



(REVIEW ARTICLE)



## Levothyroxine management in Hashimoto's thyroiditis: A comprehensive review

MONISHA S M, BABIKER BASHIR HAROUN BARAKA \*, YADAV V, ANKITH V, ANKITHA GAURAV and NIVEDITHA G

*Department of pharmacology, KLE college of pharmacy, Rajajinagar, Bangalore-560010, Karnataka, India.*

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### Abstract

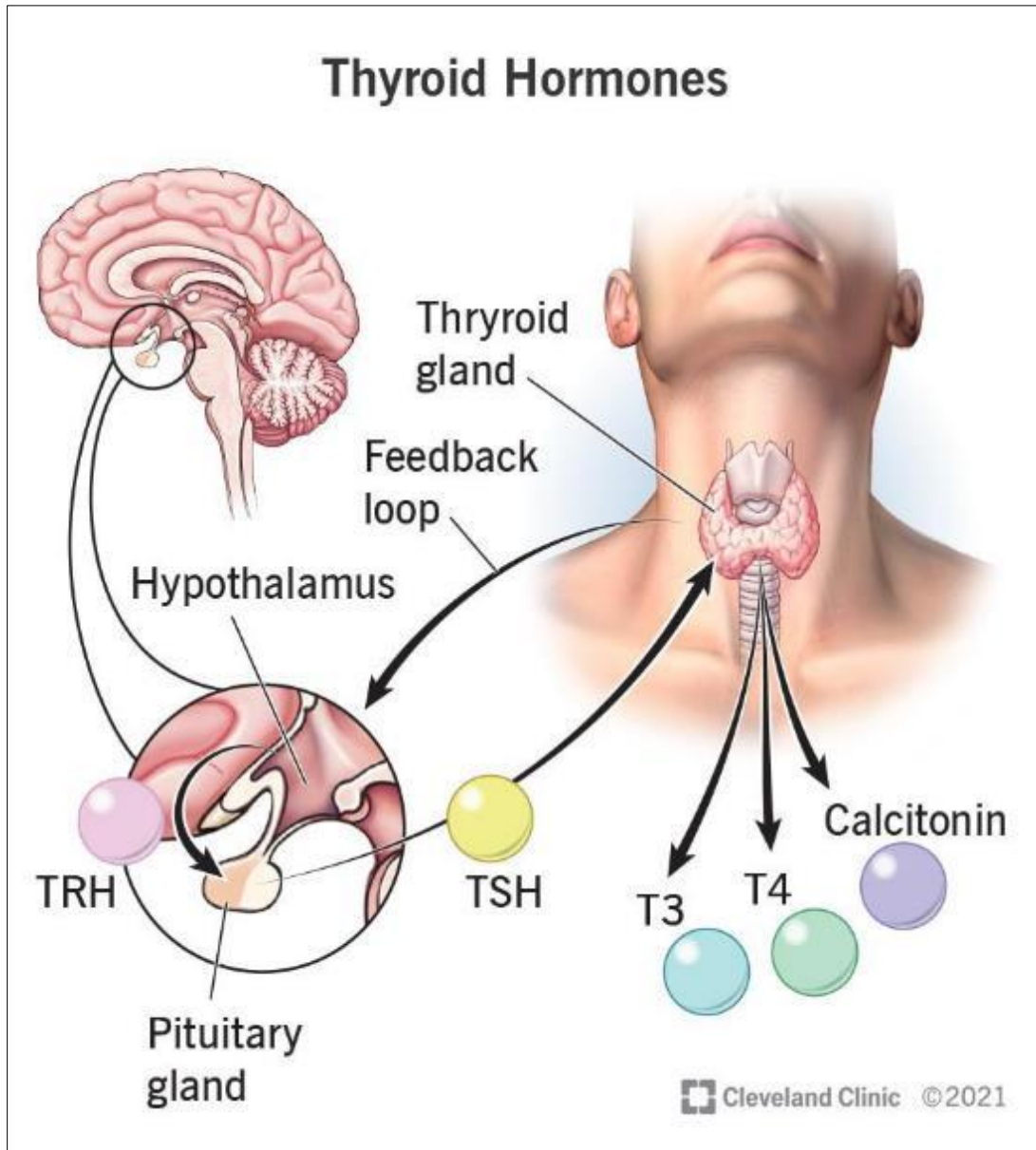
Hashimoto thyroiditis and hypothyroidism are related thyroid conditions with different aetiologies and clinical manifestations. Insufficient synthesis of thyroid hormones causes hypothyroidism, which may lead to systemic symptoms that impact energy, metabolism, and overall wellness. Thyroid tissue damage mediated by the immune system is the hallmark of the autoimmune thyroid condition known as Hashimoto thyroiditis, which is the most prevalent cause of hypothyroidism. A wide range of symptoms, such as fatigue, weight gain, cold sensitivity, constipation, dry skin, and cognitive impairment, are clinical indications of hypothyroidism and Hashimoto thyroiditis. Thyroid function tests, which measure serum levels of free thyroxine, thyroid-stimulating hormone, and thyroid autoantibodies, must be performed for the diagnosis. Imaging techniques, such as ultrasonography, may aid with nodular changes detection and thyroid morphology assessment. The goals of management plans for Hashimoto thyroiditis and hypothyroidism are to stop complications, relieve symptoms, and return the body to normal. The cornerstone of treatment is levothyroxine-based thyroid hormone replacement medication, which is customized for each patient depending on their clinical presentation and thyroid function testing. Dietary restrictions, patient education, and lifestyle changes are essential components of illness management.

