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# Preparation of Patients with Thyroid Cancer for $^{131}\text{I}$ Scintigraphy or Therapy by 1–3 Weeks of Thyroxine Discontinuation

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To assess whether the patient preparation procedure for  $^{131}\text{I}$  scintigraphy could be streamlined, we evaluated the time course of thyroid-stimulating hormone (TSH) elevation after total thyroidectomy or after discontinuation of thyroxine ( $\text{T}_4$ ) in patients with thyroid cancer. **Methods:** The clinical records of 284 patients with well-differentiated thyroid cancer were reviewed. All patients had undergone total thyroidectomy. Two groups of patients were evaluated. The immediate postoperative group consisted of 176 patients who were not given thyroid hormone replacement after surgery because of planned postoperative  $^{131}\text{I}$  therapy. The surveillance group consisted of 108 patients in whom  $\text{T}_4$  replacement was stopped (without triiodothyronine [ $\text{T}_3$ ] replacement) in preparation for surveillance whole-body  $^{131}\text{I}$  scintigraphy. We recorded the first TSH measurement and number of days after surgery or without thyroid hormone for each patient. **Results:** In the immediate postoperative group, TSH levels obtained 6–65 d (median, 17 d) after surgery ranged from 18.2 to 194.8  $\mu\text{IU/mL}$  (median, 46.6  $\mu\text{IU/mL}$ ). The TSH values exceeded 30  $\mu\text{IU/mL}$  in 89% of patients evaluated at 1–2 wk, in 88% of those evaluated at 2–3 wk, and in 90% of those evaluated after 3 wk. In patients discontinuing  $\text{T}_4$  (without  $\text{T}_3$  replacement), TSH levels obtained from 6 to 35 d (median, 20 d) later ranged from 23.4 to 214.5  $\mu\text{IU/mL}$  (median, 61.1  $\mu\text{IU/mL}$ ). The TSH levels exceeded 30  $\mu\text{IU/mL}$  in 100% of patients evaluated at 1–2 wk, in 89% of those evaluated at 2–3 wk, and in 96% of those evaluated after 3 wk. **Conclusion:** In most patients with thyroid cancer being prepared for  $^{131}\text{I}$  imaging or therapy, a TSH level exceeding 30  $\mu\text{IU/mL}$  can be achieved by withdrawal of thyroid hormone therapy for 1–3 wk.

**Key Words:** thyroid cancer; thyroid-stimulating hormone;  $^{131}\text{I}$ ; thyroxine; triiodothyronine

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**S**erum thyroid-stimulating hormone (TSH) concentrations in patients with thyroid carcinoma must be elevated before administration of  $^{131}\text{I}$  iodide either for diagnostic whole-body scintigraphy or for therapy, to ensure sufficient uptake of  $^{131}\text{I}$  in tumor tissue. The optimal TSH concentration is unknown, but a level of  $\geq 30$   $\mu\text{IU/mL}$  is generally considered sufficient for both imaging and therapy (1,2).

There are 2 distinct groups of patients in whom TSH elevation is desired: patients who are to undergo  $^{131}\text{I}$  ablation of residual thyroid tissue after total thyroidectomy for a newly diagnosed thyroid carcinoma, and patients who undergo thyroid hormone withdrawal in preparation for whole-body  $^{131}\text{I}$  scintigraphy for surveillance. Although recombinant human TSH may be administered (without the need for thyroid hormone withdrawal) to prepare patients for whole-body  $^{131}\text{I}$  scintigraphy, this approach is not optimal for use in patients in whom a positive imaging result is anticipated. Such patients will typically undergo therapeutic administration of  $^{131}\text{I}$  after imaging, and thyroid hormone withdrawal is thus a prerequisite.

After thyroidectomy, it is generally held that circulating thyroid hormone (chiefly thyroxine [ $\text{T}_4$ ]) secreted before surgery delays the postoperative TSH response and that maximal TSH values are not reached until approximately 4–6 wk. The classic recommendation has thus been that patients be maintained postoperatively on triiodothyronine ( $\text{T}_3$ ) replacement therapy for 4 wk (1,3).  $\text{T}_3$  is then withheld, with the expectation that a TSH concentration of  $\geq 30$   $\mu\text{IU/mL}$  will be achieved in 2 wk, reflecting the shorter biologic half-life of  $\text{T}_3$  than of  $\text{T}_4$ .

