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REVIEW ARTICLE

Thyroid hormone use in athletes: Physiological insights and doping controversies

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A B S T R A C T

Among the human body's most vital organs is the thyroid gland. The hormones produced by the thyroid have anabolic properties, at least when present at physiological concentrations. This paper aims to provide an overview of the current understanding of thyroid hormone use in sports doping. The physiology of skeletal muscles is significantly influenced by thyroid hormones. Exposure to T3 and T4 may enhance muscle blood flow, myogenesis, and renewal. Over an extended period, such hormones could contribute to weight loss. These methods suggest that thyroid hormones might be a likely agent in sports doping. Nonetheless, T3 and T4 aren't listed as sports doping drugs in the World Anti-Doping Code (WADA) standards; the argument over the drug's inclusion is still ongoing, and doctors must be mindful of the impact of the thyroid hormones on the metabolism of people from the standpoint of sports management. The underlying causes of the desired and negative consequences of TH exploitation, the prevalence of TH use among young adults, the legitimate medical applications of TH, the reasons why certain athletes look to utilize TH, the difficulties with identifying TH abuse, and other factors all contribute to the conclusion that, based on the available information, banning TH in highly competitive sports is not possible nor appropriate.

Keywords: *Bodybuilding Athletes; Sport; Thyroid Hormones; T3; T4; TSH*

Introduction

It is commonly recognized that the thyroid hormone regulates growth, metabolism, and a host of other biological processes. The hypothalamic-pituitary-thyroid axis is a self-regulating circuit that is made up of the thyroid gland, the anterior pituitary gland, and the hypothalamus. Thyroxine, also known as tetraiodothyronine (T4), and triiodothyronine (T3) are the two primary hormones that the thyroid gland produces. To preserve appropriate feedback processes and homeostasis, thyroid-stimulating hormone (TSH) from the anterior pituitary gland, thyroid-releasing hormone (TRH) from the brain, and T4 function in synchronized harmony.[1] The symptoms of hypothyroidism, which is brought on by an underactive thyroid gland, usually include bradycardia, bowel movements, exhaustion, and a rise in weight. On the other hand, decreased weight, heat hatred, diarrhea, fine shaking, and muscular weakness are the symptoms of hyperthyroidism, which is brought on by enhanced thyroid gland activity.[2] The small bowel absorbs iodine, a crucial trace ingredient. It is essential to both T3 and T4. Iodized salt from tables, shellfish, algae, and fruits and vegetables are among the foods that contain iodine.

Reduced thyroid hormone production and iodine insufficiency can result from reduced iodine consumption. Cretinism, goiter, myxedema coma, and hypothyroidism can all result from an iodine deficit.[3] The hypothalamus is where thyroid hormone control begins. TRH is released from the hypothalamus to the anterior pituitary gland through the hypothalamic-hypophyseal portal pathway. TSH is released by the anterior pituitary's thyrotropin cells when TRH activates them. The cellular bodies of the hypothalamic periventricular nucleus (PVN) produce the peptide hormone known as TRH. Before TRH reaches the anterior pituitary, it may concentrate in the hypophyseal portal distribution, where such cell bodies discharge their neurosecretory nerves.[4]

The pituitary gland and the hypothalamus, two brain regions, regulate the thyroid gland. TRH is released by the brain and causes the pituitary gland to secrete TSH. When the levels of thyroid hormone are inadequate, the brain and pituitary gland normally recognize this and release more TRH and TSH, which in turn encourage the production of additional thyroid hormones and conversely. The body produces more hormones when they are required. The hypothalamic-pituitary-thyroid axis (HPT), which produces thyroid hormone in its entirety, is also known as the body's regulatory system for metabolism.[5,6] The T4 is transformed into the physiologically more powerful T3 via conversion. Three iodothyronine deiodinases are responsible for this process. These enzymes are called deiodinase type 1 (D1), type 2 (D2), and type 3 (D3). T4 is converted to T3 by the removal of a 5' -iodine atom, which is catalyzed by type 1 and type 2 enzymes. To create reverse T3, the type 3 enzyme irreversible destroys a 5-iodine atom.[7] Thyroid hormone is produced by the thyroid gland and is made up of follicles where tyrosine residues in the glycoprotein thyroglobulin are iodinated to form thyroid hormone.[8]

