The endocrine system is an intricate group of organs that work together to achieve their role in the body. The thyroid gland is often overlooked when considering its global prevalence and how common its associated pathologies are. Describe how the thyroid gland works to achieve its function effectively with regards to its hormone production and outline the associated pathologies that accompany an overactive and underactive thyroid.

Abstract

The endocrine system is a crucial organ system that can affect your mood and how you grow. It is made up of a group of organs, known as glands, that release hormones and regulate hormone release to avoid any excess or suppressed production. The thyroid gland controls your metabolism which includes your heart rate, how fast you burn energy, and your heat production. The thyroid has its own blood and nerve supply to optimise its ability to carry out its function. Thyroid hormone release is tightly regulated within a loop designed to inhibit excess production and stimulate suppressed production. Drastic changes to thyroid hormone levels can result in negative changes that can impact the person's health overtime. An overactive or underactive thyroid can be diagnosed by looking at the specific physical characteristics, taking blood tests and specific imaging of the thyroid gland. Treatment options include medications for symptom relief and long-term therapy as well as surgery.

The human body is composed of numerous organ systems that work effectively together to deliver very concise and complex commands to allow survival. One of particular interest is the endocrine system, which release hormones around the body to control mood, development, and growth [1]. Another vital function done by the endocrine system is the tight regulation of its hormone release since any deviation with the optimum hormone range due to external factors can cause changes to your weight, mood, and development [1]. Of all the numerous glands that makeup the endocrine system, the thyroid gland serves a vital role in regulating metabolism, growth, and development. Thyroid disease is a global concern with a prevalence of roughly 200 million people [2]. An estimated 2.8 billion people are at risk of iodine deficiency, an essential mineral required for thyroid hormone synthesis [2]. To allow for a more focused approach, this essay will be excluding thyroid cancers. In light of this, it is important to cover the anatomy, physiology and the presenting diseases. The essay will then finish off with the diagnoses and treatments for the aforementioned conditions.

As shown on fig.1, the thyroid gland is a butterfly shaped organ located just below the thyroid cartilage [4]. It is composed of two lobes connected by the isthmus, with a pyramidal lobe shown on fig.1 extending superior to the left lobe. To achieve its vital function at monitoring the body's metabolic rate, the thyroid gland requires a large blood supply, provided by the superior and inferior thyroid arteries which arise from the external carotids and subclavian arteries respectively [4]. Each lobe is made up of follicles, which are spherical structures filled with a protein dense fluid known as colloid [4]. Sympathetic and parasympathetic nerves provide innervation to the thyroid gland to regulate hormone secretion. The sympathetic innervation is derived from the superior cervical ganglion and will stimulate hormone secretion [4]. In contrast, the parasympathetic innervation is derived from the vagus nerve

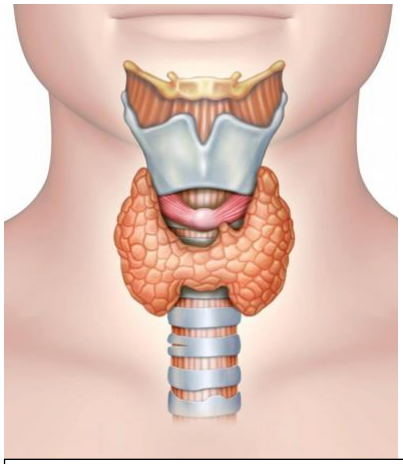

Figure 1: Image portraying the anatomy of the thyroid gland and the surrounding structures within the throat. [3]

and inhibits hormone secretion [4]. Situated posteriorly are 4 small, circular glands known as the parathyroid gland which work to tightly manage calcium and phosphate levels in the body [4]. With the anatomical perspective achieved, it is important to consider the hormones released by the thyroid glands and how they are made.

The synthesis of thyroid hormones is a tightly regulated process controlled by a three-way system composed of the hypothalamus, pituitary gland and thyroid gland (HPT) which can be shown on fig.2. The hypothalamus initiates this process by releasing thyrotropin releasing hormone (TRH) to the anterior pituitary gland, where it will release thyroid stimulating hormone (TSH) in response [5]. TSH will then act on the thyroid gland where it will control the release of the thyroid hormones triiodothyronine (T3) and thyroxine (T4) which are synthesized from iodine and tyrosine [5]. This system is a negative feedback loop where high circulating T3 and T4 levels cause inhibition to TRH and TSH release, as depicted by the red lines on fig.2. Oppositely, low T3 and T4 levels stimulate increased TSH secretion to counteract this change and maintain the thyroid levels within a small range. Once circulating in the body, the thyroid hormones increase the metabolic rate of cells in the body [5]. This can result in a rise in oxygen consumption and heat production. In addition, thyroid hormones support the heart by increasing its rate and force of contraction [5]. Since the thyroid hormone levels are kept within a controlled range, any deviation as previously mentioned can lead to numerous symptomatic presentations. A deficiency of thyroid hormones, called hypothyroidism, can lead to a reduced metabolic rate and heart rate, cold intolerance due to reduced heat production, fatigue, dry skin, and hair loss among a few others [5]. Thyroid hormone excess will result in hyperthyroidism which would cause an increased metabolic rate and heart rate, heat intolerance and perspiration due to increased head production, irritability, warm moist skin, and a tremor as well as several other symptoms [5]. With a better understanding of how the hormones are