The literature recommends a similar procedure for TSH elevation for follow-up  $^{131}\text{I}$  whole-body scintigraphy (and therapy): discontinue  $\text{T}_4$ , substitute  $\text{T}_3$  for  $\text{T}_4$  for 4 wk, withdraw  $\text{T}_3$  for 2 wk, and then determine the serum TSH level (1). If TSH is not elevated to  $\geq 30$   $\mu\text{IU/mL}$ ,  $\text{T}_3$  withdrawal is maintained for an additional 1–2 wk until the

TSH level exceeds that value. As an alternative, some institutions simply withdraw replacement thyroid hormone therapy for 4–6 wk, but this is said to lead to an unnecessarily long period of symptomatic hypothyroidism.

In our practice, we have not used  $T_3$  in any patient. We have relied on discontinuation of  $T_4$  replacement therapy and have measured serum TSH sooner than the generally recommended 4–6 wk. The purpose of this retrospective review was to evaluate the time course of TSH elevation in our patients after thyroidectomy or after  $T_4$  withdrawal without  $T_3$  substitution.

## MATERIALS AND METHODS

We retrospectively reviewed the clinical records of patients with well-differentiated thyroid carcinoma treated at our institution between July 1998 and July 2002. The institutional Human Studies Committee approved this review. All patients underwent a total thyroidectomy for well-differentiated thyroid carcinoma and subsequently received postoperative  $^{131}\text{I}$  ablation or follow-up  $^{131}\text{I}$  scintigraphy. They were prepared for  $^{131}\text{I}$  administration by withholding of thyroid hormone replacement postoperatively or simple thyroid hormone withdrawal (without  $T_3$  substitution) and had at least 1 TSH measurement. For the purposes of this study, only the first TSH measurement in each patient was considered in the analysis.

The analysis included 284 patients, 72 men and 212 women, ranging in age from 6.8 to 85.4 y (mean, 45.9 y). TSH measurements were performed in routine fashion by licensed clinical laboratories. We had planned to obtain the first TSH measurement

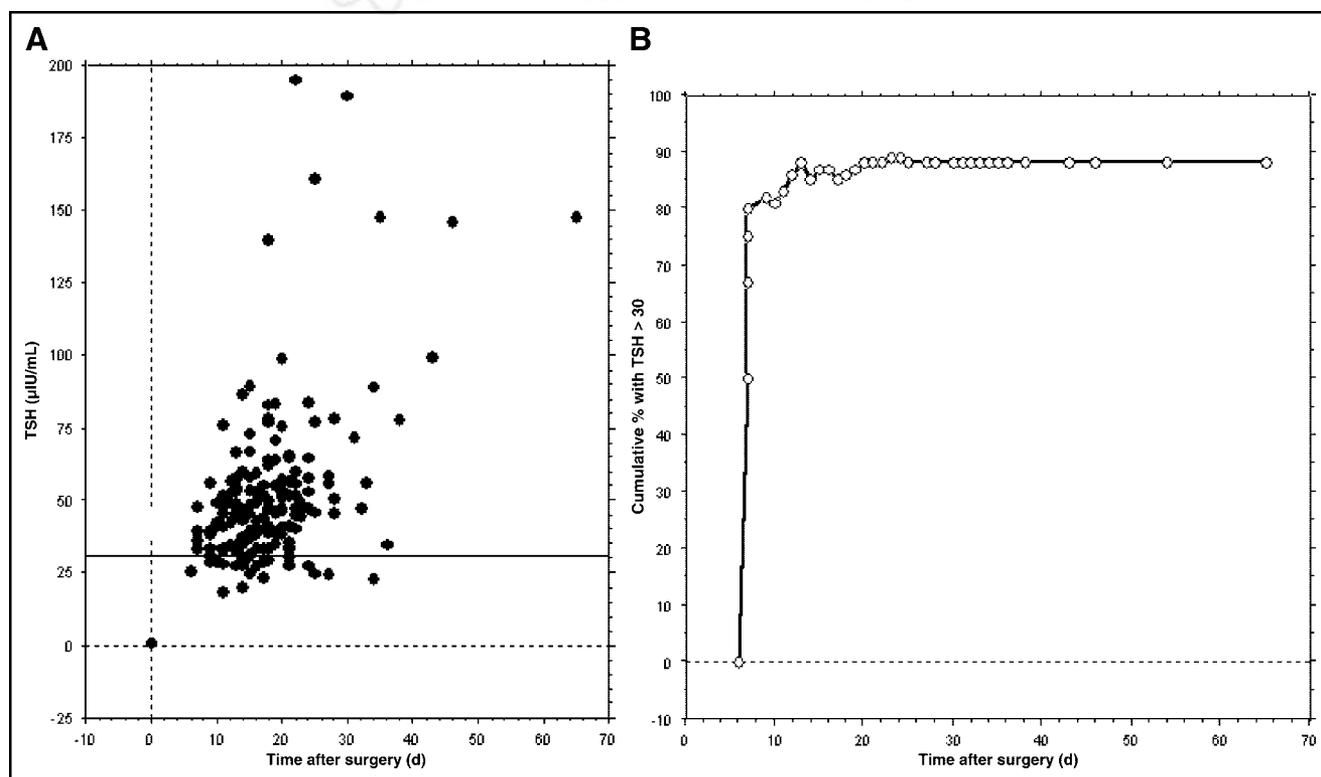
within 2–3 wk after surgery or  $T_4$  withdrawal. However, because this measurement was not obtained per a rigidly defined protocol, the actual timing of TSH measurements in our routine clinical practice ranged broadly.

