Thyroid Hormones: The Body's Main Endocrine Organ

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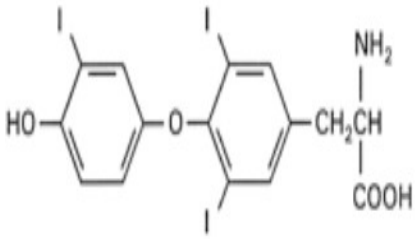
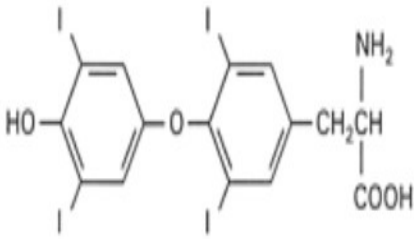
Abstract
The thyroid gland, the body's main endocrine organ, is situated in front of the thyroid cartilage in the anterior neck area. They are essential for almost all tissues to function at their best and have a big impact on a person's metabolism and oxygen consumption. The fact that thyroid-related endocrine disorders are among the most prevalent is not surprising. Around the world, hundreds of thousands of people struggle with thyroid issues. In order to clinically connect with illnesses that cause a hormone shortfall or excess, it is necessary to understand how it works. . thyroxin hormone consist of a tyrosine molecule joined to a phenyl ring by an ether bond. On their inner tyrosine rings, both have two iodine atoms. T4 and T3 are different from one another because T4 has two iodine atoms on its phenyl (outer) ring while T3 only has one. The amount of unbound or "Free" T4 and T3 (FT4 and FT3) is crucial for the biological effects of thyroid hormones, including feedback regulation to the anterior pituitary and hypothalamus. Plasma includes both bound and unbound (Free) thyroid hormones.
Keyword: thyroxin, thyronine, thyroid hormone, thyroid gland, hypothyroidism, hyperthyroidism

1 Introduction

Many physiological processes is widely known that the thyroid hormone controls these processes. The two main hormones generated by the gland that makes up the thyroid are thyroxine, also referred to as (T4) and a hormone known as (T3). TSH, T4 and thyroid-releasing hormone (TRH), both of which are produced by the anterior pituitary, as well as TRH from the brain, work in concert to keep a healthy feedback system and equilibrium. Common signs of hypothyroidism, which is caused by an underactive thyroid gland, include , cold tolerance, diarrhoea, exhaustion, and weight gain. On the other hand, hyperthyroidism, This results in weight loss, heat sensitivity, diarrhoea, mild tremors, and weak muscles and is brought on by increased thyroid gland activity. The small intestine acts as where iodine, an essential trace element, is absorbed. Important for the T3 and T4. Iodine can be found in salt, seafood, seaweed, vegetables, and other foods. Inadequate iodine intake can lead to iodine deficits and reduced thyroid hormone synthesis. Iodine deficiency can result in cretinism, myxedema coma, and hypothyroidism, among other disorders [1]. T4 is nearby metabolised in the liver, kidney, and other tissues in two separate ways, as was already explained. T3 is produced by the enzyme 5'-D's outside ring deiodination, and rT3 is produced by the enzyme 5'-D's inner ring deiodination, which is assumed to have no known biological purpose Deiodination is the hormone's primary metabolic pathway in humans Because to its dual involvement in T4 activation and inactivation, as well as the fact that T4 generates 87% of the T3 in circulation [2]. The thyroid is primarily situated on the back of the tongue during foetal growth before moving to the front of the neck, which is directly behind the larynx. The thyroid has two sizable lobes that are situated on either side of the trachea and is the largest gland in the neck, weighing less than an ounce. The isthmus, a constricted area of thyroid tissue, connects these lobes. The gland is covered in a fibrous capsule that extends inside of it and separates it into several little lobules. Because the thyroid is composed of closely spaced follicles that are encircled by capillaries, its blood flow is quite high in relation to its weight. [3] syntheses of thyroxin and thyronin:-



3,3'5-Triiodo-L-Thyronine
(T_3)



Thyroxine
(T_4)

