

Hypothyroidism: causes, effects and treatments



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Hypothyroidism is a condition characterized by abnormally low amount of the thyroid hormone synthesis. This may be due to a thyroid problem or any other reason. Thyroid hormone affects growth, development, and many cellular processes. Inadequate thyroid hormone has many consequences for the body (1, 2, 3).

Thyroid gland and thyroid hormone synthesis

Thyroid gland has two lobes connected by an isthmus. It attaches to the thyroid cartilage and trachea. Therefore it moves with swallowing. Thyroid gland consists of follicles lined by a cuboidal epithelial cell layer. These follicles filled with colloids. Parafollicular cells situated in between follicular cells which secrete calcitonine (4, 9).

Thyroid gland synthesizes mainly two hormones. They are L-thyroxin/tetraiodothyronine (T4) and triiodothyronine (T3). T3 is the active form that acts at the cellular level and T4 is the prohormone. Iodide enters the thyroid follicles primarily through a transporter. Thyroid hormone synthesis occurs in the follicular space through a series of reactions, many of which are peroxides-mediated. Thyroid hormones stored in the colloid in the follicular space that is released from Thyroglobulin by a hydrolysis reaction which occur inside the thyroid cell (4, 5, 8).

E. g. Thyroglobulin (Tgb), monoiodotyrosine (MIT), diiodotyrosine (DIT), Triiodothyronine (T3), tetraiodothyronine (T4) (5).

If there is hereditary defect of enzyme in above process, Thyroid hormone synthesis could not occur. So it's leads to congenital goiter and often results in hypothyroidism (6).

Regulation of the synthesis of thyroid hormones

Thyroid hormone synthesis is regulated by another gland located in the brain called pituitary. In turn the pituitary gland is partly regulated by the thyroid hormone via feedback mechanism and another gland called hypothalamus. The hypothalamus secretes thyrotropin hormone (TRH), which gives a signal to the pituitary gland to release thyroid stimulating hormone (TSH). TSH in turn sends a signal to the thyroid gland to release thyroid hormone. If some defect occurs in one of these levels, a lack of production of thyroid hormones can cause a deficiency of thyroid hormone (hypothyroidism) (4, 5, 8).

- Hypothalamus - TRH
- down arrow
- Pituitary- TSH
- down arrow
- Thyroid- T4 and T3

The rate of thyroid hormone synthesis is regulated by the pituitary gland. If there is an insufficient amount of thyroid hormone circulating in the body to normal functioning, the release of TSH from the pituitary increases in order to stimulate more thyroid hormone. However, when there is a large amount of thyroid hormones in circulation, TSH level decreases and the pituitary attempts to reduce the production of thyroid hormone. In people with hypothyroidism, there are low levels of circulating thyroid hormones (4, 8).

Physiological effects of thyroid hormones

- Cardiovascular system - increased cardiac output and heart rate.
- Skeletal system - increased bone turnover and resorption.

- Respiratory – maintains normal hypoxic and Hypercapnic drive in respiratory centre.
- Gastrointestinal – increases gut motility.
- Blood – increases red blood cell 2, 3-BPG facilitating Oxygen release to tissues.
- Neuromuscular – increases speed of muscle contraction and relaxation and muscle protein turnover.
- Metabolism of carbohydrates – increases hepatic Gluconeogenesis/glycolysis and intestinal glucose Absorption.
- Metabolism of lipids – increased lipolysis and Cholesterol synthesis and degradation.
- Sympathetic nervous tissue – increases catecholamine Sensitivity and β -adrenergic receptor numbers in heart, skeletal muscle, adipose cells and lymphocytes (1, 2, 4, 7, 8).

Reduces cardiac β -adrenergic receptors.