Our analysis defined 2 groups of patients. The first group consisted of 176 patients who recently underwent total thyroidectomy without immediate thyroid hormone replacement therapy. These patients had known thyroid carcinoma and were scheduled to undergo postoperative  $^{131}\text{I}$  ablation. The second group consisted of 108 patients with a history of previous total thyroidectomy and postoperative  $^{131}\text{I}$  therapy for thyroid carcinoma. These patients were evaluated with annual surveillance  $^{131}\text{I}$  scintigraphy, and  $T_4$  was simply withdrawn in preparation for this test.

## RESULTS

In the immediate postoperative group, the first TSH measurements were obtained 6–65 d (median, 17 d) after surgery, and the values ranged from 18.2 to 194.8  $\mu\text{IU}/\text{mL}$  (median, 46.6  $\mu\text{IU}/\text{mL}$ ). These data are shown in Figure 1A and Table 1. Overall, 89% of initial TSH values exceeded 30  $\mu\text{IU}/\text{mL}$  in these patients, as seen in Figure 1B (cumulative frequency). For the 11% of patients with the initial TSH level  $\leq 30$   $\mu\text{IU}/\text{mL}$ , the values ranged from 18.2 to 29.6  $\mu\text{IU}/\text{mL}$  (mean, 26.2  $\mu\text{IU}/\text{mL}$ ).

In the group of patients undergoing simple  $T_4$  withdrawal in preparation for surveillance scintigraphy, TSH values were obtained 6–35 d (median, 20 d) after discontinuation of  $T_4$ ; the TSH levels ranged from 23.4 to 214.5  $\mu\text{IU}/\text{mL}$  (median, 61.1  $\mu\text{IU}/\text{mL}$ ). These data are shown in Figure 2A



**FIGURE 1.** (A) Scatter plot of first TSH measurements as a function of time after total thyroidectomy ( $n = 176$ ). (B) Cumulative frequency of TSH concentrations  $> 30$   $\mu\text{IU}/\text{mL}$  as a function of time after total thyroidectomy ( $n = 176$ ).

**TABLE 1**  
Postoperative TSH Levels by Time Period

Time after surgery (d)	No. of patients	No. with TSH > 30 $\mu$ IU/mL
7-14	46	41 (89%) [77%-95%]
15-21	80	70 (88%) [79%-93%]
>21	50	45 (90%) [79%-96%]
Total	176	156 (89%) [84%-93%]

Ranges in brackets are 95% confidence intervals.

**TABLE 2**  
TSH Levels by Time After Abrupt T<sub>4</sub> Withdrawal

Time after withdrawal (d)	No. of patients	No. with TSH > 30 $\mu$ IU/mL
7-14	7	7 (100%) [65%-100%]
15-21	54	48 (89%) [78%-95%]
>21	47	45 (96%) [86%-99%]
Total	108	100 (93%) [86%-97%]

Ranges in brackets are 95% confidence intervals.

