LETTERS TO THE EDITOR

Hypothyroidism after Radioiodine Treatment

According to Dr. Von Hofe and his collaborators (*1*) the incidence of hypothyroidism within 1 yr after radioiodine therapy for toxic diffuse goiter appears to be increasing. They detected hypothyroidism in 69% of patients treated with 10 mCi, as contrasted with about 30–50% in earlier American studies, and they cite evidence (*2–4*) that the decreased use of thionamide pretreatment and the increase in dietary iodine may be causative or contributory factors.

However, the finding by the Glasgow group (*2,3*) of increased radioresistance after thionamide medication has not been confirmed by others (*5,6*). In one of these studies carbimazole had been used as an antithyroid drug, and the fact that this drug lacks an -SH group was offered as an explanation (*6*). It was shown later, however, that carbimazole is converted in the body to methimazole (*7*). In itself, the presence of an -SH group is a plausible explanation for a protective action, but this is then not expected to last long after discontinuing the drug. This has indeed been confirmed (*8*) and may explain the different results mentioned above.

Von Hofe et al. (*1*) further speculate that an increase in dietary iodine might render the thyroid gland more radiosensitive. However, in the study they cite on the induction of hypothyroidism by iodide after I-131 therapy (*4*), the daily dose of iodide given to the patients was of the order of 100 mg, whereas the average iodine intake in Texas has been reported as 0.3-0.4 mg per day (*9*). Furthermore, if reduction of thyroidal iodine stores were a mechanism whereby thionamide drugs render the gland more radioresistant, then perchlorate pretreatment would be expected to have a similar effect, but this was not found to be the case (*3*). I myself have speculated that the higher incidence of hypothyroidism after I-125 treatment in New York City than in Amsterdam might be explained by the higher iodine intake in America (*10*), but the mechanism proposed (different radiation doses at the level of the follicle-cell nucleus) does not hold in the case of I-131.

After all, however, I wonder whether the incidence of hypothyroidism found by Von Hofe et al. (*1*) is really higher than in other American series. One third of their patients classified as such had "extremely low" free T_4 index values but no definite symptoms of hypothyroidism. The T_3/T_4 ratio is usually clearly elevated in hyperthyroidism and may remain so for a considerable time after successful treatment; actually, judging from the figures given, a considerable number of patients classified as hypothyroid had normal T_3 values. If only those clinically hypothyroid are counted, the diffrence between their series and those of the others cited disappears completely.

The much lower incidence of post-I-131 hypothyroidism in European series can be explained partly by the lower doses given in many centers. Yet, even at doses comparable with those in most American series, the incidence was usually 20% or less after 1 yr (*6,11*). For this phenomenon there does not seem to be a ready explanation; the only obvious difference appears to be the difference in iodine intake.

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Reply

Dr. Wiener raises some valid questions about the role of decreased use of thionamides and increased dietary iodine as causative in the increased incidence of hypothyroidism we observed. As we stated in the article, the reason for the increase was not clear. We proposed that these two factors may account for an over-all increase in radiosensitivity.

Evidence that thionamides cause some radioprotective effect is greater than that indicating increased iodine consumption as causing radiosensitivity. A statistical difference in the effects of iodine-131 treatment in patients who had received thionamides was found by us and by Crooks et al. (*1,2*). Although Hagen et al. did not observe such a radioprotective effect, these results are not comparable with ours, since all their patients received SSKI after I-131 therapy (*3*). Admittedly the information is scanty, but what there is indicates that thionamides do cause some radioresistance. There is evidence from the studies of Buchanan et al. that the use of thionamides does not totally account for our observed increase in hypothyroidism (*4*). Their thionamide-treated patients, who received a mean I-131 dose of

10.7 mCi, had a 32% incidence of hypothyroidism compared with our incidence of 55% in a similar group.

The hypothesis that the "other factor" causing an increase in hypothyroidism is increased dietary iodine is certainly weakened by the observation that radioresistance was not found in carbimazole- or perchlorate-treated patients. As we stated in the article and as Dr. Wiener has emphasized, the only evidence for iodine as a cause of increased hypothyroidism depends on pharmacologic doses. In a manner similar to this last statement, the only obvious difference between our patients and earlier reports is a difference in iodine intake.