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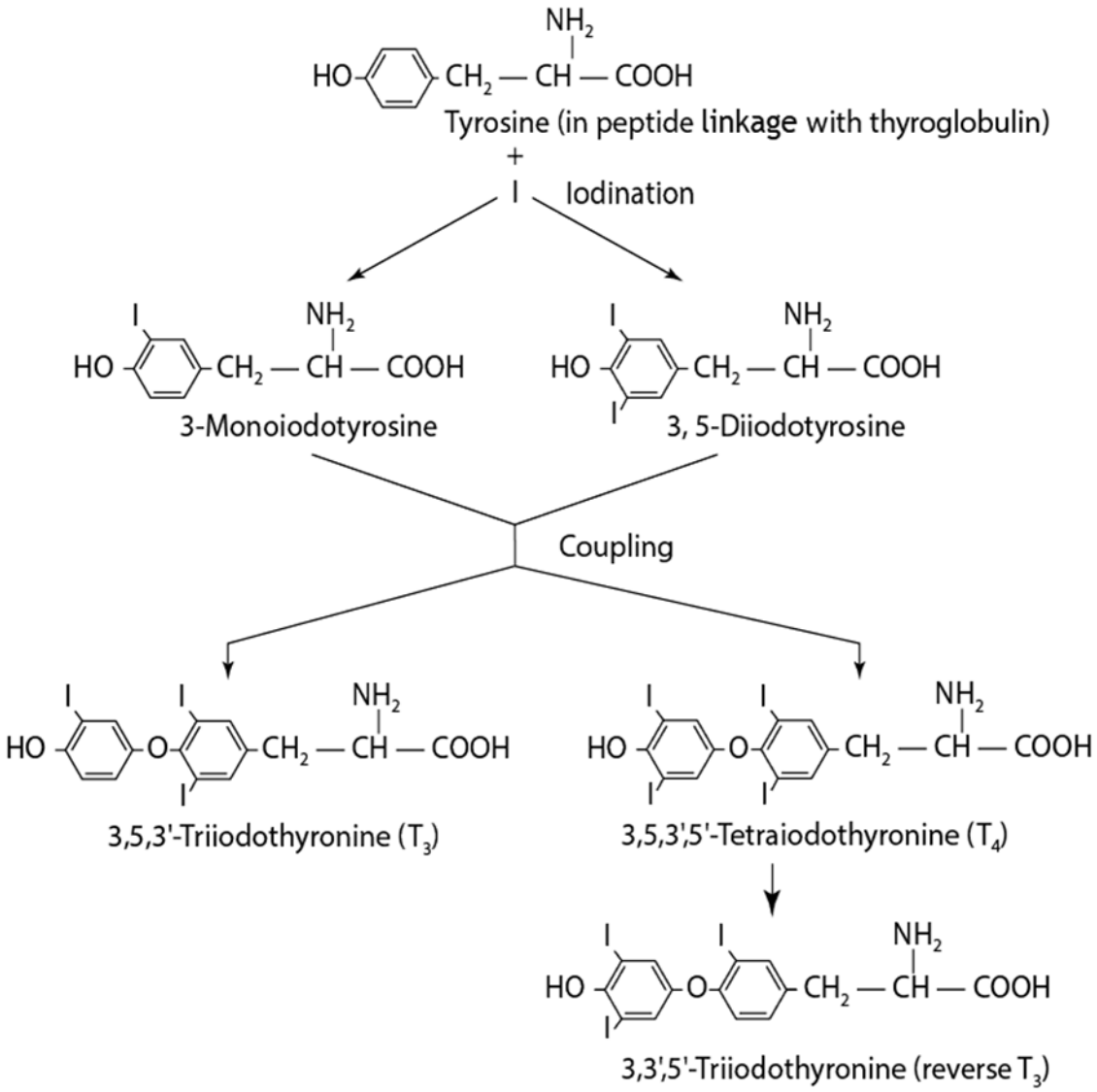

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The thyroid hormones are made by the follicular cells. The glycoprotein a substance called protein, which includes T3 and T4 precursors, is found in the colloid, a space surrounded by follicular cells and housing the hormone. The parafollicular cells, which are more commonly known as C-cells, secrete the hormone calcitonin, which controls calcium [4]. A negative feedback process that includes the brain, pituitary, thyroid, and hypothalamic-pituitary-thyroid (HPT) axis effectively regulates TH production and release. After thyroxine (T4), triiodothyronine (T3) is the second-most significant hormone generated by the thyroid gland. When administered in vivo, both compounds show metabolic action. The thyroid gland produces and stores the two iodo-amino acids as part of the large protein molecule known as (TG), which must be completely broken down to release both amino acids in an amount that prefers T4 by 10–20 tmes (6). The peripheral monodeiodination of T4 produces about 45% of the T3 pool in the extrathyroidal body .

