

# BRITISH MEDICAL JOURNAL

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We may return unduly long letters to the author for shortening so that we can offer readers as wide a selection as possible. We receive so many letters each week that we have to omit some of them. Letters should be typed with double spacing between lines and must be signed personally by all their authors, who should include their degrees. Letters critical of a paper may be sent to the authors of the paper so that their reply may appear in the same issue.

Correspondents should present their references in the Vancouver style (see examples in these columns). In particular, the names and initials of all authors must be given unless there are more than six, when only the first three should be given, followed by *et al*; and the first and last page numbers of articles and chapters should be included.

## Are antithyroid drugs immunosuppressive?

SIR,—We want to clarify two points made by Dr P Kendall-Taylor (18 February, p 509): firstly, on the evidence that immunosuppression might be mediated by normalisation of circulating thyroid hormone concentrations; and, secondly, on the intrathyroidal concentration of carbimazole.

We have already shown that microsomal antibody concentrations fall in patients with Hashimoto's disease given carbimazole, in whom euthyroidism is maintained by thyroxine supplementation.<sup>1</sup> Similarly, the immunosuppression produced by methimazole in experimental autoimmune thyroiditis in the rat is independent of thyroid hormone state.<sup>2,3</sup> We have been unable to show altered B or T cell function when excessive triiodothyronine is given to normal subjects.<sup>4</sup> T cell subset distribution is not altered in hyperthyroidism due to toxic adenoma but is clearly abnormal in Graves' disease.<sup>5</sup> On the basis of this and other evidence, there seems no good reason to invoke an indirect effect of antithyroid drugs on the immune system via the action of thyroid hormones.<sup>4</sup>

With regard to the intrathyroidal concentration of methimazole, Jansson and colleagues have reported that the concentrations achieved are only at the lower end of the effective immunosuppressive range.<sup>6</sup> This study however, was with patients with Graves' disease already rendered euthyroid with carbimazole. In fact the same researchers had previously presented data which showed that in *thyrotoxic* thyroid tissue, the concentration of drug may increase sevenfold (P A Dahlberg and others,

paper presented at the annual meeting of the American Endocrine Society, 1982). This would result in a concentration close to 100 µmol/l in the gland of an untreated patient, and this concentration is immunologically effective. Moreover, since the results of treatment depend on antithyroid drug dosage and not on thyroid hormone concentrations,<sup>7</sup> it is difficult to envisage how altered expression of antigenic sites by lowering thyroid hormones as suggested by Jansson's group (P A Dahlberg and others, paper presented at the annual meeting of the American Endocrine Society, 1982) could explain the outcome of antithyroid drug treatment.

There can be little doubt that antithyroid drugs are immunosuppressive; this has been shown *in vitro* and *in vivo*. The question now to be answered is whether this is relevant to the treatment of Graves' disease, and we have discussed this possibility at length in a forthcoming article.<sup>8</sup>

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<sup>1</sup> McGregor AM, Ibbertson HK, Rees Smith B, Hall R. Carbimazole and autoantibody synthesis in Hashimoto's thyroiditis. *Br Med J* 1980;281:968-9.

<sup>2</sup> Rennie DP, McGregor AM, Keast D, *et al*. The influence of methimazole on thyroglobulin induced autoimmune thyroiditis in the rat. *Endocrinology* 1983;112:326-30.

<sup>3</sup> Weetman AP, McGregor AM, Rennie DP, Hall R. Thyroid hormones fail to influence experimental autoimmune thyroiditis. *Clin Exp Immunol* 1982;50:51-4.

<sup>4</sup> Weetman AP, Ludgate M, McGregor AM, Hall R. Effect of tri-iodothyronine on normal human lymphocyte function. *J Endocrinol* (in press).

<sup>5</sup> Bagnasco M, Canonica GW, Ferrini S, *et al*. T lymphocyte sub-populations in Graves' disease: relationship with clinical conditions. *Acta Endocrinol* 1983;102:213-9.

<sup>6</sup> Jansson R, Dahlberg PA, Johansson H, Lundstrom B. Intrathyroidal concentrations of methimazole in patients with Graves' disease. *J Clin Endocrinol Metab* 1983;57:129-32.

<sup>7</sup> Romaldini JH, Bromberg N, Werner RS, *et al*. Comparison of effects of high and low dosage regimens of antithyroid drugs in the management of Graves' hyperthyroidism. *J Clin Endocrinol Metab* 1983;57:563-70.

<sup>8</sup> Weetman AP, McGregor AM, Hall R. Evidence for an immunosuppressive effect of antithyroid drugs in Graves' disease. *Clinical Endocrinol* (in press).

SIR,—Dr A P Weetman and others (18 February, p 518) and Dr P Kendall-Taylor extend the previous suggestion<sup>1</sup> that thiocarbamide antithyroid drugs may have an immunoregulatory role in addition to their function in suppressing thyroidal organification of iodine. The full extent of the actions of these drugs is unclear, but by virtue of their capacity to act as substrates for the many peroxidase containing tissues; mono-oxygenase systems may similarly be influenced.

We agree that zymosan induced chemiluminescence in monocytes is inhibited by methimazole, although we have found 50% inhibition with  $5.5 \times 10^{-4}$  M methimazole. Propylthiouracil and methimazole have a similar effect on polymorphonuclear neutrophilic leucocyte myeloperoxidase, although their effect on polymorphonuclear neutrophilic leucocyte function is less obvious.<sup>2</sup>