If there is a defect in the synthesis or regulation pathways or thyroid lead to many disorders. They are mainly divided in two parts. They are hyperthyroidism and hypothyroidism. Hyperthyroidism, or an overactive thyroid, is the overproduction of thyroid hormones T3 and T4, and most often caused by the development of Graves' disease which is an autoimmune disease in which antibodies are produced which stimulate the thyroid gland produces excessive amounts of thyroid hormones. This disease can lead to the development of toxic goiter due to the growth of the thyroid gland in response to the absence of negative feedback mechanisms. This is manifested by symptoms such as thyroid goiter, protruding eyes

(exophthalmos), palpitations, excessive sweating, diarrhea, weight loss, muscle weakness and unusual sensitivity to heat. Appetite is increased (2, 4, 7).

Classification of Hypothyroidism

Hypothyroidism is often classified by association with the indicated organ dysfunction (4).

- Type
- Origin
- Primary
- Thyroid gland

The most common forms are Hashimoto's thyroiditis which is an autoimmune disease and can be occur in radioiodine therapy for hyperthyroidism (4, 7, 6).

- Secondary
- Pituitary gland

Occurs if the pituitary gland does not release enough thyroid-stimulating hormone (TSH) to stimulate the thyroid gland to produce enough thyroid hormones. Although not every case of secondary hypothyroidism has a clear-cut case, it is usually caused by damage to the pituitary gland, as by a tumor, radiation, or surgery. Secondary hypothyroidism accounts for less than 5% or 10% of hypothyroidism cases (4, 7, 6).

Tertiary

Hypothalamus

Results when the hypothalamus fails to produce sufficient

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Thyrotropin-releasing hormone (TRH). TRH prompts the pituitary gland to produce thyroid-stimulating hormone (TSH). Hence may also be termed hypothalamic-pitu(4, 7, 6)

Autoimmune

Atrophic (autoimmune) hypothyroidism. The most common cause of hypothyroidism and the associated with antithyroid auto antibodies leads to lymphoid infiltration Cancer and eventually atrophy and fibrosis. It has been six Times more common in women and the incidence increases

with age. This can be associated with other autoimmune Diseases such as pernicious anemia, vitiligo and other endocrine disorders. In some cases, intermittent Hypothyroidism occurs when recovering from illness, antibodies which block the TSH receptor can sometimes be involved

in the etiology(5, 7, 10).

Hashimoto's thyroiditis.

This form of autoimmune thyroiditis, again, more common in women and the most common in the late. The average age is atrophic changes with regeneration, leading to the formation of goiter. This may be usually firm and Rubber but can vary from soft to hard. TPO antibodies very high amount (> 1000 IU / L). Patients can be euthyroid or hypothyroid, but they can pass through

the initial phase of the toxic “ Hashi toxicity, Levothyroxine therapy. The goiter may reduce the even if the patient does not Hypothyroid (7, 8, 10).

Postpartum thyroiditis.

Typically, this is a temporary phenomenon Observed after pregnancy. It can cause hyperthyroidism, Hypothyroidism or the two sequences. It is believed to cause changes in the immune system necesnecessary. In case of pregnancy, and histologically lymphocytic thyroiditis.

The process is usually self-limiting, but when Conventional antibodies are there is a strong chance this procedure of permanent hypothyroidism.

Postpartum Thyroiditis may be misdiagnosed as postnatal depression.

Thyroid function test is done to detect this situation (4, 7).

Defects in hormone synthesis

Iodine deficiency. Dietary iodine deficiency still exists in some areas as “endemic goiter” where goiter, occasionally massive is common. Patients may be euthyroid or hypothyroidism depending on the severity of iodine deficiency. The mechanism is considered borderline hypothyroidism

leading to TSH stimulation and thyroid enlargement against iodine deficiency

continues (4; 7). Iodine deficiency is this still a problem in the Netherlands,

the Western Pacific and South. East Asia for example, the mountainous

regions of the Himalayas and Africa. Some countries affected by iodine

deficiency, for example, China and Kazakhstan take measures providing

iodine in salt, but others, such as Russia, have not yet done so. Of The 500

million with iodine deficiency in India about 2 million suffering from

cretinism. Dyshormonogenesis is a rare disease is due to genetics. Defects in

the synthesis of thyroid hormones, patients Develop hypothyroidism with

goiter. One particular family Form is associated with sensorineural hearing

loss due to the removal Mutation of chromosome 7, resulting in a defect
Transporter Pendrin (Pendred syndrome author) (4, 5).

