Increased Detection of Elevated TSH Using Immunoradiometric Assay*

KARLEY Y. LITTLE, M.D.[1], KELLY S. KEARFOTT, M.D.[2], XAVIER CASTELLANOS, M.D.[3], ALAN RINKER, M.S.[4] AND RON WHITLEY, Ph.D.[5]

Using a highly sensitive immunoradiometric assay, the authors detected an increased rate of elevated thyrotropin in 2,099 patients vs 1,789 patients examined with radioimmunoassay. Closer scrutiny of mood disorder patients with elevations found confirmatory evidence of thyroid dysfunction in most.

Laboratory abnormalities suggestive of hypothyroidism are common in psychiatric patients (1). However, without sustained dimunition of thyroxine (T4) or definite nonbehavioural signs or symptoms, attributing psychiatric symptoms to thyroid deficiency solely on these findings remains controversial. Complicating the picture, Haggerty et al (2) recently noted basal TSH increases in five percent of 39 psychiatric inpatients using a radioimmunoassay (RIA) technique, compared to an increase in 11% of 85 assayed using a high sensitive immunoradiometric (IRMA) technique. Another group (3) has also noted increased rates of elevated TSH in hospitalized patients vs ambulatory controls using immunometric methods. This type of assay is now replacing the RIA at many hospitals.

We recently compared the rates of elevated TSH levels with an RIA kit* and an IRMA kit†. Consecutive serum samples were assayed for TSH using RIA in 546 nonpsychiatric inpatients (over six months preceding the switch to IRMA), 93 consecutive psychiatric inpatients (over six months) and 1,150 outpatients (over six months). Consecutive serum TSH levels were assayed using IRMA in 641 nonpsychiatric inpatients (over six months after the switch to IRMA), 97 psychiatric inpatients over six months) and 1,361 outpatients (over six months). Sixty-nine mood disorder patients admitted since the inception of the IRMA (eight months) were evaluated for decreased T4 (thyroxine), antithyroid antibodies and nonbehavioural signs of thyroid disease.

As seen in Table I, patients classified as having elevated TSH significantly increased using the IRMA vs RIA in all three patient groups. The number of psychiatric inpatients with elevated TSH increased from four to 18 (450%) vs an increase from 76 to 173 (230%) in nonpsychiatric inpatients (chi-square = 1.48, non significant). Thirteen of 39 mood disorder patients had elevated TSH vs five of 45 patients with eating disorder, schizophrenia or other diagnoses (chi-square = 3.08, p = .08).

Among an overlapping and slightly larger group of 69 mood disorder inpatients, 16 were found to have elevated TSH by IRMA. Only one of these patients had a T4 level below normal. Fourteen of these patients demonstrated confirmatory evidence of thyroid dysfunction, including a history of ongoing or previous treatment for hypothyroidism (n = 4), anti-microsomal antibodies (n = 5), elevated TSH response to TRH (n = 2), lithium therapy (n = 1) or T4 supplementation recommended by an endocrinologist based on physical exam (n = 2). Among the 16 patients with elevated TSH, T4 averaged 8.0 ± 2.6 mg/dL vs 9.2 ± 1.8 mg/dL for the remainder (t = 1.997, p = .05).

Table I
Categorization of TSH Levels in Consecutive Patients Using Either RIA or IRMA

		RIA	IRMA
Psychiatric Inpatients	Elevated	4 (4.3%)	18 (18.5%)*
	Nonelevated	89	79
Nonpsychiatric Inpatients	Elevated	76 (13.9%)	173 (27.0%)**
	Nonelevated	470	468
All Outpatients	Elevated	196 (17.0%)	354 (26.0%)***
	Nonelevated	954	1007

*chi-square = 8.08 (with Yates' correction), p = .004,
**chi-square = 29.6 (with Yates' correction), p < .0001,
***chi-square = 28.8 (with Yates' correction), p < .0001.

*Manuscript received September 1988; revised February 1989.

[1]Assistant Professor, Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, North Carolina.
[2]Resident, Department of Psychiatry, University of Kentucky College of Medicine, Lexington, Kentucky.
[3]Resident, Department of Psychiatry, University of Kentucky College of Medicine, Lexington, Kentucky.
[4]Laboratory Supervisor, Department of Pathology, University of Kentucky Medical Center, Lexington, Kentucky.
[5]Assistant Professor, Department of Pathology, University of Kentucky College of Medicine, Lexington, Kentucky.