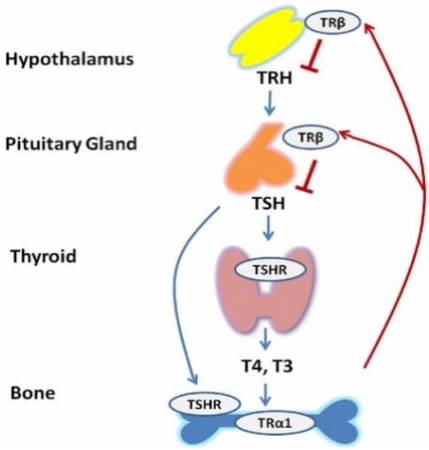

Figure 2: Image portraying HPT axis and its regulation of thyroid hormones [6]

produced we can appreciate the importance of monitoring its levels in the body as a dysregulation to the system for a long period of time results in several unwanted symptoms that arise from pathologies.

Hyperthyroidism, as previously mentioned is a condition associated with elevated thyroid hormones in the bloodstream. It can be caused by several factors such as excess iodine consumption, with Graves disease being the most common cause accounting for roughly 60% of hyperthyroid cases [7]. Graves disease is an autoimmune condition in which antibodies against the TSH receptors are produced, known as thyrotropin receptor antibodies (TRAb) [7]. The receptors are stimulated resulting in excess T4 production. Graves disease is associated with the rise of specific manifestations which include pretibial myxoedema, acropachy and exophthalmos [7]. Pretibial myxoedema involves the anterior side of the lower legs and includes swelling with thick scaly skin, whereas acropachy is soft tissue swelling around the hands accompanied with clubbing of the fingers [7]. Exophthalmos is known as bulging of the eyeballs caused by increased muscle swelling leading to irreversible fibrosis of extraocular muscles [7]. Another known cause of hyperthyroidism found in adults and chronic iodine deficiency is toxic multinodular goitre (TMNG) [8]. TMNG involves the development of nodules over the course of a few years until the nodules gain independent control outside of the normal feedback loop controlled by TSH [8]. Once autonomous, the nodules secrete excess T4 hormones giving rise to the typical symptoms found in hyperthyroidism. In addition to this, TMNG can result in the enlargement of the thyroid gland which may compress the oesophagus causing difficulty swallowing [8]. Thyroiditis is the inflammation of the thyroid glands, and it is classified based on the specific presenting features. Subacute thyroiditis typically occurs due to a viral infection and can involve several phases during its disease progression [8]. It begins with a hyperthyroid picture with painful swellings lasting up to 6 weeks [8]. This is then reduced into a euthyroid state for up to 3 weeks before turning into a hypothyroid state lasting several months [8]. Postpartum thyroiditis can occur within the first year after childbirth, acting as a targeted health concern for new mothers, resulting in a hypo- or hyperthyroid

state within the body [8]. Hashimoto's thyroiditis which will be covered in more detail later, is characterized by an autoimmune process also resulting in thyroid inflammation; however, this results in a hypothyroid clinical manifestation rather than an overactive state [9]. If these conditions were left untreated, thyrotoxicosis becomes a serious life-threatening risk. Thyrotoxicosis is an excess of thyroid hormone resulting in shock, fever, and delirium [8]. Whilst covering the pathologies outlining an overactive state, it is important to recognise what is occurring when the body is suffering from an underactive thyroid state.

When the body experiences an uncompensated deficiency in circulating thyroid hormone, it results in a clinical presentation consistent with hypothyroidism. As mentioned, hypothyroidism results in a myriad of symptoms ranging from tiredness to depression and hair loss [9]. Iodine deficiency remains the most common cause of hypothyroidism in developing countries, with Hashimoto's thyroiditis accompanying it especially in developed countries.[9]. Hashimoto's thyroiditis is an autoimmune condition in which antibodies are produced against thyroid peroxidase (TPO) which is an enzyme responsible for a crucial step in the production of thyroid hormones [9]. It is important to note that up to 15% of hypothyroid patients have none of the antibodies present and others can have different antibodies produced, but anti-TPO is the most common antibody produced [9]. If untreated, it can lead to a myxoedema coma which is a clinical state of shock, hypothermia and confusion as a result of very little T4 circulating the body [9]. It is a medical emergency and requires immediate treatment. Recognising the difference in presentation between an overactive and underactive thyroid is paramount in confirming and diagnosing the presence of the exact condition.