Hypothyroidism causes many symptoms. The term “ myxedema” refers to the accumulation of mucopolysaccharides. In the subcutaneous tissue. The classical pictures are Slow in working, dry hair, thick-skinned, deep voice, Weight gain, cold intolerance, bradycardia, and constipation. These features make the diagnosis easy. Milder symptoms, however, more common and difficult to distinguish from other causes Nonspecific tiredness. Many of the cases on the biochemical detection (4, 6, 7)

Screening

Particular difficulties in diagnosis may occur in certain circumstances:

Children with hypothyroidism may not classical Properties, but often have a slow growth rate, poor School performance and sometimes arrests of pubertal Development.

Young women with hypothyroidism may not show obvious signs.

Hypothyroidism is excluded in all Patients with oligomenorrhea / amenorrhea, Menorrhagia, infertility and hyperprolactinemia.

the elderly show many clinical features that are difficult Distinct from normal aging (7, 10, 11).

Investigation of primary hypothyroidism

The Serum TSH is the examination of choice, a high TSH level Confirmed primary hypothyroidism. A low free T4 level confirms the hypothyroidism is

(and is also essential for TSH to close a deficiency and clinical hypothyroidism is strongly suspected and TSH is normal or low). Thyroid and other organ-specific antibodies are present (7, 10).

Other exceptions are the following:

- Anemia, usually normochromic and normocytic In type but can macrocytic (sometimes this is by Associated pernicious anemia) or microcytic (in women, By menorrhagia)
- increased serum aspartate transferase levels, from Muscle and / or liver
- increased serum creatine kinase levels, with associated myopathy
- Hypercholesterolemia and hypertriglyceridemia
- Hyponatremia due to an increase in ADH and reduced Free water clearance (7, 10).

Treatment

Replacement therapy with levothyroxine (thyroxin, that is to say, T4) is Data for life. The starting dose will depend upon the severity of the failure and the age and condition of the patient, especially their cardiac function: 100 $\hat{1}$ /₄g per day during the Young and fit, 50 $\hat{1}$ /₄g (up to 100 $\hat{1}$ /₄g after 2-4 weeks) for the small, old or weak. Patients with ischemic heart disease Illness an even lower initial dose, especially if the Hypothyroidism is a severe and prolonged.

Most doctors

Would then start with daily 25 $\hat{1}$ /₄g and performing serial ECG, increasing the dose at 3 - to 4-week intervals as angina Not occur or worsen and the ECG is not Deteriorate(8, 10, 11).

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Monitoring

The goal is to recover well within T4 and TSH The normal range. The adequacy of the replacement is reviewed Clinical and thyroid function tests after at least 6 weeks at a constant dose. If serum TSH remains high, the dose of T4 Should is increased in increments of 25-50 g if→ the tests Repeated 6-8 week intervals until TSH returns to normal. Complete suppression of TSH should be avoided atrial fibrillation and the risk of osteoporosis. The usual The Maintenance dose is 100 to 150 g if→ administered as a single daily Dose. An annual thyroid function test is recommended - this is usually done in the first line, often assisted and in response to the district ' thyroid registers (5, 8, 11).

Clinical improvement T4 cannot start 2 weeks or more and complete resolution of symptoms 6 months. The need for lifelong therapy should be emphasized and the possibility of other autoimmune endocrine disease development, Especially Addison's disease or pernicious anemia,

Should be considered. During pregnancy, an increase of T4 Dosage of about 25-50¹/₄g is often necessary to maintain normal TSH and the need for replacement during optimal. Pregnancy is highlighted by the finding of the reduction of Cognitive function in children of mothers with elevated TSH during pregnancy. A few patients with primary hypothyroidism complain incomplete symptomatic response to T4 replacement. Combination T4 and T3 replacement is advocated in this Context, but randomized clinical trials show no consistent Benefit from the quality of life symptoms (4, 8).