The frontal pituitary's released hormone known as TSH directly affects the thyroid follicular cell's TSH receptor (TSH-R). The processes required for thyroid hormone production to occur are initiated by TSH, which also controls the sodium iodide symporter. When T3 and T4 leave the thyroid gland and reach the circulatory system, they attach to a protein known as Thyroid Binding Protein (TBP) and move through the bloodstream. They get at the particular cells through the bloodstream.[9] The hypothalamus and pituitary gland are regulated by the thyroid gland to create T4 in the body. To become functioning, either type 1 (D1) or type 2 (D2) deiodinase enzyme needs to change T4 to T3. The primary component needed for the synthesis of thyroxine is iodine. Iodide from the consumed iodine is required to synthesize a normal level of thyroxine.[10]

T3 is the functional thyroid hormone that is produced by the thyroid gland. The majority of bodily physiological functions, including development, metabolism, and heartbeat are influenced by it. T4 has a longer duration of impact than hypothalamic T3 and T4 is four times more effective than T3. Because T3 has a lower affinity for plasma proteins than T4, it escapes rapidly and has an impact more promptly than T4.

80 to 90% of circulating T3 is derived from peripheral tissue that converts T4 to T3 by outer ring deiodination. T4 is released from the thyroid in greater quantities than T3 (90 vs. 30 µg/day).[11] The functions of TH are essential for metabolic processes, growth, and reproduction. T4 is often administered for individuals with deficient TH production at a level of 1.6 µg/kg/day to ensure complete replacement. The question of whether adding T3 to standard T4 regimens is useful is no longer as contentious as it once was. Some work has examined the physiological limits of T4 monotherapy and how they could account for a worse quality of life while on T4 replacement treatment.[12] T4 monotherapy and T4/T3 combination treatment had similar therapeutic effects, according to more recent studies.[13] On the other hand, T3 is highly recommended in "alternative" medicine practices and particularly favored in illegal usage, such as bodybuilding and doping that are promoted online. Accordingly, it is possible to utilize the prevalence of T3 usage among top athletes as a proxy for the occurrence of TH misuse.[14]

T4 is mostly recommended to treat original hypothyroidism and, less commonly, secondary hypothyroidism. It is additionally prescribed for avoiding the return of cancer of the thyroid. Globally, iodine deficiency is a highly common cause of hypothyroidism and is seen in nations with extensive inland mountains. To regain the euthyroid state, T4 medication is necessary for primary hypothyroidism in iodine-replete locations, which is mostly caused by autoimmune thyroid dysfunction (Hashimoto thyroiditis). To minimize circulating thyrotropin levels and lower the risk of cancer recurring a full T4 substitute is frequently needed after surgery or radioiodine ablation for thyroid carcinoma. This replacement therapy is often prescribed at a gently overpowering dosage for a brief to medium period.[15]

With less than 1% of primary hypothyroidism's incidence, secondary (or central) hypothyroidism is uncommon. It results from treatments for tumors in the pituitary gland or hypothalamic diseases that lower pituitary synthesis of enough TSH to sustain thyroidal TH synthesis. Individuals with unmanaged secondary hypothyroidism have low or undetected blood TSH levels together with low amounts of T4 and T3. To treat these individuals, adequate replacement of T4 is needed to raise and sustain circulating T4 levels.[16]

T4 is one of the most often given medications in the USA and the UK, surpassing the incidence of overt hypothyroidism, due to long-standing concerns about TH misuse, particularly regarding the management of subclinical hypothyroidism.[17] Based on data from the National Health and Nutrition Examination Survey (NHANES) research, the projected incidence of TH consumption in the general population of adults in the USA is 4.6%.[18] The overall incidence of this condition is 3.2% in men and 9.3% in women. Of these, less than 10% have overt biochemical hypothyroidism, with the remaining percentage being subclinical. Likewise, the overall estimate of the average rate of TH usage in Europe is 5.9% among women and 3.5% among men; however, as previously mentioned, only 0.8% and 0.3%, respectively are attributable to overt hypothyroidism. The requirements for treating borderline hypothyroidism (elevated serum TSH) with uncertain therapeutic effects are "creeping" downward over time, and this tendency may also affect top athletes.[19,20] According to an international epidemiology investigation, there is a variance in the incidence of visible hypothyroidism among iodine-replete nations. In Europe, the incidence ranges from 0.2 to 5.3%, whereas in the USA, it is between 0.3% and 3.7%. T4 therapy is utilized more frequently worldwide than therapy for severe hypothyroidism. If TH were banned in sports, these differences in the justifications that are prescribed would present severe and time-consuming challenges when it comes to Therapeutic usage Exemptions for proper medical TH usage.[21]