A healthy man's thyroid generates about 100 pg of T4 every day, of which 30% is monodeiodinated to make about 25 pg of T3, and 20% is lost in the faeces. The other 70% is gradually deiodinated to create intermediates that are assumed to be physiologically inactive. Only about 7 pg of the daily needed 32 pg of T3 are produced by the thyroid.

Moreover, the faeces lose about 5 pg of T3. The bloodstream contains over 99% of the thyroid hormone, which is bound to certain serum proteins. A small amount of unbound hormone and the protein-bound hormone are in reversible balance, and the inner cell hormone pool is then in balance. The corresponding free circulating hormone concentrations are thus 2.5 and 0.3 ng/dl, although the mean serum total contents of T4 and T3 are 8.5 and 0.12 pg/dl, respectively[7][8] [9].

The iodothyronines gain macromolecular characteristics by the relationship of the hormones with the serum-bound proteins, which reduces their urine loss. These hormone-binding proteins may also protect the organism from sudden variations in hormonal output by keeping the level of free hormone content steady and acting as a store for easily available hormone. The modest additional thyroidal pool of free hormone is expected to be depleted shortly after a sudden cessation of hormone synthesis if the serum's binding proteins weren't there [10].

The main thyroid hormone (TH) in circulation is the prohormone T4, which is converted into the thyroid

hormone (T3), a more powerful form. Three iodothyronine deiodinases control how TH is metabolised. By removing a 5′-iodine atom, the type 1 and type 2 enzymes (D1 and D2) catalyse the conversion of T4 into T3. When a 5-iodine atom is irreversibly removed from either T4 or T3 by the type 3 enzyme (D3), the resultant 3,3′,5′-L-triiodothyronine (reverse T3, rT3) and 3,3′-diiodothyronine (T2) are inert substances [11]. Since skeletal cells do not express D1 [12]. D1 cannot directly affect how T3 acts on bone. D2 is only present in primary osteoblasts that are fully developed; it is absent from chondrocytes and osteoclasts [13].

The set point, also known as the connection between the quantity of blood T4 and serum TSH, is constant for a person but significantly varies between individuals when regularly assessed prospectively [14]. This population-wide variation in set point raises the possibility that the thyroid hormone system may have one or more genes with a genetic component. [15]. Pituitary TSH set points have been found to be affected by D2 polymorphisms [16]. And a slowed rise in serum T4 following an abrupt rise in serum TSH induced by thyrotropin-releasing hormone (TRH) stimulation [17]. Hypothyroid patients with certain D2 polymorphisms have been shown to respond better to T4 and T3 together than T4 alone [18].

The hypothalamus, pituitary, and other components of the feedback system regulate the thyroid gland, along with other endocrine system glands, and anterior pituitary, a particular gland (the thyroid). The HPT axis refers to the relationship between the hypothalamus, pituitary, and thyroid glands. The brain creates the tripeptide TRH, which leaves the bloodstream and travels to the pituitary gland. TSH, also known as thyrotropin, is produced and secreted by the pituitary gland when TRH binds to a receptor in thyrotroph cells. The thyroid gland produces and secretes the thyroid hormones T3 and T4 when thyroid stimulating hormone interacts with TSH receptors in the follicular cells of the thyroid gland. The thyroid gland exhibits both types of feedback, as do all endocrine glands, but the negative feedback mechanism predominates [19].

Thyroid hormones have a variety of effects on growth, metabolism, and other organ-specific activities. Thyroid hormones naturally burn calories and, from a metabolic standpoint, produce oxygen. consumption and body heat production. They boost gluconeogenesis, boost glucose consumption, and boost lipid metabolism, in addition to increasing protein catabolism. Other organ-specific effects of thyroid hormones include an increase in heartbeat, contractility of the myocardium, blood flow, and cardiac output, as well as a decrease in periphery vascular volume. To promote bone development and growth, they increase the creation of cytokines, growth factors, and other substances[20]. Iodine is used in the making of T3 and T4. Iodine deficiency impacts T3 and T4 production. Thyroxine (T4), which has a half-life of around one week, is the main type of thyroid hormone found in blood as opposed to T3, which has a shorter half-life. T4 to T3 blood emission in humans is 14:1 [21].