*Amersham Corporation, Arlington Heights, IL 60005
†Allegro™ HS-TSH Immunoassay System, Nichols Institute, San Juan Capistrano, CA 92675

Careful scrutiny of our 16 mood disorder patients with TSH elevations found indirect evidence that many of these patients might be suffering thyroid dysfunction. It remains uncertain, however, what percentage of patients with elevated basal TSH by IRMA have true thyroid axis disease. Spencer et al (3) attributed many elevations to medications or non-thyroidal illnesses (also called the euthyroid sick syndrome) and suggested that a wider reference range might be appropriate for hospitalized patients. Generally, patients with the euthyroid sick syndrome have low T3 and/or T4 attributed to altered protein binding, altered degradation, or assay interference. Basal TSH and TSH after TRH stimulation are usually normal or low, but occasionally elevated, reflecting the effects of a variety of factors on the pituitary, as well as normal thyroid hormone feedback. Although TSH levels have been considered the best indicator of thyroid availability, Boles et al (4) recently found that thyrotroph response to illness varies independently of age, sex, severity or type of illness, mean serum total T4 and T3 levels or patterns, or clinical outcome. Anti-mouse antibodies that positively interfere with antibody dependent assays (including RIA) may account for some presumably small proportion of elevations (5). In any event, psychiatrists can anticipate a more challenging task in interpreting TSH results as the IRMA method replaces RIA. Repeating the assay in one to two weeks may be necessary.

Studies of the efficacy of supplemental T4 or T3 in non-thyroidally ill patients have failed to demonstrate an impact on eventual clinical outcome (6). Among depressed patients there has been evidence that the addition of T3 may improve a poor response to antidepressants (7), possibly related (8) or not (9) to TSH levels. If these elevations are in fact a sign of thyroid deficiency, their frequency supports the hypothesis that significant numbers of psychiatric inpatients (especially those with mood disorders) might benefit from thyroid supplement.

References

1. Gold MS, Pearsall HR. Hypothyroidism—or is it depression? Psychosomatics 1983; 24(7): 646-656.
2. Haggerty JJ, Simon JS, Evans DL, et al. Relationship of serum TSH concentration and antithyroid antibodies to diagnosis and DST response in psychiatric inpatients. Am J Psychiatry 1987; 144(11): 1491-1493.
3. Spencer C, Elgen A, Shen D, et al. Specificity of sensitive assays of thyrotropin (TSH) used to screen for thyroid disease in hospitalized patients. Clin Chem 1987; 33(8): 1391-1396.
4. Boles J-M, Morin J-F, Garre MA. Ultrasensitive assay of thyroid stimulating hormone in patients with acute non-thyroidal illness. Clin Endocrinol 1987; 27: 395-401.
5. Zweig MH, Csako G, Benson CC, et al. Interference by anti-immunoglobin G antibodies in immunoradiometric assays of thyrotropin involving mouse monoclonal antibodies. Clin Chem 1987; 33(6): 840-844.
6. Brent GA, Hershman JM. Thyroxine therapy in patients with severe nonthyroidal illnesses and low serum thyroxine concentration. J Clin Endocrinol Metab 1986; 63(1): 1-8.
7. Prange AJ Jr, Wilson IC, Rabon AM, et al. Enhancement of imipramine antidepressant activity by thyroid hormone. Am J Psychiatry 1969; 126: 457-469.
8. Targum SD, Greenberg RD, Harmon RL, et al. The TRH test and thyroid hormone in refractory depression. Am J Psychiatry 1984; 141(3): 463.
9. Schwarcz G, Halaris A, Baxter L, et al. Normal thyroid function in desipramine non-responders converted to responders by the addition of L-triodothyronine. Am J Psychiatry 1984; 141(12): 1614-1616.

Résumé

Les auteurs ont comparé les résultats des dosages effectués chez 2 099 malades à l'aide d'une méthode radio-immunométrique très sensible à ceux obtenus chez 1 789 malades par dosage radio-immunologique et ont détecté un pourcentage plus élevé de malades présentant un taux élevé de thyrotropine avec la première méthode. Un examen plus approfondi des malades atteints de troubles de l'humeur et présentant une élévation de la thyrotropine a permis de conclure que la plupart souffraient d'un dérèglement thyroïdien.