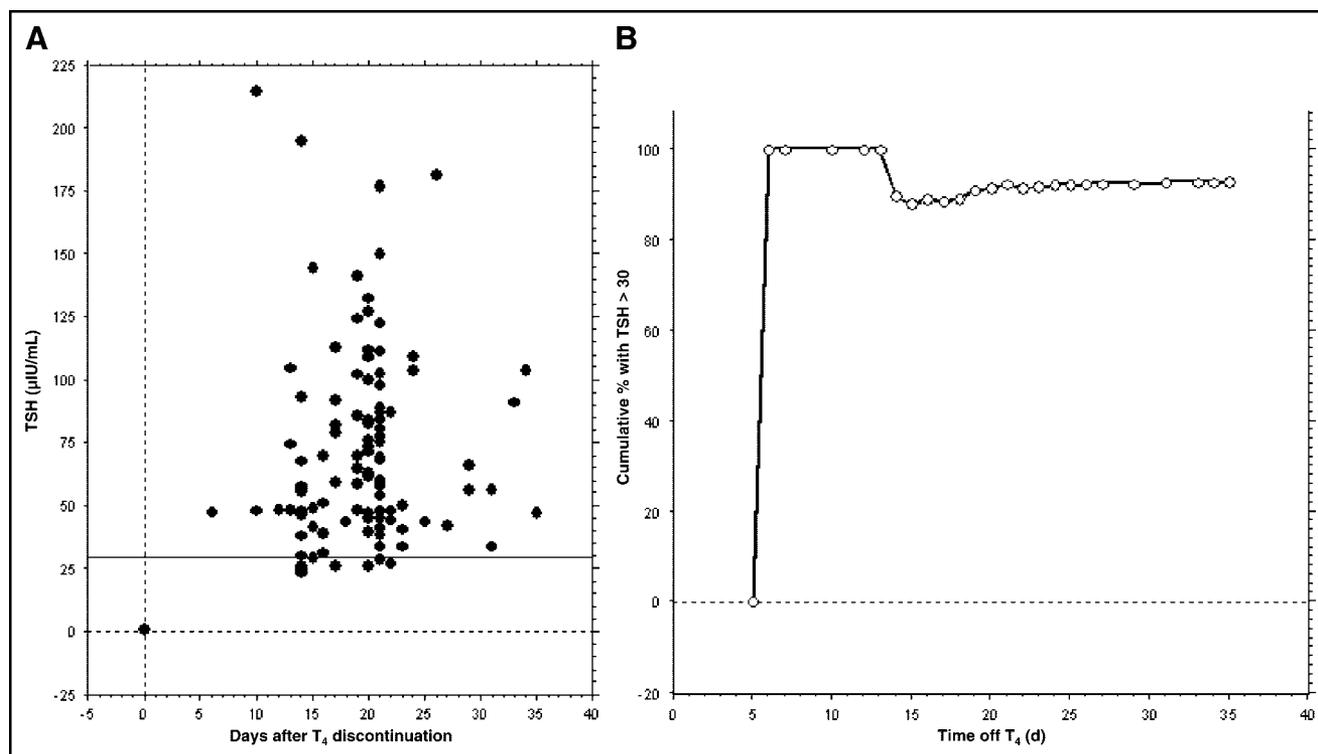
and Table 2. Overall, 93% of initial TSH values exceeded 30  $\mu$ IU/mL in these patients, as demonstrated in Figure 2B (cumulative frequency). For the 7% of patients with an initial TSH level  $\leq$  30  $\mu$ IU/mL, the values ranged from 23.4 to 29.1  $\mu$ IU/mL (mean, 26.2  $\mu$ IU/mL).