**Keywords:** Levothyroxine; Hashimoto thyroiditis; Hypothyroidism; Thyroid Hormones; Pathogenesis of hashimoto's thyroiditis (HT)

### 1. Introduction

The prevalent pathological disease of thyroid hormone insufficiency is referred to as hypothyroidism. It may result in major negative health repercussions and even cause death if left untreated. The term hypothyroidism is primarily biochemical because there is a broad spectrum of clinical presentation and a general lack of symptom specificity [1][2][3] [4]. TSH (thyroid-stimulating hormone), it is possible to diagnose independent of free thyroxine concentrations falling or rising within the standard range, overt or clinical primary hypothyroidism. Generally considered to be the indicator in moderate or subclinical hypothyroidism, a sign of thyroid dysfunction, is characterized by TSH levels and free thyroxine levels within normal limits [4][5]. Elevated levels of total as well as low-density lipoprotein cholesterol are frequently seen in hypothyroidism, that is the secondary cause of dyslipidemia. It is evident that lowering total cholesterol levels is linked to medication that causes the serum TSH to return to normal [6].

\* Corresponding author: BABIKER BASHIR HAROUN BARAKA.



**Figure1** Thyroid Hormones

## 2. Levothyroxine

### 2.1. Metabolism of levothyroxine

Deiodination to T3, or reversing T3 (rT3), is the initial stage of T4 metabolism. MDI types I, II, and III help with iodothyronines' progressive deiodination. T3 is generated whenever the beta or outer ring is monodeiodinated with respect to the alanine side chain. T3 is three to four times more metabolically efficient than T4. When the alpha or inner ring is monodeiodinated, rT3, which has a low metabolic activity, is produced. The thyroid gland produces and releases a significant quantity of T3 and a negligible quantity of rT3. Consequently, peripheral synthesis as well as secretion are reflected during the levels of T3 and rT3 in circulation. Ten to twenty-five percent comes from the thyroid gland, while between seventy and ninety percent comes via peripheral conversion. The corresponding values for rT3 are 2% to 4% and 96% to 98%. T3 and rT3 are broken down into noniodinated thyronine, monoiodo, and diiodo through progressive tissue monodeiodination processes.[7]