Thyroid Hormone Abuse Among Elite Athletes

The World Anti-Doping Agency (WADA) has not banned performance-enhancing drugs (THs) from usage in sports, despite allegations of misuse in this regard.[21] If two of the three equally weighted criteria that are, whether the drug or procedure is speed-expanding,[2] damaging to athletes, or against the spirit of sport are fulfilled, then it may be barred from use in sports under the World Anti-Doping Code.[18] Antidoping bodies have the authority to issue treatment exceptions for legitimate medicinal uses of prohibited drugs Since skilled athletes seek to prevent career-ending penalties if antidoping violations of regulations are established, they engage in highly private, hidden practices that make it extremely difficult to quantify the general prevalence of doping in top sports.[22] Through an average estimate of less than 10%, overall predictions are still less than 5%. Reduced estimates are derived from biological examinations of athlete specimens, while greater projections are derived from athlete questionnaire surveys that heavily rely on truthful responses and awareness of anti-doping regulations.[22]

The information that is currently available indicates that using high (i.e., supraphysiological) dosages of thyroxine in euthyroid people would result in thyrotoxicosis, with crushed serum thyrotropin illustrating sensitive TH sensing with unfavorable hypothalamic-pituitary feedback. This condition is believed to be harmful to athletic performance because it results in an absence of heart and skeletal muscle mass, which reduces one's ability to exercise with either naturally occurring or experimentally generated thyrotoxicosis, despite anecdotal suggestions of improvement that are not objectively verified.[23] Moreover, TH misuse can result in serious, serious thyrotoxicosis. However, sports medicine physicians and managers continue to be worried about the incidence, security, and doping aspects of TH use due to anecdotal allegations of athletes using nonprescription THs, particularly those participating in weight-classified exercises (weightlifting, combat sports), with the goal of "making-weight" at official precompetition weigh-ins. However, there hasn't been a thorough investigation of the frequency of TH misuse among athletes passing anti-doping tests for competitiveness in sports that comply with WADA.[24]

Why Do Athletes Use Thyroid Hormone Without Medical Indications?

It helps to clarify why sportsmen take TH apart from medical purposes to comprehend the contradiction of attitudes about and reasons why they utilize the drug. Sportspeople and bodybuilders that use TH lacking permission from their doctor typically combine it with other non-banned substances rather than TH by itself. To find out why people take THs, internet websites like steroidology.com and social media sites like Reddit, Instagram, and Facebook were polled.[25] Below is a discussion of several justifications for utilizing TH that is not prescribed. The main justification for using TH is, by far, to modulate weight reduction such that fat loss takes precedence over a decrease in muscle mass. The need to "make weight" to compete in weight-classified sports (e.g., fighting sports, lifting weights, propelling) and other activities in which the power-to-weight ratio determines energetic efficiency (e.g., cycling, strength sports) is particularly apparent for image-based activities, including bodybuilding. T3, also known by the commercial name Cytomel (other names for T3 include Triostat, Triomet, and Thybon), is thought to be more costly and more difficult to get than T4, but it acts more quickly. The writers had little trouble finding Cytomel promoted and/or advertised on a variety of supplementation websites.[25]

Therapeutic dosages of TH are not effective in helping people lose weight, much less in helping them lose fat instead of muscles. Early research on obese euthyroid people on low-calorie diets revealed no loss of weight benefit from T3.[26] While there has been not enough proof of T3 impacts on total body catabolic and structural breakdown of protein in muscles for assessment of particular shedding of fat, a new meta-analysis of TH usage, either as T4 or T3, found no convincing proof of an overall weight reduction.[27] However, losing weight may result from the harmful overdosage impact of purposefully utilizing high dosages of TH that produce hyperthyroidism. Because there is a dearth of reliable effectiveness and safety evidence, the American Thyroid Association strongly advises against utilizing T3 for the treatment of obese euthyroid individuals.[28]

Drug mixtures that combine testosterone and thyroxine are one way that testosterone is used to "improve" the composition of the body. This seems to indicate an understanding that exogenous testosterone is catabolic at both of these supraphysiological dosages, which may be a rationale for integrating it with an artificial being's androgen (such as oxandrolone) in an attempt to achieve equilibrium through the "anabolic" (i.e., weight-gaining) effects of androgens.[25]