Borderline hypothyroidism or " Compensated euthyroidism ' Patients are

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often seen with a low-normal serum T4 levels and slightly elevated TSH values. Sometimes this follows surgery or radioactive iodine therapy when it can be reasonably seen as 'compensatory'. Treatment with levothyroxine is normally recommended where the TSH is consistently above 10 mu / L, or if possible symptoms, high titers of thyroid Antibodies or lipid abnormalities are present (4, 8, 10).

When the TSH is only marginally increased, the tests must be repeated three to six Months later. Conversion to overt hypothyroidism is more common in men or TPO antibodies are present in

Practice, vague symptoms in patients with marginal Elevated TSH (less than 10 mu / L) rarely responds to treatment, However, a "therapeutic trial" of substitution may be required to confirm that the symptoms are not related to the thyroid gland(4, 8, 10).

It is also is considered to be the best time (TSH level normalization, the ideal case, the former)

Pregnancy, in order to avoid the side effects of the fetus. Myxedema coma severe hypothyroidism, especially in the elderly, may be with confusion and even coma. Myxedema coma is very rare. Low temperature is often there, the patient may have severe heart failure, hypoventilation, hypoglycemia, and hyponatremia. The best treatment Controversial, there is no data, most doctors recommend T3 oral or intravenous injection, a dose of 1-2, and 5-5 grams every 8 hours then, such as the above-mentioned increase. High-dose intravenous cannot be used (4, 7, 8). Other measures, although there is no proof of Include:

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- Oxygen (by ventilation if necessary)
- monitoring of cardiac output and pressure
- Gradual warming
- Hydrocortisone 100 mg intravenously 8-hour
- Glucose infusion to avoid hypoglycemia.

“ Myxedema madness” Depression is common in hypothyroidism but rarely with severe hypothyroidism in the elderly can the patient be said demented or psychotic, sometimes with prominent delusions. This may occur shortly after starting T4 replacement (6, 5).

Screening for hypothyroidism

the incidence of congenital hypothyroidism is Approximately 1 in 3500 births. Untreated, severe Hypothyroidism produces permanent neurological and Intellectual damage (cretinism). Routine screening of the newborn with a bloodstain, like Guthrie test, a high TSH level as an indicator of primary detecting Hypothyroidism is efficient and cost effective; cretinism is prevented if T4 is started within the first few months of life.

screening of elderly patients for thyroid dysfunction a low pick-up rate and is controversial and not currently recommended. However, patients who have undergone Thyroid surgery or radioactive iodine should receive Regular thyroid function tests, should be as those who Lithium or amiodarone therapy (6, 5).

Signs and symptoms

early hypothyroidism is often asymptomatic, can have very mild symptoms. Subclinical hypothyroidism normal levels of thyroid hormones, thyroxin (T4)

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and triiodo thyroxin (T3), moderate to high thyroid-stimulating hormone, thyroid stimulating hormone (TSH) conditions. TSH and low free T4 at a higher level; the symptoms are more obvious in clinical hypothyroidism (4, 6, 5).

Hypothyroidism may be associated with the following symptoms:

Early

- cold intolerance, increased sensitivity to cold
- Constipation
- weight gain, water retention
- bradycardia (low heart rate – less than 65 times per minute)
- Fatigue
- decreased sweating
- Muscle cramps and joint pain
- dry, itchy skin
- thin, brittle nails
- Quick thoughts
- Depression
- muscle tension difference (hypotonia)
- female infertility and problems in the menstrual cycle
- Hyperprolactinemia and galactorrhea
- elevated serum cholesterol(10, 11)