## 2.2. Excretion of levothyroxine

In contrast to those who suffer from primary hypothyroidism, the daily turnover rate for T4 is roughly 10%, whereas it is between 50% and 70% for T3. The turnover rate for normal volunteers is marginally faster. For hypothyroid patients, this means a half-life of 7.5 days, and for euthyroid people, 6.2 days. For volunteers, it means roughly 1.4 days for hypothyroid people and 1.0 days for euthyroid people. In subjects who were hypothyroid and euthyroid, respectively, clearance for T4 was comparable at 0.056 and 0.054 L/h. Comparable values have been reported for hypothyroid patients (0.0385 L/h/70 kg)<sup>27</sup> and normal control subjects (0.053 to 0.064 L/h).[8]

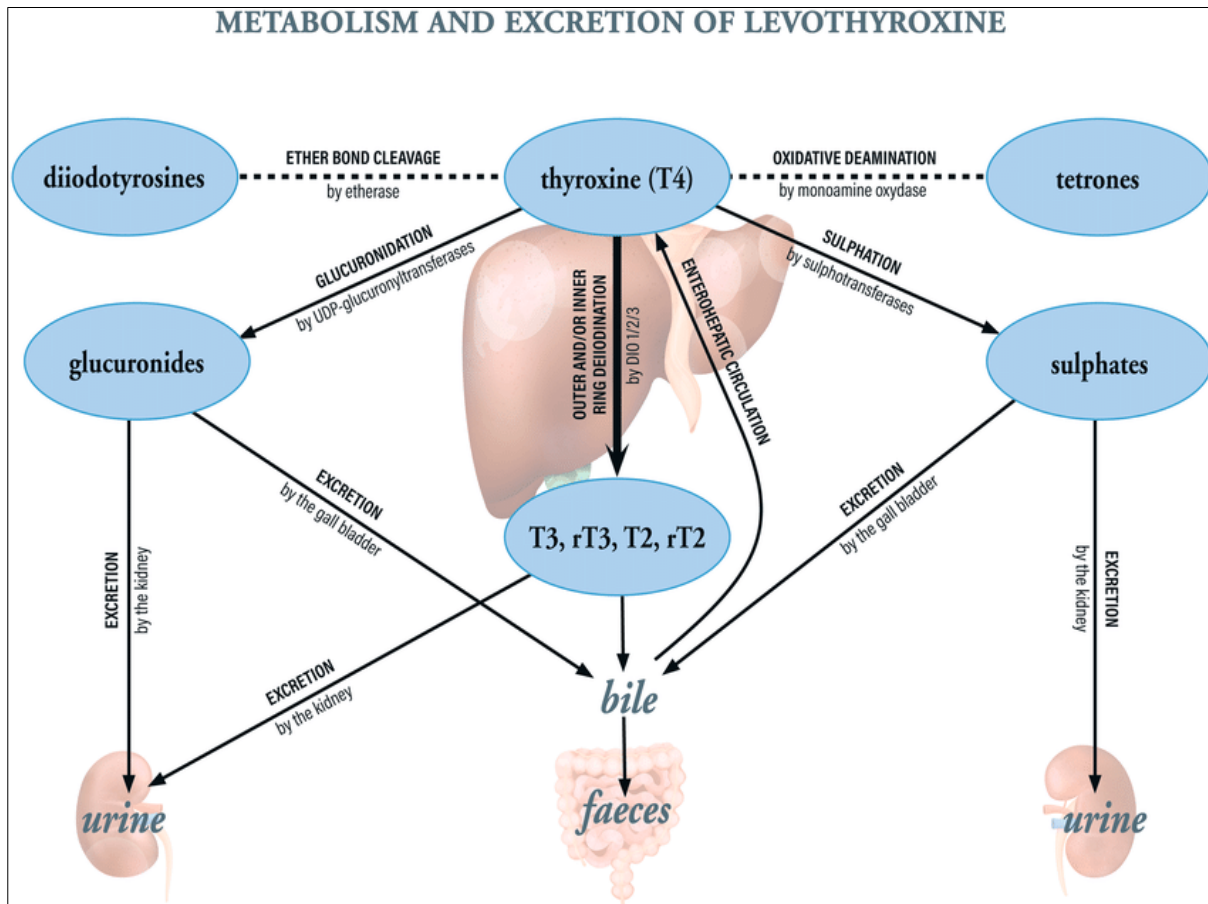


Figure 2 Metabolism and extract of levothyroxine

## 2.3. Hashimoto thyroiditis

Hashimoto thyroiditis, often referred to as chronic lymphocytic or autoimmune thyroiditis, is an autoimmune thyroid illness that is typified by antibodies that are specific to thyroid antigens, increased thyroid volume, and lymphocyte infiltration of parenchyma. Jointly with Graves' disease (GD), HT is classified as an autoimmune thyroid condition (AITD). [9]

