



Educational Discussion: TSH Testing

2022-B Harmonized Thyroid (ABTH)

Putting together a commutable Survey for thyroid function tests has proven more difficult than for other tests we have targeted. To ensure commutability as well as a good range of concentrations, we have had success with assays like steroid hormones (pooling specimens from healthy males and healthy females of different ages), hemoglobin A1c (pooling specimens from healthy individuals as well as individuals with diabetes mellitus with different degrees of glycemic control), and lipids (pooling specimens from otherwise healthy people with different types of lipid disorders). For Vitamin D, we have succeeded in getting appreciable concentrations of 25-OH Vitamin D by supplementing with vitamin D2 volunteers whose 25-OH Vitamin D is low (after obtaining IRB approval and informed consent).

For thyroid function tests, we have been drawing specimens from healthy donors, whose TSH values have almost always been in the reference interval, but pooling their specimens by separating those with the lowest TSH values, the highest TSH values, and the mid-range TSH values. Unfortunately, that technique has not provided as much variation in TSH (or any of the other thyroid function tests) as we would like.

For this Survey, we tried a different approach, one on which we have been working for several years. We collaborated with an endocrinologist at Tufts Medical Center in Boston, Massachusetts, who has identified patients in her practice with reasonably stable thyroid diseases, from whom she obtained informed consent to donate several additional tubes of blood after a routine clinic visit. For each specimen, we measured TSH and the thyroid hormones, and then pooled the specimens with the lowest and highest TSH values.

As a result, you can see that we were successful in obtaining specimens ABTH-05 and ABTH-06, with TSH values of ~0.10 and ~6.10, much lower and higher than we achieved previously, representing values outside the typical reference interval.

Unfortunately, we have only two groups reflected in the accompanying report. The CAP statisticians require **at least 3 participants** to report minimum and maximum values and **at 10 participants** for additional statistics. We do have some data from other platforms, but there are too few participants to draw any conclusions. It would be extremely valuable to have more participants, so please spread the word about this Accuracy-Based Survey.

We would also draw your attention to the fact that some of these samples were drawn when the patients were on thyroid replacement or thyroid inhibitors. And, like many patients, some did not take their medications regularly. In other words, one might expect that at least some of the patients whose TSH is outside the reference interval would also have abnormal free T4, T4, or T3, but these pooled specimens did not.

Nonetheless, we think that the TSH values are interesting in themselves. From our previous Surveys and confirmed here by data collected but not reported, it appears that TSH assays are still not standardized and that the manufacturers' suggested reference intervals, though different, do not explain those differences. That is, platforms that have higher values for TSH have lower reference intervals. At least one recent publication confirms this conundrum (1).



COLLEGE of AMERICAN PATHOLOGISTS

The take home message is that it is important for laboratories to verify manufacturers' proposed reference intervals and to communicate with clinical colleagues to ensure that your reported values and reference intervals are meeting clinical needs at your institutions.

Reference:

1. Kalaria T, Sanders A, Fenn J, et al. The diagnosis and management of subclinical hypothyroidism is assay-dependent- Implications for clinical practice. *Clin Endocrinol.* 2021;94(6):1012-1016.

Gary Horowitz, MD, FCAP
Accuracy-Based Programs Committee