Late

- goiter

- slow speech and a hoarse, breaking voice – deepening of the voice can also be noticed. Reinke edema.
- Dry puffy skin, especially in the face
- Thinning of the outer third of the eyebrows (sign of Hertoghe)
- Menstrual cycle abnormalities
- Low basal body temperature
- thyroid related depression(10, 11)

Uncommon

- Impaired memory
- Impaired cognitive function (brain fog) and inattentiveness.
- A slow heart rate with ECG changes including low voltage signals.
Diminished cardiac output and decreased contractility
- slow reflexes
- Yellowing of the skin due to impaired conversion of beta-carotene to vitamin A (carotoderma)
- Difficulty swallowing(dysphagia)
- Shortness of breath with a shallow and slow respiratory pattern(dyphnea)
- myxedema madness (a rare presentation)
- Decreased libido due to impairment of testicular testosterone synthesis
- Gynecomastia(enlarge breast tissue)
- Loss of hearing(10, 11)

Diagnosis

thyroid function test

the only validation test diagnosis of primary hypothyroidism is thyroid stimulating hormone (TSH) and free thyroxin (T4) level. However, these levels can be varying without thyroid disease (10, 11).

High TSH levels, the thyroid gland does not produce enough thyroid hormone levels (primarily thyroxin (T4) and a small amount of iodine Thyroid three original leucine (T3)). However, measuring just TSH can diagnose secondary and tertiary thyroid function loss, resulting in the following recommended a blood test, if the TSH is normal hypothyroidism remains skeptical(10, 11).

Free triiodothyronine (ft3)

Free thyroxin (ft4)

Total T3

Total T4

Additionally, the following measurements may be needed:

Free T3 from 24-hour urine catch

Antithyroid antibodies – for evidence of autoimmune diseases that may be damaging the thyroid gland

Serum cholesterol – which may be elevated in hypothyroidism

Prolactin – as a widely available test of pituitary function

Testing for anemia, including ferritin

Basal body temperature(4, 8, 10)

Exams and Tests

A physical examination may reveal a smaller than normal thyroid gland, although sometimes the gland is normal size or even enlarged (goiter). The examination may also reveal:

- Brittle nails
- Coarse facial features
- Pale or dry skin, which may be cool to the touch
- Swelling of the arms and legs
- Thin and brittle hair
- A chest x-ray may show an enlarged heart (12, 13).

Laboratory tests to determine thyroid function include:

TSH test

T4 test(10, 12, 13)

Lab tests may also reveal:

Anemia on a complete blood count (CBC)

Increased cholesterol levels

Increased liver enzymes

Increased prolactin

Low sodium(8, 13)

Treatment

The treatment of hypothyroidism is levorotatory forms of thyroxin (thyroid hormone) (L-T4) and triiodo thyroxin liothyronine (L-T3). Thyroxin is a name, and in the USA, the most common form of thyroxin tablets. Thyroxin is a doctor of the most common drugs, wherein a synthetic thyroid hormone predetermined. This medicine can improve symptoms of thyroid deficiency such as speech delay, lack of energy, weight gain, hair loss, dry skin, cold feeling. This will also help in the treatment of goiter. It can also be used to treat certain types of thyroid cancer, surgery and other medicines. Both synthetic and animal thyroid tablets available, and may be required in patients with the additional thyroid hormone (8, 10). Daily doses of thyroid hormone, doctors can monitor blood pressure, in order to help ensure that the correct dose. Thyroxin is the best 30-60 minutes before breakfast, because some foods can reduce absorption. Calcium can interfere with absorption levothyroxine. Compared with water, the coffee can be reduced about 30% of the absorption of thyroxin. Some patients may be anti-thyroxin, in fact, they do not have good absorption sheet - to solve the problem by spraying. There are several different treatment options for thyroid replacement therapy (8, 10, 12, 13).

T4 only such treatment methods include supplementary levothyroxin separately, a synthetic form. This is the current standard treatment of mainstream medicine.

A combination of T4 and T3 in This treatment method involves the combination simultaneously manage two synthetic L-T4 and L-T3 (8, 10, 11).