## DISCUSSION

The classic protocol that is described in the literature (1,2) and recommended in the practice guidelines of several professional organizations (4-6) for elevation of serum TSH in preparation for <sup>131</sup>I therapy or diagnostic imaging requires discontinuation of T<sub>4</sub> replacement therapy, use of maintenance T<sub>3</sub> therapy for 4 wk, and then discontinuation of T<sub>3</sub> for 2-3 wk before TSH values are measured. Acceptance of this method of TSH elevation does not appear to be evidence based, as the literature contains scant data support-

ing this approach (7,8). Only recently did Liel (9) report on 13 patients who underwent T<sub>4</sub> withdrawal and find that the mean interval to reach a TSH of  $\geq$ 30  $\mu$ IU/mL was 17 d. Also, Sanchez et al. (10) recently reported the results of a prospective study of 31 patients. In that study, 10 patients were in the immediate postoperative group and 100% achieved a TSH level of >30  $\mu$ IU/mL within 3 wk. Sanchez et al. also studied 21 patients who discontinued T<sub>4</sub>; 90% had a TSH level of >30  $\mu$ IU/mL within 3 wk.

The serum TSH concentration increases exponentially after total thyroidectomy (11) and after thyroid hormone withdrawal (7). Our data indicate that about 90% of patients with TSH values determined 1-3 wk postoperatively or after T<sub>4</sub> withdrawal had TSH levels exceeding 30  $\mu$ IU/mL. Accordingly, our results suggest that preparation of patients for <sup>131</sup>I administration can be simpler (thyroid hormone



**FIGURE 2.** (A) Scatter plot of first TSH measurements as a function of time after abrupt T<sub>4</sub> withdrawal ( $n = 108$ ). (B) Cumulative frequency of TSH concentrations > 30  $\mu$ IU/mL as a function of time after abrupt T<sub>4</sub> withdrawal ( $n = 108$ ).

withdrawal alone) and quicker (2–3 wk) than has classically been described.

One presumed advantage of the classic approach is that  $T_3$  is metabolized more quickly than  $T_4$ , such that the hypothyroid state (and TSH elevation) can be achieved more quickly after stopping  $T_3$  than after stopping  $T_4$ . One important limitation of our study is that we did not compare TSH measurements in patients undergoing  $T_3$  withdrawal with those in patients undergoing  $T_4$  withdrawal. However, our data do demonstrate that sufficient TSH elevation occurred within 1–3 wk in both of our patient groups, and this is the same period that classic protocols recommend for discontinuing  $T_3$  substitution therapy.

A major limitation of this study is its retrospective nature. TSH measurements were obtained but not routinely recorded before thyroidectomy. The presence of hypothyroidism in the clinical setting of thyroid cancer is rare (12). Also, baseline TSH measurements were not routinely recorded for the  $T_4$  withdrawal group. However, patients in this group were regularly followed clinically with routine TSH measurements, and TSH suppression to  $\leq 0.10$   $\mu\text{IU/mL}$  was typical. None were known to be hypothyroid before  $T_4$  withdrawal. Unsuppressed TSH measurements were not obtained in accordance with a rigid schedule, but rather per clinical routine, with the initial planned measurement at 2–3 wk. Most patients did not have serial measurements of TSH because of the known exponential rise in TSH after withdrawal. Thus, we did not assess the time course of TSH elevation. In practice, we may repeat the measurement in 1 wk if the initial measurement is sufficiently low (72% of our patients with a TSH of  $< 30$   $\mu\text{IU/mL}$  had a value between 25 and 29.9  $\mu\text{IU/mL}$ , and these measurements were not repeated).

All patients in this study underwent a total thyroidectomy. However, the completeness of a total thyroidectomy is well known to be unpredictable (13). The presence of greater amounts of residual thyroid tissue may account for the failure of the TSH concentration to increase to  $> 30$   $\mu\text{IU/mL}$  within 2–3 wk in some of our patients.

We did not assess the prevalence of hypothyroid symptoms in our patients while they were not receiving thyroid hormone replacement. Thus, another limitation of our study is that we do not know if such symptoms are more or less frequent with our method than with the classic method of  $T_3$  substitution and withdrawal. However, the frequency and

severity of symptoms have been shown to correlate with the degree of hypothyroidism (14). We assume that since the degree and the duration of hypothyroidism are comparable in our patients and in patients managed in accordance with the literature recommendations, symptoms of hypothyroidism should not be worse with our methods.

## CONCLUSION

An alternative to the classic approach to TSH elevation has been presented. Our method of no thyroid hormone replacement after initial surgery and discontinuation of  $T_4$  in preparation for whole-body  $^{131}\text{I}$  scintigraphy is less cumbersome than the classic method and appears to sufficiently elevate TSH within an acceptable time frame.

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