Being able to recognise the signs shown in hypo- and hyperthyroidism can help guide medical professionals in inspecting more closely through blood tests and imaging to accurately diagnose the presenting issues. The presence of swellings, nodules and pain around the anterior neck can often distinguish and exclude certain thyroid conditions from others [8]. For hyperthyroidism, examining the thyroid can reveal a diffuse enlargement in Graves disease, a diffuse non-symmetric nodule enlargement in TMNG, and a tender thyroid in subacute thyroiditis [8]. Once a clinical suspicion is gained for the suspected condition, a thyroid profile blood test is done which looks at the TSH, T3 and T4 levels to help confirm the diagnosis [8]. Fig.3 contains the normal range of the hormones in the thyroid profile for adults. Low TSH with elevated T4 is associated with hyperthyroidism, whereas subclinical hyperthyroidism would be recognised with a low TSH and a normal T4 [8]. A high TSH with reduced T4 is associated with hypothyroidism, whereas subclinical hypothyroidism has a high TSH with a normal T4 level [9]. Looking for autoantibodies can help diagnose Graves disease or Hashimoto's thyroiditis [9]. Patients can undergo a radioactive iodine uptake (RAIU) scan to assess the levels of iodine taken up by the thyroid gland [8]. Graves will have a high diffuse uptake, TMNG will have a high patchy uptake, and thyroiditis would have a low/absent uptake [8]. An ultrasound can also be done to assess thyroid size and the presence of nodules [8]. By outlining the current options to aid medical professionals in diagnosing thyroid condition, we can get closer to finally treating the underlying cause and help patients improve their quality of life.

Hormone	Reference Range
TSH	0.4 – 4.5 μU/ml
Total thyroxine (total T_4)	4.0 – 12.0 μg/dl
Free thyroxine (free T_4)	0.7 – 1.8 ng/dl
Total triiodothyronine (total T_3)	100 – 200 ng/dl
Free triiodothyronine (free T_3)	208 – 596 pg/dl

Figure 3: Table outlining the normal ranges for thyroid hormones in adults [5]

The aim of treating an overactive or underactive thyroid is to recognise the underlying cause and treat it to return the body's normal thyroid balance, and work to maintain that range long term. Treatment options can be separated from symptomatic relief to definitive therapy [8]. Certain symptoms for hyperthyroidism such as anxiety, tremors, and

palpitations can be managed with a beta-adrenergic antagonist like atenolol [8]. Hyperthyroid conditions can be treated pharmacologically with thionamide drugs such as carbimazole and propylthiouracil, which work as TPO competitive inhibitors [8]. Medication is generally continued for up to 18 months before evaluating remission, and if TRAb levels are normal then medication can be discontinued [8]. Radioactive iodine therapy can also be used which destroys thyroid follicular cells thereby reducing thyroid hormone synthesis [8]. Surgery can be done which involves partial or complete removal of the thyroid gland, known as a partial or total thyroidectomy respectively [8]. Once completed, the patient will be started on lifelong weight-based thyroid hormone replacement. Levothyroxine would be used in this case which is the same medication given for hypothyroidism [8]. Once the dosage is calculated then the patient should take it as advised everyday lifelong. Blood tests are done within the first 2 months to ensure the right dosage is selected then every 6-12 months to monitor thyroid levels for general health and to assess if the dosage needs to be corrected [8]. Thyrotoxicosis is treated with warm blankets, symptomatic treatment such as paracetamol, intravenous (IV) propranolol, carbimazole/propylthiouracil, and IV hydrocortisone [8]. Myxoedema coma is another life-threatening complication and is treated with IV fluids, IV thyroxine for T4, and IV hydrocortisone to help rule out other medical possibilities [9].

The thyroid gland presents itself as a major player within the whole-body system. With such a pivotal role in regulating the body's natural rate, the thyroid gland performs an exceptional job in maintaining and monitoring its hormone levels within a precise range. This is achieved through negative feedback loop that works to inhibit excess production and vice versa. When the balance is dysregulated, the body reacts negatively giving rise to characteristic signs and symptoms associated with an increased or decreased metabolic rate. Hyperthyroidism and hypothyroidism have numerous causes, each with their unique presentation. Blood tests looking into thyroid hormones as well as imaging can help confirm the diagnosis of an overactive or underactive thyroid. Depending on several factors, pharmacological or surgical intervention become options considered. Thyroid awareness is

an important aspect overlooked globally, especially considering the ones that remain undiagnosed. With so many affected and even more at risk, it is crucial to continue spreading more information and increasing overall awareness in order to help treat those in need and help provide an explanation regarding the manifestation of their symptoms.

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