Dried thyroid extract

Dried thyroid extract is an animal thyroid extract; the most common is from porcine sources. It is also a combination therapy, containing a natural form of L-T4 and L-T3.

Dealing with controversial

T4 T3 generation has been investigating the potential benefits, but has proved to be no conclusive combination therapy benefit. Laboratory Medicine Practice Guidelines in 2002, the clinical biochemical state of the U. S. National Academy of Sciences during pregnancy: " L-T4 dose should be increased (usually 50 micrograms / day) maintained at 0. 5 ~ 2. 0 mIU / L and serum serum TSH FT4 within the normal reference interval the upper third." Doctors tend to assume that if your TSH is in the normal range, sometimes defined as high as 5. 5 mIU / L has no effect on fertility. But there is an approximately 1. 0 mIU / L, TSH level in healthy pregnant women (8, 12, 13)

Subclinical hypothyroidism

there are a series of biochemical and point thyroxin treatment, the typical treatment of hypothyroidism symptoms views. Reference range has been debated. As of 2003, the American Association of Clinical Endocrinologists (ACEE) that within the normal range of 0. 3-3. 0 mIU /L.

There is always an excess risk of hyperthyroidism. Some studies suggest that subclinical hypothyroidism does not require treatment. In 2007, the Cochrane Collaboration, a meta-analysis found that, in addition to the " no benefit of thyroid hormone replacement lipids and left ventricular function in

2002 meta-analysis checks whether subclinical hypothyroidism may increase the risk of heart disease increase, some of the parameters previously thought, a slight increase, and recommended to be updated for the current recommendations for further research with the end point of coronary heart disease (11, 12, 13).

Replacement therapy

The connection has been a slow release combination of T3 and T4, supporters will be able to thyroid dysfunction symptoms and functional quality of life. This is still a matter of debate, refused by the traditional medical community (3, 8, 10).

Remember, the important thing when are taking thyroid hormone are:

Do not stop taking the drugs, and when you feel better. Continue the medication completely guidance of a doctor.

If change the brand of thyroid drugs, let doctor know. levels may need to be checked.

Some dietary changes can change your body absorb thyroid drugs. Contact your doctor, if you eat a lot of soy products, or in the high-fiber diet.

Thyroid medicine best on an empty stomach, and if any other drugs before one hour.

Do not take the thyroid hormone supplement fiber, calcium, iron, multivitamins, aluminum hydroxide, sulfuric acid agent, cholesterol, or in combination with a bile acid drugs(4, 13).

Start taking replacement therapy, the doctor tells, if there are symptoms of increased thyroid activity (hyperthyroidism), such as

- Palpitations
- Rapid weight loss
- Restlessness or shakiness
- Sweating

Myxedema coma is a medical emergency; the thyroid hormone the body becomes very low. Intravenous replacement thyroid hormone and steroids. Some patients may need support therapy (oxygen, breathing assistance, fluid replacement) and intensive care (8, 10, 11).

Outlook (prognosis)

in most cases, thyroid levels to normal, and appropriate treatment. However, thyroid hormone replacement for the rest of life. Myxedema coma can result in death (12, 13).

Possible complications

Hypothyroidism, myxedema coma, the most severe form is rare. This can be caused by infection, illness, exposure to cold, or certain medications in untreated hypothyroidism (12, 13).

The symptoms and signs of myxedema coma include:

- room temperature
- Reduce breathing
- low blood pressure
- Hypoglycemia

- unresponsive

Other complications include:

- Heart disease
- Increased risk of infection
- Infertility
- Abortion(8, 12, 13)

Untreated hypothyroidism are at increased risk:

- gave birth to birth defects
- heart disease, the higher the level of LDL (“ bad” cholesterol)
- heart failure

Too much thyroid hormone treatment are at risk of angina or a heart attack, as well as the risk of osteoporosis(the bone thinning)(11, 12, 13).