The symptoms of a thyroid problem might occasionally be hard to spot. This is because a number of other reasons might generate symptoms that are similar, and typically, treatment is administered in accordance with the symptoms. For example, extreme fatigue may be linked to sleep apnea, narcolepsy, etc., but the symptoms may truly be thyroid-related at their root. Nervousness, poor attention, and memory loss are some of the prevalent thyroid symptoms. Changes in the menstrual cycle increased the heart rate, caused muscle pain, and resulted in weight gain and high cholesterol levels.The main component of thyroid hormones is iodine, and in the developing world, iodine shortages are a key contributor to hypothyroidismIodide, a type of iodine that circulates in plasma and has a half-life of 24 hours, is absorbed from the GI tract and is a source of iodine. Iodide is primarily eliminated by the kidney 24 to 48 hours after ingestion [22]. Iodine can be estimated using a variety of techniques, including mass spectrometry, neutron activation analysis, iodine-specific electrodes, calorimeters employing spectrophotometry, and other techniques [23]. Thyroid hormones play a critical role in virtually every bodily tissue's metabolism as well as the development of the foetus' and child's CNS. The metabolic processes required for healthy growth and development are regulated by thyroid hormones. For healthy bone growth and development, TH is essential. Small stature and a delayed rate of epiphyseal closure are also effects of hypothyroidism. Both bone production and bone resorption are influenced by THs [24,25].

Almost all of the cells in the body are impacted by thyroid hormones. It influences protein synthesis, aids in regulating the length of the long bones (in conjunction with growth hormone), encourages permissiveness, which regulates the maturity of the brain, it makes the body more susceptible to catecholamines (like adrenaline) [26].

All of the body's cells must properly develop and differentiate, and this is made possible by thyroid hormones. These hormones also control how human cells utilise energy molecules by regulating the metabolism of protein, fat, and carbohydrates. Additionally, they promote vitamin metabolism. A variety of physiological and pathological triggers affect the synthesis of thyroid hormone. Human produce heat as a result of thyroid hormone. However, the thyronamines work through an unidentified method to decrease neural activity, which is crucial for the moulting behaviour of birds and the hibernation cycles of mammals. The anterior pituitary gland's thyrotropes produce TSH, which controls the thyroid follicular cells' capacity to produce the thyroid hormones (T4 and T3). A mediator of T4's effects in vivo is T3, which T4 in the target tissues is transformed. The activity of T3 is

three to five times that of T4. The thyroid gland's follicular cells produce thyroxine (3,5,3′,5′-tetraiodothyronine). Thyroglobulin precursor (which is separate from thyroxine-binding globulin, or TBG) is the starting point, and enzymes degrade it to form active T 4[27].

The thyroid gland alone can use Thyroglobulin (Tg), a 660 kDa dimeric protein, is produced by the follicular cells of the thyroid.Triiodothyronine (T3) has three iodine atoms per molecule as opposed to thyroxine (T4)'s four iodine atoms per molecule. The remaining tyrosine in this protein is converted to thyroxine by adding iodine atoms to its ring arrangements. [28].

Disorders can result from thyroxine excess or shortage. Iodine, apoptosis, and thyroxine triiodothyronine effects Measurement-related illnesses The clinical illness known as hyperthyroidism, which includes Graves' disease as an example, is brought caused by a high concentration of free T4, free T3, or both, in the blood. It is a widespread condition that affects 0.2% of males and 2% of females. Although thyrotoxicosis and hyperthyroidism are frequently used interchangeably, there are some minor distinctions. While hyperthyroidism only refers to an overactive thyroid, thyrotoxicosis This refers to an increase in the blood levels of thyroid hormones, which can be brought on by either a hyperactive thyroid or by taking thyroxine tablets. When there is an insufficiency of thyroxine, triiodothyronine, or both, the condition is known as hypothyroidism (Hashimoto's thyroiditis is one example). Hypothyroidism can occasionally result in clinical depression. [29]

According to certain studies [30], T 3 is present at the synaptic connections and controls the brain's production of serotonin, norepinephrine, and -amino butyric acid (GABA). T 3 and T 4 issues have been linked to hair loss on occasion. The normal cycle of hair growth could be impacted, interrupting hair growth. Heart problems can be brought on by either an overactive or underactive thyroid gland, or they might worsen pre-existing diseases. Thyroid hormone excess and insufficiency have been linked for than 200 years to disorders such as cardiac failure, atherosclerotic vascular disorders, and arrhythmias [31].

