the Buffalo rat (9) and the NOD mouse (10) does increase the incidence and severity of lymphocytic thyroiditis.

References

- 1 Reinhardt W, Luster M, Rudorff KH, Heckmann C, Petrasch S, Lederbogen S, Haase R, Saller B, Reiners C, Reinwein D & Mann K. Effect of small doses of iodine on thyroid function in patients with Hashimoto's thyroiditis residing in an area of mild iodine deficiency. *European Journal of Endocrinology* 1998 139 23–28.
- 2 Paul T, Reinhardt W, Meyers B, Ingbar SH & Braverman LE. Small increase in iodine intake does not induce hypothyroidism in

- euthyroid patients with Hashimoto's disease. *Clinical Research* 1987 **35** 400A.
- 3 Galofre JC, Fernandez-Calvet L, Rios M & Garcia-Mayor RV. Increased incidence of thyrotoxicosis after iodine supplementation in an iodine sufficient area. *Journal of Endocrinological Investigation* 1994 **17** 23–27.
 - 4 Elnagar B, Eltorn M, Karlsson FA, Ermans AM, Gebere-Medhin M & Bourdoux PP. The effects of different doses of oral iodized oil on goiter size, urinary iodine, and thyroid-related hormones. *Journal of Clinical Endocrinology and Metabolism* 1995 **80** 891–897.
 - 5 Bourdoux PP, Ermans AM, Mukalay A, Mukalay WA, Filetti S & Vigneri R. Iodine induced thyrotoxicosis in Kivu, Zaire. *Lancet* 1996 **347** 552–553.
 - 6 Todd CH, Allain T, Gomo ZA, Hasler JA, Ndiweni M & Oken E. Increase in thyrotoxicosis associated with iodine supplements in Zimbabwe. *Lancet* 1995 **346** 1563–1564.
 - 7 Allen EM, Appel MC & Braverman LE. The effect of iodine ingestion on the development of spontaneous lymphocytic thyroiditis in the diabetes prone BB/Wor rat. *Endocrinology* 1986 **118** 1977–1981.
 - 8 Bagchi N, Brown TR, Vrdaniria E & Sundick RS. Induction of autoimmune thyroiditis in chickens by dietary iodine. *Science* 1985 **230** 375.
 - 9 Allen EM & Braverman LE. The effect of iodine on lymphocytic thyroiditis in the thymectomized buffalo rat. *Endocrinology* 1990 **127** 1613–1616.
 - 10 Rasooly L, Burek CL & Rose NR. Iodine induced autoimmune thyroiditis in NOD-H-2h4 mice. *Clinical Immunology and Immunopathology* 1996 **81** 287–292.
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