X chromosome inactivation patterns that can be affected by environmental variables and the makeup of the microbiome, as well as hereditary predisposition, generate an imbalance in self-tolerance mechanisms and afflict women 7–10 times more frequently than males. Thyrocyte death results from the ensuing lymphocyte infiltration of the thyroid, which is exacerbated by an antibody-mediated autoimmune response via antibodies against thyroid peroxidase (TPOAbs). TPOAbs are linked to a two- to four-fold elevated risk of early birth and recurrent abortions in pregnant women [8]. The three main symptoms of hypothyroidism (HT) are (A) thyrotoxicosis, which occurs when destroyed thyroid follicles release stored thyroid hormones into the bloodstream; (B) euthyroidism, a condition in which the thyroid's remaining tissue replaces the lost thyrocytes and (C) hypothyroidism, which occurs when it is affected to thyroid gland, thyroid hormones are not produced in appropriate levels.[19]

## 2.4. Mechanism of action

Mechanism of action in HT aim to alleviate symptoms, lessen inflammation and return the normal range of thyroid hormones. To replace insufficient thyroid hormones, levothyroxine replacement treatment is frequently used. Occasionally, immune response modulation medicine is also used. [10]

When an autoimmune disease targets the thyroid gland, thyroid cells are reviled. Thyroid hormones that have been held within the gland may be released because of this damage, temporarily causing hyperthyroidism and then hypothyroidism as the gland's function deteriorates.

Cytokines are messenger molecules that control inflammation and immune-mediated responses, and they are produced by immune cells during the autoimmune response. Thyroid inflammation and injury are correlated with elevated levels of pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-alpha).[11]

The Essential Function of T Cells: An important factor in Hashimoto's thyroiditis is T lymphocytes, which are a subset of white blood cells involved in the immunological response. Helper T cells, specifically Th1 and Th17 cells, are stimulated and have a part in the thyroid gland's autoimmune assault. In patients with Hashimoto's thyroiditis, regulatory T cells—which typically aid in regulating immune responses and suppressing autoimmunity—may not be functioning efficiently. [12]

In reaction to thyroid antigens, B cells—an intermediate portion of white blood cells—produce antibodies. Thyroid proteins, in particular to thyroglobulin (Tg) and thyroid peroxidase (TPO), are the target of B cell production in Hashimoto's thyroiditis, which results in the production of immune complexes that inflame and destroy tissue.[13]

## 2.5. Etiology

Hashimoto's thyroiditis has a hereditary component, which means that it typically runs in families. The condition's likelihood of development can be raised by specific genetic variants.

Autoimmune Response: The immune system generates antibodies to destroy thyroid cells because it misinterprets them as foreign invaders. Inflammation and thyroid gland damage result from this.

Triggers in the environment: There are numerous environmental factors that might either cause or worsen Hashimoto's thyroiditis. Radiation exposure and viral illnesses like hepatitis C or Epstein-Barr virus are two examples of this.[14]

Hormonal Imbalances: Variations in the amounts of hormones, especially oestrogen, can affect how Hashimoto's thyroiditis starts and progresses. Because of this, the illness affects more women than men—and frequently arises during or after pregnancy.