Using TH to covertly increase natural androgen activity is another justification. A possible explanation for this could be that hyperthyroidism raises serum sex hormone–binding globulin (SHBG), the primary circulation attaching proteins for testosterone, leading to a rise in the circulation of SHBG and consequently in testosterone levels.[29] The rise in hepatic SHBG production and the release, which is apparent in TH overload of either endogenous or exogenous source, is caused by TH promotion of hepatocyte nuclear factor-4α gene expression in both men and women, including children.[30] Nonetheless, elevated levels of SHBG in the blood decrease the rates of testosterone (and estradiol) whole-body metabolism clearance levels, extending its circulatory residency duration and diminishing tissue androgen effects.[31] For instance, increased levels of circulatory SHBG decrease rather than increase net androgen impact in the bones, and the high incidence of gynecomastia associated with hyperthyroidism can be explained by the decreased androgen: estrogen balances.[25]

Overcoming Low Circulating T3

Correcting the low levels (or anticipated drop) of serum T3 observed in a power deficit situation of some top athletes enduring rigorous training and/or nutrition is another justification for utilizing non-prescription TH.[32] Relative Energy Deficit in Sports (RED-S) in 2014 to expand the definition of the formerly known athlete's triad, which had previously been defined to encompass functional hypothalamic a period in females. This concept includes men who exhibit low serum testosterone levels and cover a broader range of physical activity and dietary states. These reversible functional modifications in circulating THs correspond with this concept.[33]

This expanded definition of the female athlete's triad, which has been criticized by proponents of the original theory, is becoming more widely accepted when it comes to athletes who have reduced their physical abilities as a result of a lack of energy that is insufficient to sustain normal bodily processes. This can result in secondary a period and osteoporosis.[34] Similar results have been observed in various catabolic states brought on by significant calorie restriction (severe undernutrition, for example) and/or energy depletion (intense exercise, for example), which lead to weight losses as a pathophysiological reaction to energy deficit conditions.

According to[35] energy shortage syndromes, such as RED-S, are associated with persistently low serum T3 and elevated reverse T3. However, there are less consistent, if any, alterations in serum T4 and serum TSH, which are occasionally slightly decreased but not nonexistent. These catabolism state symptoms align with the changeable alterations in tests for thyroid function observed in the broader unwell euthyroid syndrome (also known as non-thyroidal disease). These might be a compensatory hypothalamic reaction to stressful events in surroundings during virtually any severe or protracted non-thyroidal sickness. Tests for thyroid function show distinctive, changeable abnormalities in this illness, including a typical decrease in serum T3 and a rise in reverse T3, but neither serum T4 nor TSH consistently changes. Although there is still some debate, it is generally agreed that neither the biochemical characteristics nor the data support TH replacement treatment as a means of treating a TH deficit condition.[36]

Biochemical Effects of TH:

The baseline metabolic rate, which is decreased in hypothyroidism and raised in hyperthyroidism, indicates that TH is a crucial controller of whole-body the process of thermogenesis and could also impair the performance of athletes.[37,38] TH-induced activation of several futile energy processes in the cardiac and skeletal muscles in addition to white and brown fat appears to be the primary cause of these thermogenic influences. Such stimulation mostly occurs via impacts on mitochondrial energies and uncoupling molecules. For instance, animal research indicates an adaptive reaction in myocytes and skeletal muscle, even though hyperthyroidism is linked to decreased exercise tolerance.[39]

When pigs are given T3, their hearts' cross-sectional dimensions and beta-adrenergic receptor number rise temporarily, causing tachycardia and a rise in oxygen demand. T3 injection with a higher heart rate is similarly linked with an upsurge in lactic acid generation; however, it is unclear how this enhances or reduces efficiency.[38] Acute enhancement of TH was not detrimental to skeletal muscle blood supply or muscle oxygen delivery during dynamic exercises in human participants, but it did enhance blood circulation to skeletal muscles in rats given extra T3 during exercising by up to three times.[40]

Adverse Effects of Thyroid Hormone Overuse:

The narrow therapeutic index of THs, a phrase that is often used in pharmaceutical research to refer to the boundary between therapeutic and harmful effects of dose (or, more precisely, systemic hormone exposure), is a significant aspect of TH abuse.[41] Due to the limited therapeutic index of T4 along with more T3, even slight dose adjustments may have harmful consequences. This is in stark contrast to the excellent therapeutic index of testosterone. Its extremely broad dosage response in beneficial consequences, mainly on muscle, which ranges in dosage from below to over the physiological limit by a factor of 24, is the cause of that. Amongst all the mammalian hormones, testosterone is the only one that does not normally cause a hormone overabundance condition in males.