2. Conclusion

Thyroid hormones (THs) are crucial metabolic regulators. They significantly affect metabolic rate and oxygen intake and are necessary for practically all tissues to function at their best. Thyroxine (T4) and 3,5,3'-triiodothyronine are two physiologically active thyroid hormones secreted by the thyroid gland (T3). The hypothalamus, pituitary, and thyroid gland make up the intricate HPT axis, which controls TH production and secretion. Since iodine is a key component of thyroid hormones, developing nations' iodine shortages are a significant contributor to hypothyroidism. Both genomic and non-genomic mechanisms are used by thyroid hormones to affect their target cells.

Both bone resorption and creation are regulated by THs. Brown and white adipose tissue depend on them for development and function, and T3 is essential for regulating lipogenesis and lipolysis. They are crucial for the production and metabolism of cholesterol, and it is well recognised that a lack of them can lead to hypercholesterolemia. Thyrotropin, prolactin, and TSH production are all regulated by THs in the pituitary. THs are necessary for the differentiation of particular cell types as well as the accumulation of foetal mass in the growing foetus. They play significant functions in the maturation and differentiation of key organs like the heart and lungs. Thyroid hormone actions are crucial to human survival and health due to their pleotropic effects. Thyroid hormones play crucial roles in controlling cholinergic pathways in the brain as well as neuronal differentiation, maturation, and migration. They guard against lactic acidosis, have cardiac and peripheral artery inotropic and vasodilatory actions, and are essential for aerobic mitochondrial activity.

References

Núñez A, Bedregal P, Becerra C, Grob L F. [Neurodevelopmental assessment of patients with congenital hypothyroidism]. Rev Med Chil. 2017 Dec;145(12):1579-1587. [PubMed]

Sorisky A. Subclinical Hypothyroidism - What is Responsible for its Association with Cardiovascular Disease? Eur Endocrinol. 2016 Aug;12(2):96-98. [PMC free article] [PubMed]

Singh S, Sandhu S. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 19, 2022. Thyroid Disease And Pregnancy. [PubMed]

Bertholf R. Laboratory Evaluation of Thyroid Function. In: Clarke W. ed. Contemporary Practice in Clinical Chemistry. 2nd ed. Washington, DC:AACCPress;2011

Fekete C, Lechan RM. Central regulation of hypothalamic-pituitary-thyroid axis under physiological and pathophysiological conditions. Endocr Rev. 2014;35:159-94.

NAGATAKI, S., UCHIMURA, H., MASUYAMA, Y., NAKAO, K. & ITO, K. (1972) Triiodothyronine and thyroxine in thyroid glands of euthyroid Japanese subjects. Journal of Clinical Endocrinology, 35,18-23.

CHOPRA, I.J., FISHER. D.A., SOLOMON, D.H. & BEALL, G.N. (1973a) Thyroxineand triiodothyronine in the human thyroid. Journal of Clinical Endocrinology, 36, 31 1-316.

SURKS, M.I., SCHADLOW, A.R., STOCK, J.M. & OPPENHEIMER, J.H. (1973) Determination of iodothyronine absorption and conversion of L-thyroxine (T,) to L-trlodothyronine (T,) using turnover techniques. Journal of Clinical investigation, 52,805-81 1

BROWN, J., CHOPRA, I.J., CORNELL, J.S., HERSHMAN, J.M., SOLOMON, D.H., ULLER, R.P. & VAN HERLE, A.J. (1974) Thyroid physiology in health and disease. Annals of Internal Medicine, 81,68-81.

DAVIS, P.J., HANDWERGER, B.S. & GLASER, F. (1974) Physical properties of a dog liver and kidney cytosol protein that binds thyroid hormone. Journal of Biological Chemistry, 249,6208-6217.