The third of our patients who were not definitely clinically hypothyroid were not asymptomatic. They had mild-to-moderate symptoms compatible with hypothyroidism, T_4 levels of less than 4, and even lower levels of FT_4I. They usually also had low T_3 levels of RIA and high TSHs. The studies that we used for comparison used criteria of low PBIs plus some symptoms. As such, our criteria for hypothyroidism were as rigid as the studies we used for comparison, if not more so.

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Ventilation Studies and the Perfusion Lung Scan

The letter of Drs. Coates and Garnett in a recent issue of the *Journal* regarding ventilation studies and their relation to the perfusion lung scan is of interest, but it overlooks one simple, direct, practical point.

Admittedly, because of the difference between the energies of Xenon-133 and technetium-99m, theoretically the technetium scan should precede the xenon scan. In practice, however, this appears to be of no importance. To demonstrate this I would like to recommend a simple experiment to those who are interested. Let us take a patient on whom we have just carried out a perfusion scan, pick any view we wish, and re-scan him, changing the windows to those used to scan xenon. Let the patient be scanned for the same time as the ventilation scan usually takes. We have found, and I think this can be easily corroborated, that on most of today's equipment the separation remains so good that virtually nothing is seen of the technetium scan when the xenon windows are used. A little further thought would tell us that if one chooses obviously abnormal perfusion-scan views, then even if some of the perfusion scan is to be seen with xenon windows, the "match" of the two scans would be accentuated rather than diminished. Similarly, it is extremely unlikely that on good xenon studies the "mismatching" would be obscured. This is not to deny that Xe-127 certainly looks like a better scanning agent than Xe-133, but since the latter is not yet freely available to most of us, there is absolutely no reason, in my opinion, why the ventilation scan should not follow the perfusion scan with all the advantages that Drs. Coates and Garnett point out.

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Reply

In reply to Dr. Lewis' letter, we draw his attention to a paper published by Coates and Nahmias in 1977 (*1*). In this study we performed the "simple experiment" suggested by Dr. Lewis, in which we measured the contribution of the Compton scatter from 1 mCi of Tc-99m into the Xe-133 window of a gamma camera*. We expressed this contribution as a fraction of the counts recorded for the same time from 1 mCi of Xe-133. For every 100 counts contributed by the Xe-133 there were 169 counts from the Tc-99m. If one extrapolates this to the clinical situation in which the patient receives 2 mCi of Tc-99m MAA and up to 20 mCi of Xe-133, the number of counts from Xe-133 would be 2000 and from Tc-99m would be 338. This is presumably what Dr. Lewis found in his patient, although he did not state the doses used. The point, which was discussed in the above-mentioned paper (*1*), is that 20 mCi of Xe-133 delivers an unacceptably large radiation dose to the trachea and bronchial mucosa (*2*). As the Xe-133 dose is reduced, the contribution of Tc-99m to the Xe-133 image becomes more and more significant.

With regard to Dr. Lewis' second point, we agree that in an abnormal perfusion scan the Tc-99m contribution to the Xe-133 image would tend to accentuate a ventilation defect if one is present. However, this is usually not the issue. The important fact is that for the same reasons there will be an apparent ventilation defect when, in fact, the ventilation is normal. This point was highlighted in Fig. 4 of our paper. We must disagree, therefore, with Dr. Lewis' conclusion that "mismatching would not be observed," since, in fact, the opposite has been shown to be true.

Finally, despite Dr. Lewis' statement to the contrary, Xe-127 is readily available from Brookhaven National Laboratories to anyone who obtains approval to use it.

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FOOTNOTE

*Ohio Nuclear Series 100

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Technical Errors in Scintigraphic Measurements of Gastric Emptying

We read with interest the paper on Technical Errors in Scintigraphic Measurements of Gastric Emptying by Tothill et al. (*1*). We feel, however, that their results might discourage others from using a gamma camera to measure gastric emptying. We have been performing gastric emptying measurements for over 5 years and feel that the problems that they highlight are insignificant. A great advantage of the gamma camera is that the