As a result, even high supraphysiological dosages of testosterone are generally tolerated in short-term use, with little to no persistent negative physical or symptomatic consequences.[42] The most well-known negative consequences of high TH exposures are caused by hyperthyroidism, which can be brought on by excessive TH dosages or spontaneous thyrotoxicosis. TSH restriction from hyperthyroidism compromises bone wellness and cardiovascular function. To avoid thyroid cancer from recurring, the American Thyroid Association has updated its recommendations for long-term TSH stabilization with the use of somewhat supraphysiological amounts of T4. Instead, in low- to intermediate-risk patients, researchers now support a dynamic risk classification with early relaxing of post-thyroidectomy TSH inhibition.[43]

Detection of Thyroid Hormone Overuse:

TH abuse, irrespective of exogenous T4 or T3, might theoretically be easily identified with a fully hidden, nonexistent blood TSH. Furthermore, levels of T4 could fall under the usual range if T3 is being given. Therefore, it would be quite likely that someone is taking exogenous T3 based on the biochemical profile of undetected blood TSH, minimal serum T4, and elevated serum T3. Consuming exogenous T4 would result in a similar picture, with the possible exception that the transformation of exogenous T4 to T3 might result in a lesser drop in serum T3. This implies that if used in an extended endocrine component of the Athlete Biological Passport (ABP) with a Bayesian approach to serial modification of individual blood TSH values, sequential monitoring of blood TSH levels may be able to identify TH misuse. Unable to differentiate TH doping from natural thyrotoxicosis caused by autoimmune Hashimoto disease, toxic thyroid adenoma, thyroiditis, or even during early pregnancy since flowing human chorionic gonadotropin (hCG) increases, any positive outcome of undetected serum TSH would merely demonstrate hyperthyroidism.[44]

In the event of an abnormal finding, the athlete would undergo a specialized endocrine examination, which would include further blood tests and a thyroid absorption scan to differentiate between repressed and strong thyroidal secretions and rule out endogenous hyperthyroidism. This would be considered comparable to how the outcomes of a positive urine hCG test in men are managed, wherein a medical assessment is necessary to rule out a tumor releasing hCG before classifying an outcome as a detrimental analytical discovery, which is assumed to be a potential violation of the antidoping rule triggering anti-doping sanctions.[25]

Possibility variables on serum TSH measurements other than TH overload need to be taken into account when evaluating the possibility of sequential serum TSH surveillance to identify TH misuse in top athletes. Serum TSH levels inside a human being are less variable and consistent over time than those between humans, indicating an elevated number of genetic determinants of individual set points and favorable conditions for successful integration into an ABP-style Bayesian screening framework.[45] Determining population thresholds can be difficult in an otherwise healthy population since factors such as age, sex, pregnancy, body weight, iodine consumption, and ethnicity all have little impact on serum TSH levels. Once more, that follows more in line with an ABP-style assessment that uses criteria that are individual-specific as opposed to population-based. Because of the lengthy half-life of T4 and the strict guidelines for safe use for therapy (storing T4 in the refrigerator, implementing it on a vacant stomach, and preventing simultaneously consumption of calcium, iron, and any other medications that inhibit T4 absorption), maintaining T4 treatment in individuals with hypothyroidism may take some time, and some patients may experience temporary low serum TSH through the optimization of doses.[46] Serum levels of TSH that are undetected are, however, seldom caused by these causes of variability. Utilizing a third-generation TSH immunoassay that is currently in use, indistinguishable serum TSH combined with normal or elevated serum T4 and/or T3 suggests an elevated level of thyroid hormone that is either the result of exogenous thyroid hormone intake or thyroid abnormalities (such as subclinical in nature or explicitly thyrotoxicosis from hazardous adenoma, thyroiditis, or autoimmune thyroid a medical condition).[47]

Conclusion

The bodily functioning of skeletal muscles is significantly influenced by thyroid hormones. Exposure to T3 and T4 may enhance muscle blood flow, myogenesis, and renewal. Over an extended period, such hormones could contribute to weight loss. These methods suggest that thyroid hormones might be a likely agent in sports doping. Though the World Anti-Doping Code (WADA) standards do not currently identify T3 or T4 as sport doping the argument over their inclusion is ongoing physicians should be aware of the impact of the hormones in the thyroid on metabolism in humans from the standpoint of athletic medicine.