Gereben B, Zavacki AM, Ribich S, Kim BW, Huang SA, Simonides WS, Zeold A, Bianco AC . Cellular and molecular basis of deiodinase-regulated thyroid hormone signaling. Endocr Rev. 2008;29:898–938.
Gouveia CH, Christoffolete MA, Zaitune CR, Dora JM, Harney JW, Maia AL, Bianco AC . Type 2 iodothyronine selenodeiodinase is expressed throughout the mouse skeleton and in the MC3T3-E1 mouse osteoblastic cell line during differentiation. Endocrinology. 2005;146:195–200.
Williams AJ, Robson H, Kester MH, van Leeuwen JP, Shalet SM, Visser TJ, Williams GR . Iodothyronine deiodinase enzyme activities in bone. Bone. 2008;43:126–134.
Andersen S, Pedersen KM, Bruun NH, Laurberg P. Narrow individual variations in serum T(4) and T(3) in normal subjects: a clue to the understanding of subclinical thyroid disease. J Clin Endocrinol Metab. 2002;87(3):1068–1072.
Medici M, et al. A large-scale association analysis of 68 thyroid hormone pathway genes with serum TSH and FT4 levels. Eur J Endocrinol. 2011;164(5):781–788.
Hoftijzer HC, et al. The type 2 deiodinase ORFa-Gly3Asp polymorphism (rs12885300) influences the set point of the hypothalamus-pituitary-thyroid axis in patients treated for differentiated thyroid carcinoma. J Clin Endocrinol Metab. 2011;96(9):E1527–E1533.
Peltsverger MY, et al. The -258A/G (SNP rs12885300) polymorphism of the human type 2 deiodinase gene is associated with a shift in the pattern of secretion of thyroid hormones following a TRH-induced acute rise in TSH. Eur J Endocrinol. 2012;166(5):839–845.
Panicker V, et al. A common variation in deiodinase 1 gene DIO1 is associated with the relative levels of free thyroxine and triiodothyronine. J Clin Endocrinol Metab. 2008;93(8):3075–3081.
Liu Y, Brent G. Thyroid hormone crosstalk with nuclear receptor signaling in metabolic regulation. Trends Endocrinol Metab 2012;21:166-73.
Kleerekoper M. Hormones. In: Burtis C., Ashwood E., Bruns D. eds. Tietz Fundamentals of Clinical Chemistry. 6th ed. Philadelphia:W.B. Saunders Company;2008.
Hill RN, Crisp TM, Hurley PM, Rosenthal SL, Singh DV (August 1998). "Risk assessment of thyroid follicular cell tumors". Environ. Health Perspect. 106 (8): 447–57
Spitzweg C, Heufelder AE, Morris JC. Thyroid iodine transport. Thyroid. 2000 ;10:321-30. Review.
Taurog A. Hormone synthesis. In Werner and Ingbar's The Thyroid, Braverman L, Utiger R (eds), Lippincott-Raven, Philadelphia, PA 1996. pp 47–81.
Allain TJ, McGregor AM. Thyroid hormones and bone. J Endocrinol.1993; 139:9–18.
Huang BK, Golden LA, Tarjan G et al. Insulin-like growth factor I production is essential for anabolic effects of thyroid hormone in osteoblasts. J Bone Miner Res. 2000; 15:188–197.
World Health Organization(2019). Essential medicines: 21st list 2019
Synthesis of Thyroid Hormones" in: Walter F. Boron; Emile L. Boulpaep (2012).
Medical Physiology (2nd ed.). Elsevier/Saunders. ISBN 9781437717532.
Dabbs DJ (2019). Diagnostic Immunohistochemistry . Elsevier. pp. 345–389.
Kirkegaard C, Faber J (January 1998). "The role of thyroid hormones in depression European Journal of Endocrinolog. 138 (1): 1–9. Dratman MB, Gordon JT (December 1996). "Thyroid hormones as neurotransmitters". Thyroid . 6 (6): 639–647.
Dratman MB, Gordon JT (December 1996). "Thyroid hormones as neurotransmitters".
Thyroid.6(6): 639–647.
Parry CH. Elements of Pathology and Therapeutics, Being the Outlines of a Work. Bath,England: R. Cruttwell, 1815.