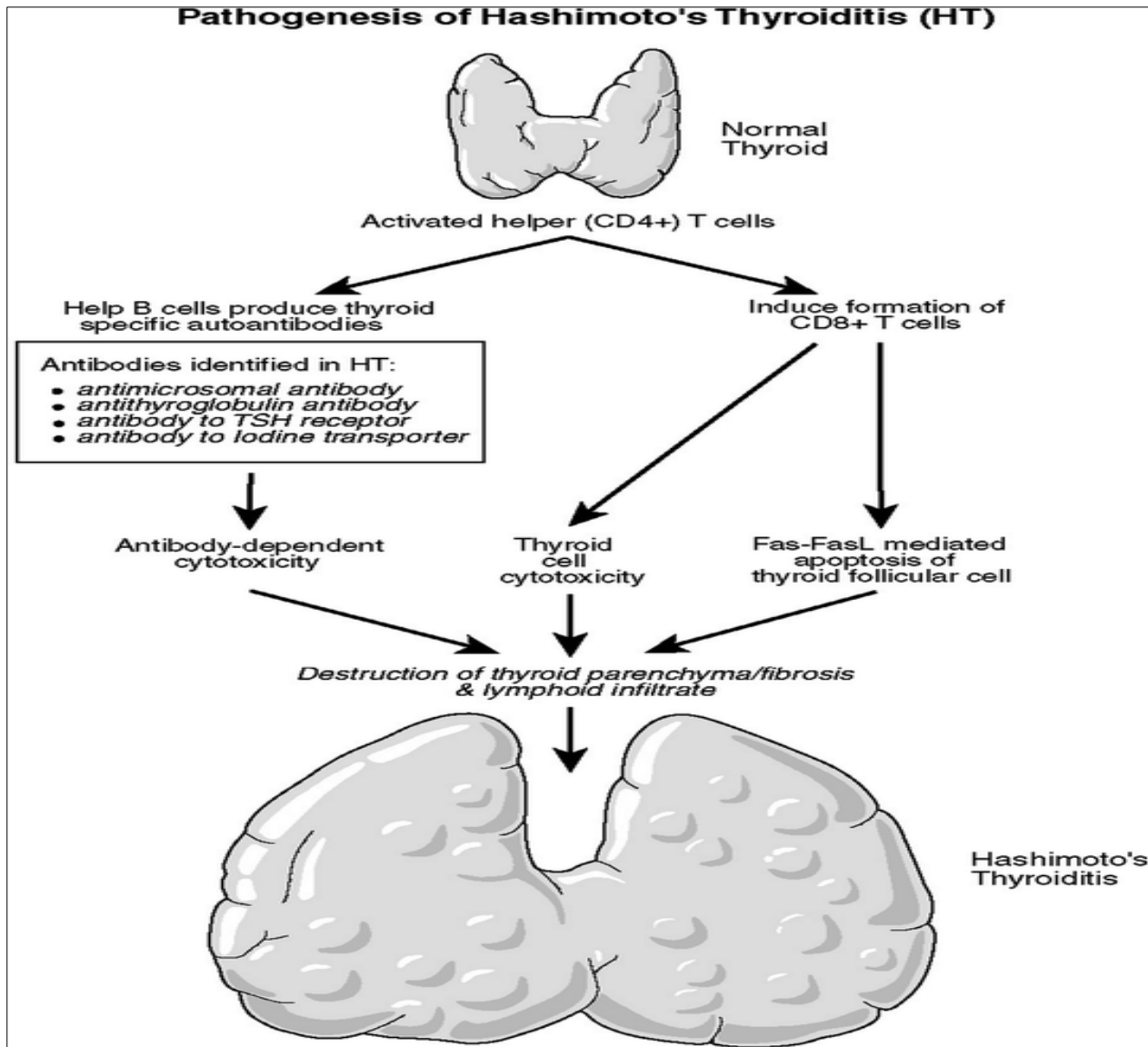
Iodine Intake: Thyroid inflammation in susceptible individuals can occasionally be induced or exacerbated by excessive iodine intake, whether from food or medicine. Alternatively, in some communities, iodine deficiency can also be associated with danger. [15]

## 2.6. Pathophysiology

Hashimoto's Thyroiditis is the complex interaction between the immune system also thyroid gland, which causes thyroid problems and the onset of hypothyroidism. It offers a more extensive view of the disease's complexity and its effects on diagnosis, therapy, and care. When thyroid hormone (HT) is present, the immune system misinterprets the proteins in the thyroid glands as foreign invaders and launches an attack on them. Thyroid gland infiltration is specifically caused by lymphocytes that release cytokines that cause inflammation and damage to thyroid cells.[16]

Thyroxine (T4) in addition to triiodothyronine (T3) these are the two thyroid hormones that the thyroid gland gradually loses its ability to produce at an acceptable level as long as it is damaged, and inflammation continues. Hypothyroidism ensues, presenting with symptoms like lethargy, rise in body weight, sensitivity to cold, xerostomia, and constipation.