Overall, it is not currently warranted for the Code to forbid TH in elite sports. More compelling data about the frequency of TH use among elite athletes and, more importantly, whether TH usage has any benefits for performance might eventually tip the scales, even if this is still a difficult field. Top athletes' hypothalamus pituitary thyroid (HPT) axis is impacted by extensive bodybuilder activity. Administration of anabolic drugs simultaneously causes significant alterations in the hypothalamic-pituitary-gonadal (HPGA) Aaxis, which controls testosterone levels.

References

1. Chen J, You H, Li K. A review of thyroid gland segmentation and thyroid nodule segmentation methods for medical ultrasound images. Comput Methods Programs Biomed. 2020; 185:105329. DOI: https://doi.org/10.1016/j.cmpb.2020.105329.
2. Dilmurodovna TD. Morphological aspects of the thyroid gland in various forms of its pathology. Am J Ped Med Health Sci. 2023; 1(8):428-31.
3. Sharma S, Hashmi MF, Chakraborty RK. Treasure Island: StatPearls Publishing; 2021.
4. Babić Leko M, Gunjača I, Pleić N, Zemunik T. Environmental factors affecting thyroid-stimulating hormone and thyroid hormone levels. Int J Mol Sci. 2021; 22(12):6521. DOI: https://doi.org/10.3390/ijms22126521.
5. Köhrle J. Selenium, iodine and iron–essential trace elements for thyroid hormone synthesis and metabolism. Int J Mol Sci. 2023; 24(4):3393. DOI: https://doi.org/10.3390/ijms24043393.
6. Rajalakshmi AN, Begam F. Thyroid hormones in the human body: A review. J Drug Deliv Ther. 2021; 11(5):178-82. DOI: https://doi.org/10.22270/jddt.v11i5.5039
7. Cioffi F, Giacco A, Goglia F, Silvestri E. Bioenergetic aspects of mitochondrial actions of thyroid hormones. Cells. 2022; 11(6):997. DOI: https://doi.org/10.3390/cells11060997.
8. Liu YY, Milanesi A, Brent GA. Thyroid hormones. InHormonal Signaling in Biology and Medicine. Academic Press; 2020. 487-506.

