LETTERS TO THE EDITOR

Re: Clinical Assessment of a Radioimmunoassay for Free Thyroxine using a Modified Tracer

We read with interest the letter by Drs. Bayer and McDougall (*1*) regarding Dr. Chan's evaluation of the single-step free-thyroxine (FT_4) assay marketed by Amersham Corporation (*2*). While we agree in general with their comments, there is one point that we feel we need to clarify, and a second upon which we wish to comment.

Our initial experience with Corning Medical's single-step FT_4 assay (Immophase Single-Step Free-T_4 (I-125) Radioimmunoassay) was presented at the meeting of the American Association for Clinical Chemistry in the summer of 1983. Information published in our abstract was included in Bayer's Table 1 (her Ref. *14*). Unfortunately, this represents information obtained with a prototype assay system and is not representative of the performance of Corning Medical's present single-step system, on which we report elsewhere (*4*). In 45 seriously nonthyroidally ill patients, 20% of results using the present Corning system fell below the lower limit for normal, while 42% of the same patients had results below the lower limit for normal using the Amersham FT_4 system (*4*). This difference reflects an awareness on the part of the Corning development staff that T_4 derivatives are bound by serum albumin. Their present assay system was modified after our original observations, such that these effects are minimized.

We agree that the Clinical Assays two-step system produces apparently normal results in patients who are nonthyroidally ill (*5*). We have, however, two concerns regarding this conclusion. First, we find that the antibody-extracted mass of total thyroxine is low in patients with nonthyroidal illness (*5,6*). If the mass extracted is quantified as extracted fraction times total T_4, the result is a low free-T_4 estimate. It is difficult to understand why this very same low extracted mass produces a quantitatively normal free-T_4 estimate in the Clinical Assays two-step system. Secondly, we, like Braverman (*7*), frequently find free-T_4 results that are apparently spuriously elevated when using the Clinical Assays two-step method. We have discussed this in some detail with Clinical Assays and have been informed that the problem does indeed exist and may or may not be explained by tubes into which serum is collected, as was suggested by Braverman (*7*). In our own laboratory we have repeated the experiment described by Braverman and his group, and have not been able to relate elevated FT_4 results to the brand of tube, whether the tube is glass or plastic, whether it is siliconized, or whether the red rubber top is used or not. Our inability to produce consistently reproducible results with this assay system is disturbing to us, because it certainly differs from the experience reported by the Stanford group (*1*).

In our experience, equilibrium dialysis most often produces normal FT_4 results in patients with nonthyroidal illness (*5*). In the absence of an equilibrium-dialysis assay, we most often successfully evaluate thyroid functional status in ill, hospitalized patients by measuring total thyroxine and T_3 uptake, followed by measurements of TSH and reverse T_3 concentration. We are unable to recommend any currently available commercial FT_4 system for FT_4 estimation in nonthyroidally ill patients.

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Reply

We thank Drs. Witherspoon and Shuler for their comments. We agree with them that the Clinical Assays two-step FT_4 procedure demands more technical skills from the analyst. As stated previously (Ref. *10* of our original letter), we have amended the kit protocol to obtain more reproducible results.

In agreement with Ekins et al. (*1*), we find it conceptually wrong to use any of the analog methods to measure FT_4, in particular in sick patients, if the tracer analog can be shown to bind to serum albumin or other serum binding proteins.

In view of earlier reports (*2*) and our own data, we believe it unusual that Drs. Witherspoon and Shuler find the measurement of total T_4 and T_3 uptake useful in ill, hospitalized patients.

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Re: Decreased Sensitivity of Early Imaging with In-111 Oxine-Labeled Leukocytes in Detection of Occult Infection

Datz et al., in their article in the March, 1984, issue of the