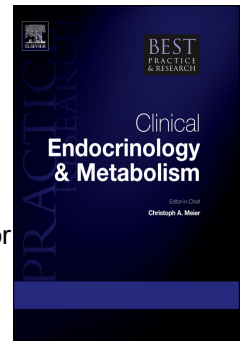
Accepted Manuscript



Resistance to thyrotropin

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PII: S1521-690X(17)30010-6

DOI: 10.1016/j.beem.2017.03.004

Reference: YBEEM 1139

To appear in: *Best Practice & Research Clinical Endocrinology & Metabolism*

Please cite this article as: Grasberger H, Refetoff S, Resistance to thyrotropin, *Best Practice & Research Clinical Endocrinology & Metabolism* (2017), doi: 10.1016/j.beem.2017.03.004.

Resistance to thyrotropin

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ABSTRACT

Resistance to thyrotropin (RTSH) is broadly defined as reduced sensitivity of thyroid follicle cells to stimulation by biologically active TSH due to genetic defects. Affected individuals have elevated serum TSH in the absence of goiter, with the severity ranging from nongoitrous isolated hyperthyrotropinemia to severe congenital hypothyroidism with thyroid hypoplasia. Conceptually, defects leading to RTSH impair both aspects of TSH-mediated action, namely thyroid hormone synthesis and gland growth. These include inactivating mutations in the genes encoding the TSH receptor and the PAX8 transcription factor. A common third cause has been genetically mapped to a locus on chromosome 15, but the underlying pathophysiology has not yet been elucidated. This review provides a succinct overview of currently defined causes of nonsyndromic RTSH, their differential diagnoses (autoimmune; partial iodine organification defects; syndromic forms of RTSH) and implications for the clinical approach to patients with RTSH.

KEYWORDS

Thyrotropin receptor; TSHR; paired domain; PAX8; mutations; congenital hypothyroidism; subclinical hypothyroidism; hormone resistance