Hyperthyroidism and Thyrotoxicosis

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KEYWORDS

• Hyperthyroidism • Thyrotoxicosis • Thyroid storm • Thyroiditis • Graves disease

KEY POINTS

- Thyroid storm is uniformly fatal if untreated and, even with treatment, mortality ranges from 20% to 50%.
- Consider thyroid storm in any ill patient with signs and symptoms of a hypermetabolic state.
- Be wary in the elderly, children, and pregnant patients who may present with subtle or atypical symptoms of thyroid storm.

Hyperthyroidism is defined as the excess production and release of thyroid hormone by the thyroid gland resulting in inappropriately high serum levels. The disproportionate amount of thyroid hormone leads to an accelerated metabolic state. The most common causes include diffuse toxic goiter (Graves disease), toxic multinodular goiter (Plummer disease), and toxic adenoma.[1] Thyrotoxicosis also refers to a hypermetabolic state that results in excessive amounts of circulating thyroid hormone, but includes extrathyroidal sources of thyroid hormone such as exogenous intake or release of preformed stored hormone. Thyroiditis, inflammation of the thyroid gland resulting in release of stored hormone, is a frequent cause of thyrotoxicosis. The clinical presentation of thyrotoxicosis varies from asymptomatic (subclinical) to life threatening (thyroid storm). Thyroid storm is a true endocrine emergency. The diagnosis is based on history, clinical signs and symptoms, and laboratory analyses including thyroid-stimulating hormone (TSH), free T4 (thyroxine), and T3 (triiodothyroxine).

Thyroid hormone affects virtually every organ system and can result in an amalgam of complaints that can be challenging to identify. However, when undiagnosed, serious complications can occur including delirium, insomnia, anorexia, osteoporosis, muscle weakness, atrial fibrillation, congestive heart failure (CHF), thromboembolism, altered mental status, cardiovascular collapse, and death.[2,3] Populations that are at increased risk for serious sequelae include pregnant women, children, and the elderly.[4] It is

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Emerg Med Clin N Am 32 (2014) 277–292
http://dx.doi.org/10.1016/j.emc.2013.12.001 **emed.theclinics.com**
0733-8627/14/$ – see front matter

essential that the emergency medicine provider has a high clinical suspicion for hyperthyroidism and thyrotoxicosis in patients with a myriad of seemingly unrelated symptoms, especially when coupled with dysautonomia. Thyroid storm needs to be identified rapidly and treated aggressively to avoid multiorgan dysfunction and death.[5]

EPIDEMIOLOGY

The prevalence of thyrotoxicosis in the United States is estimated at 1.2%, which comprises 0.5% symptomatic and 0.7% subclinical.[6] Occurrences are seen at all ages but presentation peaks between 20 and 50 years of age secondary to the higher prevalence of Graves disease. Toxic multinodular goiter typically occurs after age 50 years, as opposed to toxic adenoma, which presents at a younger age. All forms of thyroid disease are more common in women. Graves disease is the most common cause of thyrotoxicosis in the United States, accounting for 60% to 80% of cases, whereas subacute thyroiditis accounts for 15% to 20%, toxic multinodular goiter accounts for 10% to 15%, and toxic adenoma accounts for 3% to 5%.[7] Of those with thyrotoxicosis only 1% to 2% develop thyroid storm.[8] Although the overall incidence of thyroid storm is low, the morbidity and mortality associated with the diagnosis make it a disease state that all emergency medicine physicians should be adept at identifying and treating.

PATHOPHYSIOLOGY

The production and release of thyroid hormones is regulated by a sensitive negative feedback loop involving the hypothalamus, pituitary gland, and thyroid gland (**Fig. 1**). The hypothalamus releases thyroid-releasing hormone (TRH), which stimulates the pituitary to release TSH, in turn stimulating the thyroid gland to release thyroid hormones, T4 and T3. The increased production of thyroid hormone normally causes inhibition of TRH and TSH release by the hypothalamus and pituitary respectively. Disruption of this delicate system leads to additional production and release of thyroid hormone and subsequent hyperthyroidism.

The production of thyroid hormones in the thyroid gland depends on iodine.[3] Dietary iodide is transported into cells and converted to iodine. The iodine is then bound to thyroglobulin by thyroid peroxidase and subsequently forms monoiodotyrosine (MIT)

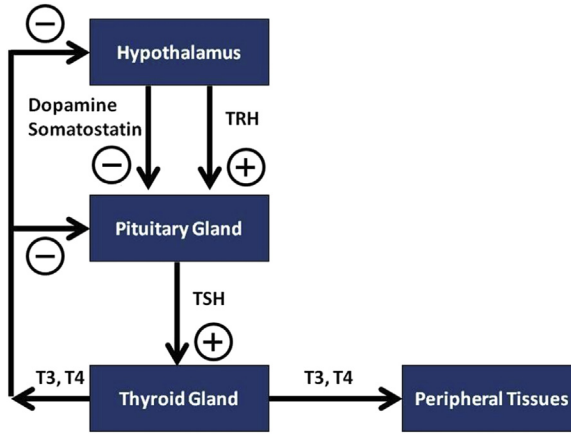

Fig. 1. Negative feedback loop regulating production and release of thyroid hormones.