**Topic:** THYROGLOBULIN MEASUREMENTS IN THE FOLLOW-UP OF THYROID CANCER PATIENTS

**Title:** Monitoring thyroglobulin in a sensitive immunoassay has comparable sensitivity to recombinant human TSH-stimulated thyroglobulin in the follow-up of thyroid cancer patients.

**Authors:** Smallridge RC, Meek SE, Morgan MA, Gates GS, Fox TP, Grebe S, & Fatourechi V (Mayo Clinic of Medicine, Jacksonville & Rochester, USA)

**Reference:** Journal of Clinical Endocrinology and Metabolism 92: 82-87, 2007

**SUMMARY**

**Context:** Most thyroglobulin (Tg) assays have a sensitivity of 0.5-1 ng/ml. A minority of patients with undetectable T4-suppressed Tg levels have a recombinant human TSH (rhTSH)-stimulated Tg above 2 ng/ml and identifiable residual disease.

**Objective:** The objective was to determine whether a Tg assay with improved sensitivity could eliminate the need for rhTSH stimulation when baseline Tg is below 0.1 ng/ml.

**Design:** A retrospective study of two academic endocrine practices was conducted.

**Population:** A total of 194 patients undergoing rhTSH stimulation participated in the study.

**Results:** Of the 80 patients with Tg below 0.1 ng/ml, two (2.5%) had rhTSH-stimulated Tg above 2 ng/ml. One other patient with stimulation to 0.3 ng/ml and negative 123I scan had an ultrasound-detected malignant lymph node resected. None had 131I/123I imaging after rhTSH stimulation suggestive of local recurrence or distant metastasis. If T4-suppressed Tg was 0.1-0.5 or 0.6-2.0 ng/ml, rhTSH Tg was above 2 ng/ml in 24.2 and 82.4%, respectively.

**Conclusions:** Patients with differentiated thyroid carcinoma and a T4-suppressed serum Tg below 0.1 ng/ml rarely have a rhTSH-stimulated Tg above 2 ng/ml, and none of these patients had 131I or 123I imaging after rhTSH stimulation suggestive of local recurrence or distant metastasis. The authors recommend monitoring such patients with a T4-suppressed Tg level and periodic neck ultrasonography. An increase in T4-suppressed serum Tg to a detectable level or the appearance of abnormal lymph nodes by physical or ultrasound examination should prompt further investigation.

**COMMENT**

The development of Tg assays and recombinant human TSH (rhTSH) have provided the means for clinicians to detect residual (or recurrent) thyroid cancer. The combined use of serum Tg and whole body scan (WBS) after stimulation with rhTSH is particularly effective in identifying small residual foci of thyroid tissue (either normal glandular remnants and/or cancer). This study is based on the experience of the Mayo Clinic group, using a serum Tg assay with a clinical detection limit of 0.1 ng/ml, i.e. a sensitivity considerably lower than the 0.5 to 1.0 ng/ml levels reported in
other studies. The data showed that in 80 patients with T₄-suppressed (i.e. under treatment) Tg below 0.1 ng/ml, Tg remained undetectable in 47/80 patients (59%) after rhTSH; furthermore in 78/80 patients (97.5%), stimulated Tg was below 2 ng/ml. Only one of 80 patients had treatment for recurrent disease. Thus, a rare patient may have detectable disease despite a very low serum Tg (and in their case negative imaging by scintigraphy), emphasizing the importance of neck ultrasonography in the follow-up of patients with differentiated thyroid cancer (DTC).

What is proposed in this report is that by using a sensitive Tg-immunoassay with a very low cut-off, it is possible to follow patients with DTC and a T₄-suppressed Tg below 0.1 ng/ml without the need to perform rhTSH stimulation. If T₄-suppressed Tg levels are detectable, the recent guidelines of ATA/ETA should be followed because 24-82% of such patients have a rhTSH-stimulated Tg above 2 ng/ml, hence prompting additional work-up to identify residual cancer.

Two last comments: a) the testing laboratory has to ensure consistent assay performance over time; and b) patients should always be tested with the same highly sensitive Tg assay. Finally, additional studies using Tg assays with improved sensitivity and longer follow-up are needed before deciding universally that monitoring such patients with a low risk cancer grade could be recommended by carrying out a yearly T₄-suppressed Tg measurement and periodic neck ultrasound imaging, but without rhTSH stimulation.  
(Daniel Glinoer, M.D.; Ph.D.)

See Figure below

Upper panel: the results from Mayo Clinic (Florida): only 1 of 47 patients with a baseline Tg (‘pre’) below 0.1 ng/ml had a rhTSH-stimulated Tg (‘post’) above 2 ng/ml.

Lower panel: the results from Mayo Clinic (Rochester): in 15/33 patients (45.4%), baseline Tg (‘pre’) below 0.1 ng/ml remained undetectable after rhTSH (‘post’) and in 17/33 patients (51.3%) stimulated Tg levels were less than 2 ng/ml.