9. Hershman JM, Beck-Peccoz P. Discoveries Around the Hypothalamic–Pituitary–Thyroid Axis. Thyroid. 2023; 33(7):785-90.
DOI: https://doi.org/10.1089/thy.2022.0258.
10. Nikanorova, AA., Barashkov, NA, Pshennikova, VG, Teryutin, FM, Nakhodkin, SS., Solovyev, AV, et al. A Systematic Review and Meta-Analysis of Free Triiodothyronine (FT3) Levels in Humans Depending on Seasonal Air Temperature Changes: Is the Variation in FT3 Levels Related to Nonshivering Thermogenesis? Int J Mol Sci, 24(18)14052.
DOI: https://doi.org/10.3390/ijms241814052.
11. Salvatore D, Davies TF, Schlumberger MJ, Hay ID, Larsen PR. Thyroid physiology and diagnostic evaluation of patients with thyroid disorders. InWilliams textbook of endocrinology. Elsevier; 2016; 333-368.
12. Liu J, Zhao K, Qian T, Li X, Yi W, Pan R, et al. Association between ambient air pollution and thyroid hormones levels: A systematic review and meta-analysis. Sci Total Environ. 2023; 166780.
DOI: https://doi.org/10.1016/j.scitotenv.2023.166780.
13. Toloza FJ, El Kawkgi OM, Spencer HJ, Mathews SE, Garcia A, Gamboa A, et al. Determinants for thyroid hormone replacement therapy in subclinical hypothyroidism: a multicenter electronic health records-based study. Thyroid. 2023; 33(9):1045-54.
DOI: https://doi.org/10.1089/thy.2023.0062.
14. Ettleson MD, Ibarra S, Wan W, Peterson S, Laiteerapong N, Bianco AC. Demographic, healthcare access, and dietary factors associated with thyroid hormone treatments for hypothyroidism. J Clin Endocrinol Metab. 2023; 108(12):e1614-23.
DOI: https://doi.org/10.1210/clinem/dgad331.
15. Jin J, Li J, Liu Y, Shi Q, Zhang B, Ji Y, et al. Thyroid hormone changes correlate to combined breast cancer with primary thyroid cancer. Breast Cancer: Targ Therap. 2024; 31:15-22.
DOI: https://doi.org/10.2147/BCTT.S442707.
16. Stedman M, Taylor P, Premawardhana L, Okosieme O, Dayan C, et al. Trends in costs and prescribing for liothyronine and levothyroxine in England and wales 2011–2020. Clin Endocrinol. 2021; 94(6):980-9.
DOI: https://doi.org/10.1111/cen.14414.
17. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, et al. Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab. 2002; 87(2):489-99.
DOI: https://doi.org/10.1210/jcem.87.2.8182.
18. Handelsman DJ, Gild M, Clifton-Bligh R, Speers N, Kouzios D, McMartin MC, et al. Thyroid hormone abuse among elite athletes. J Endocr Soc. 2023; 7(5):bvad027.
DOI: https://doi.org/10.1210/jendso/bvad027.
19. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nat Rev Endocrinol. 2018; 14(5):301-16.
DOI: https://doi.org/10.1038/nrendo.2018.18.
20. Bereda G. Definition, causes, pathophysiology, and management of hypothyroidism. Mathews J Pharma Sci. 2023; 7(1):1-5.
DOI: https://doi.org/10.30654/MJPS.10014
21. Bernet VJ. Thyroid hormone misuse and abuse. Endocrine. 2019; 66(1):79-86.
DOI: https://doi.org/10.1007/s12020-019-02045-1.
22. Gleaves J, Petróczi A, Folkerts D, De Hon O, Macedo E, Saugy M, et al. Doping prevalence in competitive sport: evidence synthesis with "best practice" recommendations and reporting guidelines from the WADA Working Group on Doping Prevalence. Sports Med. 2021; 51(9):1909-34.
DOI: https://doi.org/10.1007/s40279-021-01477-y.
23. Stangierski A, Ruchała M, Krauze T, Moczko J, Guzik P. Treatment of severe thyroid function disorders and changes in body composition. Endokrynol Pol. 2016; 67(4):359-66.
DOI: https://doi.org/10.5603/EP.a2016.0025.
24. Handelsman DJ, Hirschberg AL, Bermon S. Circulating testosterone as the hormonal basis of sex differences in athletic performance. Endoc Rev. 2018; 39(5):803-29.
DOI: https://doi.org/10.1210/er.2018-00020.
25. Gild ML, Stuart M, Clifton-Bligh RJ, Kinahan A, Handelsman DJ. Thyroid hormone abuse in elite sports: the regulatory challenge. J Clin Endocrinol Metab. 2022; 107(9):e3562-73.
DOI: https://doi.org/10.1210/clinem/dgac223.
26. Juiz-Valiña P, Cordido M, Outeiriño-Blanco E, Pértega S, Varela-Rodríguez BM, García-Brao MJ, et al. Central resistance to thyroid hormones in morbidly obese subjects is reversed after bariatric surgery-induced weight loss. J Clin Med. 2020; 9(2):359.
DOI: https://doi.org/10.3390/jcm9020359.
27. Volke L, Krause K. Effect of thyroid hormones on adipose tissue flexibility. Eur Thyroid J. 2021; 10(1):1-9.
DOI: https://doi.org/10.1159/000508483.
28. Sagoe D, McVeigh J, Bjørnebekk A, Essilfie MS, Andreassen CS, Pallesen S. Polypharmacy among anabolic-androgenic steroid users: a descriptive metasynthesis. Subst Abuse Treat Prev Policy. 2015; 10:1-9.
DOI: https://doi.org/10.1186/s13011-015-0006-5.
29. Brown ED, Obeng-Gyasi B, Hall JE, Shekhar S. The thyroid hormone axis and female reproduction. International J Mol Sci. 2023; 24(12):9815.
DOI: https://doi.org/10.3390/ijms24129815
30. Barbagallo F, Cannarella R, Condorelli RA, Cucinella L, La Vignera S, Nappi RE, et al. Thyroid diseases and female sexual dysfunctions. Sex Med Rev. 2024; 10:qeae021.
DOI:https://doi.org/10.1093/sxmrev/qeae021.
31. Kjaergaard AD, Marouli E, Papadopoulou A, Deloukas P, Kuś A, Sterenborg R, et al. Thyroid function, sex hormones and sexual function: a Mendelian randomization study. Eur J Epidemiol. 2021; 36:335-44.
DOI: https://doi.org/10.1007/s10654-021-00721-z.
32. Mountjoy M, Sundgot-Borgen J, Burke L, Ackerman KE, Blauwet C, Constantini N, et al. International Olympic Committee (IOC) consensus statement on relative energy deficiency in sport (RED-S): 2018 update. Int J Sport Nutr Exerc Metab. 2018; 28(4):316-31.
DOI: https://doi.org/10.1123/ijsnem.2018-0136.
33. Grossmann M, Wittert GA. Dysregulation of the hypothalamic–pituitary–testicular axis due to energy deficit. J Clin Endocrinol Metab. 2021; 106(12):e4861-71.
DOI: https://doi.org/10.1210/clinem/dgab517.
34. McCall LM, Ackerman KE. Endocrine and metabolic repercussions of relative energy deficiency in sport. Curr Opin Endocr Metab Res. 2019; 9:56-65.
DOI: https://doi.org/10.1016/j.coemr.2019.07.005
35. Bloise FF, Cordeiro A, Ortiga-Carvalho TM. Role of thyroid hormone in skeletal muscle physiology. J Endocrinol. 2018; 236(1):R57-68.
DOI: https://doi.org/10.1530/JOE-16-0611.
36. Maiden MJ, Torpy DJ. Thyroid hormones in critical illness. Crit Care Clin. 2019; 35(2):375-88.
DOI: https://doi.org/10.1016/j.ccc.2018.11.012.
37. Guerri G, Bressan S, Sartori M, Costantini A, Benedetti S, Agostini F, et al. Hypothyroidism and hyperthyroidism. Acta Bio Medica: Atenei Parmensis. 2019; 90(Suppl 10):83.
DOI: https://doi.org/10.23750/abm.v90i10-S.8765.

