



## THYROID HORMONE ACTION

### Patients with two abnormal copies of the thyroid hormone receptor gene have more severe symptoms of thyroid hormone resistance

#### BACKGROUND

Patients who have persistently high thyroid hormone levels but whose TSH values are persistently normal (or high) may be resistant to thyroid hormone. After ruling out other possible diagnoses, most cases of thyroid hormone resistance turn out to be due to a mutation in the thyroid hormone receptor gene, which is responsible for all of the actions of thyroid hormone. Each person has 2 copies of every gene, with only 1 being active at any one time. There have been multiple mutations in the thyroid hormone receptor described and they differ widely in their effects and in the degree of resistance observed in different tissues. The same mutation can be associated with very different clinical manifestations, even in members of the same family. Some patients are unaware of symptoms or merely have a long-standing goiter, while others may have symptoms suggesting hyperthyroidism. In children, delays in neurologic and skeletal development can suggest hypothyroidism. Part of the difference is related to whether the mutation affects one copy or both copies of the gene. This study examines the difference in presentation of thyroid hormone resistance.

#### THE FULL ARTICLE TITLE

Ferrara AM et al. Homozygous thyroid hormone receptor  $\beta$ -gene mutations in resistance to thyroid hormone: three new cases and review of the literature. *J Clin Endocrinol Metab.* February 8, 2012 [Epub ahead of print]. doi: 10.1210/jc.2011-2642.

#### SUMMARY OF THE STUDY

Three children from two families were noted to have tachycardia, goiter, deafness, defective speech and delays

in growth and intellectual development. In both of the families, the parents were related to each other. In one family, both parents had mild hearing loss as the only manifestation of thyroid hormone resistance. In the other family, the father had a goiter and the mother had abnormal thyroid levels but was otherwise normal. Analysis of the thyroid hormone receptor genes showed that the parents had one normal copy of the gene and one mutated copy of the gene. The children all had 2 mutated copies of the gene.

#### WHAT ARE THE IMPLICATIONS OF THIS STUDY?

These reports suggest that patients with severe forms of thyroid hormone resistance will have 2 mutated copies of the thyroid hormone receptor gene. Further, individuals with one normal and 1 mutated copy of the gene may have few, if any, symptoms. These patients may be more common than initially thought, especially if there is a family history of the thyroid abnormalities starting at a young age. Identification of such individuals will help future generations of their families avoid unnecessary treatment, which may include surgery.

— Alan P. Farwell, MD

#### ATA THYROID BROCHURE LINKS

Thyroid Function Tests: <http://www.thyroid.org/blood-test-for-thyroid>

Goiter: <http://www.thyroid.org/what-is-a-goiter>

#### ABBREVIATIONS & DEFINITIONS

**Thyroid hormone receptor genes:** genes that bind thyroid hormone and are responsible for causing all of the actions of thyroid hormone. There are 2 copies of each thyroid hormone receptor gene, with only one being active at any one time.

**Genes:** a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

**Mutation:** A permanent change in one of the genes.

*continued on next page*



## **THYROID HORMONE ACTION**, continued

**Goiter:** a thyroid gland that is enlarged for any reason is called a goiter. A goiter can be seen when the thyroid is overactive, underactive or functioning normally. If there are nodules in the goiter it is called a nodular goiter; if there is more than one nodule it is called a multinodular goiter.

**TSH: Thyroid Stimulating Hormone** — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.