In Hashimoto's thyroiditis, thyroglobulin antibodies are another kind of antibody. Thyroid inflammation and dysfunction can also be caused by antibodies against thyroglobulin, a protein that serves as a precursor to thyroid hormones.



**Figure 3** Pathogenesis of hashimoto's thyroiditis (HT)

## 2.7. Management

The management of HT is individualized based on how strong the signs are, thyroid hormone level, and the presence of any other underlying health conditions. Close collaborations between healthcare providers and patients are essential for achieving for optimal outcome and maintaining thyroid health.[17]

As Hashimoto's thyroiditis is a major cause of hypothyroidism, the primary mode of treatment is TH hormone replacement therapy. For the reason of controlling hypothyroidism and improving its symptoms, levothyroxine, a synthetic form of the thyroid hormone thyroxine (T4), is typically given.

To ensure acceptable TH levels and modify medication dosage, thyroid function must be evaluated through blood tests that measure thyroid-stimulating hormone (TSH), free thyroxine (T4), and occasionally triiodothyronine (T3). [18]

Certain dietary components, such gluten or iodine, may make symptoms worse for certain people with Hashimoto's thyroiditis. It might help to identify and address any food triggers by working with a dietician or healthcare physician.

Thyroid gland enlargement, or goitre, is a potential side effect of Hashimoto's thyroiditis in certain individuals. Medications, radioactive iodine therapy, or, in extreme situations, surgery to remove all or portion of the thyroid gland are possible treatments for a goitre, depending on its size and symptoms.

**Pregnancy Management:** Pregnant or prospective mothers with Hashimoto's thyroiditis need some extra attention because replace in the thyroid hormone levels can have an effect on the mother's and the foetus's health. To keep thyroid hormone levels at optimal levels during pregnancy, careful monitoring about thyroid function and dosage adjustments are essential.[20]

**Alternative Therapies:** In order to control symptoms or promote general health, some people with Hashimoto's thyroiditis investigate complementary and alternative therapies including acupuncture, herbal supplements, or mind-body techniques like yoga or meditation. Even though these methods might help some people with their symptoms, it's crucial to talk to a healthcare professional about them and make sure they support traditional medical care.

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### 3. Conclusion

The challenges encountered in treating (subclinical) hypothyroidism and linking its symptoms to a biochemical diagnosis. The majority of thyroid-related symptoms are non-specific and can affect people who are euthyroid as well. Many patients report only somewhat effective symptom reduction following L-T4 therapy. This occurrence has a number of possible reasons. The crucial significance of plasma TSH and FT4 concentrations, which may not always reflect tissue thyroid hormone state, might lead to the disparity between patient satisfaction and biological thyroid hormone status. In addition, symptoms could be the consequence of other conditions like autoimmunity or a chronic illness that requires medical care. Particular circumstances, such aging, pregnancy, NTIS, and central hypothyroidism, provide additional difficulties for measuring, interpreting, and monitoring TSH and FT4 values throughout treatment. There's cause for anticipation. Numerous genetic factors and environmental factors that might trigger an autoimmune response have been identified, but the precise pathogenic pathways of HT are still unknown. Further research is necessary to completely understand the role of epigenetic factors, even though they need to be implicated in the etiopathogenesis of HTC. One autoimmune disorder that causes hypothyroidism is Hashimoto's thyroiditis. Anybody can develop it; however adult females are more likely to have it. To replenish the thyroid hormone that the body is lacking as part of the treatment, a daily medicine must be taken.

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### Compliance with ethical standards

#### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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