LABORATORY MEDICINE PRACTICE GUIDELINES
Laboratory Support for the Diagnosis and Monitoring of Thyroid Disease

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Section 1. Foreword and Introduction

Physicians need quality laboratory testing support for the accurate diagnosis and cost-effective management of thyroid disorders. On occasion, when the clinical suspicion is strong, as in clinically overt hyperthyroidism in a young adult or with the presence of a rapidly growing thyroid mass laboratory thyroid hormone testing simply confirms the clinical suspicion. However in the majority of patients, thyroid disease symptoms are subtle in presentation so that only biochemical testing or cytopathologic evaluation can detect the disorder. However overt or obscure a patient's thyroid problem may be, an open collaboration between the physicians and clinical laboratory scientists is essential for optimal, cost-effective management of the patient with thyroid disease.

Thyroid dysfunction, especially thyroid insufficiency caused by a deficiency in iodide, is a worldwide problem. Iodide deficiency is not always uniform across a nation. Studies in both Europe and the United States suggest

that iodide deficiency should be considered more as a "pocket disorder", meaning that it can be more prevalent in some areas of a country compared with others *(1-3)*. The creation of this updated monograph was a collaborative effort involving many thyroid experts from a number of professional organizations concerned with thyroid disease: American Association of Clinical Endocrinologists (AACE), Asia & Oceania Thyroid Association (AOTA), American Thyroid Association (ATA), British Thyroid Association (BTA), European Thyroid Association (ETA) and the Latin American Thyroid Society (LATS). These organizations are the authoritative bodies that spearhead thyroid research and have published standards of care for treating thyroid disease in each region of the world. Because geographic and economic factors impact the clinical use of thyroid tests to some extent, this monograph will focus on the technical aspects of thyroid testing and the performance criteria needed for optimal clinical utility of thyroid tests in an increasingly cost-sensitive global environment. Individual clinicians and laboratories around the world favour different thyroid hormone testing strategies. *(4)*. This monograph cannot accommodate all these variations in thought and opinion but we hope that readers of this monograph will appreciate our efforts to consolidate some of these differences into a recommended strategy. We believe that most of the commonly performed tests and diagnostic procedures used to diagnose and treat thyroid disorders are included in this text. The monograph is designed to give both clinical laboratory scientists and practicing physicians an overview regarding the current strengths and limitations of those thyroid tests most commonly used in clinical practice. Consensus recommendations are made throughout the monograph. The consensus level is > 95%, unless otherwise indicated. We continue to welcome constructive comments that would improve the monograph for a future revision.

A. Additional Resources

Current clinical guidelines are published in the following references *(4-11)*. In addition, the textbooks "Thyroid" and "The Thyroid and Its Diseases" (www.thyroidmanager.org) are useful references *(12,13)*. A list of symptoms suggesting the presence of thyroid disease together with the ICD-9 codes recommended to Medicare by the American Thyroid Association is available on the ATA website (www.thyroid.org). Clinical practice guidelines may vary, depending on the region of the country. More information can be obtained from each of the thyroid organizations: Asia & Oceania Thyroid Association (AOTA = www.dnm.kuhp.kyoto-u.ac.jp/AOTA); American Thyroid Association (ATA = www.thyroid.org); European Thyroid Association (ETA =www.eurothyroid.com) and Latin American Thyroid Society (LATS = www.lats.org).

B. Historical Perspective

Over the past forty years, improvements in the sensitivity and specificity of biochemical thyroid tests, as well as the development of fine needle aspiration biopsy (FNA) and improved cytological techniques, have dramatically impacted clinical strategies for detecting and treating thyroid disorders. In the 1950s, only one serum-based thyroid test was available - an indirect estimate of the total (free + protein-bound) thyroxine (T4) concentration, using the protein bound iodide (PBI) technique. Today, urine iodide concentrations are measured directly by dry or wet-ash techniques and are used to estimate dietary iodide intake. The development of competitive immunoassays in the early 1970s and more recently, non-competitive immunometric assay (IMA) methods have progressively improved the specificity and sensitivity of thyroid hormone testing. Currently, serum-based tests are available for measuring the concentration of both the total (TT4 and TT3) and free (FT4 and FT3) thyroid hormones in the circulation *(14,15)*. In addition, measurements of the thyroid hormone binding plasma proteins, Thyroxine Binding globulin (TBG), Transthyretin (TTR)/Prealbumin (TBPA) and Albumin are available *(16)*. Improvements in the sensitivity of assays to measure the pituitary thyroid stimulating hormone, thyrotropin (TSH) now allow TSH to be used for detecting both hyper- and hypothyroidism. Furthermore, measurement of the thyroid gland precursor protein, Thyroglobulin (Tg) as well as the measurement of Calcitonin (CT) in serum have become important tumor markers for managing patients with differentiated and medullary thyroid carcinomas, respectively. The recognition that autoimmunity is a major cause of thyroid dysfunction has led to the development of more sensitive and specific tests for autoantibodies to thyroid peroxidase (TPOAb), thyroglobulin (TgAb) and the TSH receptor (TRAb). Current thyroid tests are usually performed on serum by either manual or automated methods that employ specific antibodies *(17)*. Methodology continues to evolve as performance standards are established and new technology and instrumentation are developed.