38. Yau WW, Yen PM. Thermogenesis in adipose tissue activated by thyroid hormone. Int J Mol Sci. 2020; 21(8):3020.
DOI: https://doi.org/10.3390/ijms21083020.
39. Johann K, Cremer AL, Fischer AW, Heine M, Pensado ER, Resch J, et al. Thyroid-hormone-induced browning of white adipose tissue does not contribute to thermogenesis and glucose consumption. Cell Rep. 2019; 27(11):3385-400.
DOI: https://doi.org/10.1016/j.celrep.2019.05.054.
40. Machado M, Bachini F, Itaborahy A. Thyroid Hormones and Skeletal Muscle Beyond Thermogenesis. J Sci Sport Exerc. 2023; 26:1-9.
DOI: https://doi.org/10.1007/s42978-023-00235-y
41. Negro R, Attanasio R, Nagy EV, Papini E, Perros P, Hegedüs L. Use of thyroid hormones in hypothyroid and euthyroid patients; the 2019 Italian survey. Eur Thyroid J. 2020; 9(1):25-31.
DOI: https://doi.org/10.1159/000502057.
42. Twitchell DK, Pastuszak AW, Khera M. Controversies in testosterone therapy. Sex Med Rev. 2021; 9(1):149-59.
DOI: https://doi.org/10.1016/j.sxmr.2020.09.004.
43. Chen DW, Lang BH, McLeod DS, Newbold K, Haymart MR. Thyroid cancer. The Lancet. 2023; 401(10387):1531-44.
DOI: https://doi.org/10.1016/S0140-6736(23)00020-X
44. Abbey EJ, McGready J, Oh E, Simonsick EM, Mammen JS. Thyroid hormone use and overuse in dementia: Results from the Health, Aging and Body Composition Study. J Am Geriatr Soc. 2022; 70(11):3308.
DOI: https://doi.org/m 10.1111/jgs.17961.
45. Kuś A, Chaker L, Teumer A, Peeters RP, Medici M. The genetic basis of thyroid function: novel findings and new approaches. J Clin Endocrinol Metab. 2020; 105(6):1707-21.
DOI: https://doi.org/10.1210/clinem/dgz225.
46. Virili C, Antonelli A, Santaguida MG, Benvenga S, Centanni M. Gastrointestinal malabsorption of thyroxine. Endoc Rev. 2019; 40(1):118-36.
DOI: https://doi.org/10.1210/er.2018-00168.
47. Palacios-Bayona KL. Optimizing TSH Testing: Minimizing Overdiagnosis and Unnecessary Interventions.2024.
DOI: https://doi.org/10.5772/intechopen.1005108