Hypothyroidism

Introduction

Hypothyroidism is **decrease in the functionality of the thyroid gland**. It is **decrease in the secretion of T3 and T4**.

Previous Summary

- All theses gland are responsible for thyroid hormones secretion like Thyroid gland, Pituitary gland, and Hypothalamus.
- Pituitary gland and Hypothalamus are responsible for controlling the thyroid gland.
- Pituitary gland secretes TSH hormone that stimulates thyroid hormones secretion of T3 and T4.
- Hypothalamus secretes TRH that in turn stimulates Pituitary gland to secrete TSH then thyroid hormones secretion of T3 and T4.

Causes of Hypothyroidism

- Primary Hypothyroidism

Iodine deficiency	Iodine is found in sea fish and food salt. Iodine deficiency is only found in developing countries, low economic state areas and areas away from seas and fishes especially in African countries. This cause is rarely seen in developed countries and good economic state areas, as salt is very available. Iodine is important as it is incorporated in the structure of T3 and T4.

Hashimoto's thyroiditis

(Anti-TPO,Anti-TG, TSH receptors block AB)

It is very important and is seen very often in clinical life.

That is an autoimmune disease.

The immune system attacks the thyroid gland by Cell mediated immunity at first T- cells then also B-cells. B-cells produce antibodies that attack important and dangerous structures in the Thyroid gland.

Eg. If A thief came into a house, he will target gold, jewelleries, and money. The autoimmune system attack important structures in the thyroid gland.

T- cells mainly attack the thyroid gland as cell mediated immunity. Eventually, B cells make antibodies and attack the thyroid gland as well. B cells antibodies attack important structures like Thyroperoxidase (an important enzyme used to merge iodine and thyroglobulin) (Anti-TPO), thyroglobulin (Anti-TG), and TSH receptors (TSH receptors block AB)(These AB block TSH receptors unlike what happens in Grave's disease).

Hashimoto's is more common in women 5-7 times more than men. It is also more common in older people

Post-thyroidectomy

A patient with thyroid hypertrophy or cancer in the thyroid gland undergoes thyroidectomy weather partial, sub-total, or total. All can cause Hypothyroidism

Atrophic hypothyroidism

(DM, and Addison's)

Atrophy happens with age especially in patients with other diseases like DM, and Addison's.

The thyroid atrophies without the immune system attacking it

Enzymopathy

It is defeat in the enzymes function especially Thyroperoxidase enzyme

Drugs (Lithium, Amiodarone, L- thyroxin) like Calcium, Iron, Omeprazole, Rifampicin	Drugs that interfere with the thyroid functions or lead to their impairment like Lithium and Amiodarone. Drugs that decrease the absorption of Thyroxine (if the patients are on drug like L- thyroxin) like Calcium, Iron, Omeprazole, Rifampicin
Elevated hormones	Extensive hemangioma especially in the liver that converts T4 into rT3 instead of T4 to T3 which lead to decrease in thyroid functions even when the hormones are sensitized normally by the thyroid gland

In all the first 5 causes, the problem lies within the thyroid gland. So, all these previous causes are **primary** to the thyroid gland. In **primary hypothyroidism**, there is **decrease in T3&T4** and an **increase in both TSH and TRH**. As both pituitary gland and the hypothalamus increase their secretion in hope of stimulations of thyroid gland till hormones reach back to their normal level.

- Secondary Pituitary Hypothyroidism

The **pituitary gland is the problem**. If there is a **tumour** or **Sheehan's syndrome**, **trauma** or **infection** that lead to **death of the pituitary gland**, **TSH will decrease** and so will **T3& T4** as consequence. As there will be not stimulation of the thyroid gland from the pituitary. So, decrease in **TSH will lead to decrease in T3 &T4**.

- Tertiary Hypothalamus Hypothyroidism

The **Hypothalamus gland is the problem**. If there is a problem with theHypothalamus that lead to **death of the Hypothalamus**, **TRH will decrease** and so will **TSH& T3& T4** as consequence. As there will be not stimulation of either the pituitary or the thyroid gland from the Hypothalamus. So, **decrease in TRH will lead to decrease in TSH,T3 &T4**.

Clinical features of Hypothyroidism

* It is easier to remember hypothyroidism symptoms if we started from upward (the hair) to downward

Clinical features of Hypothyroidism	
Hair loss, Dry and Thick skin	In cases of hypothyroidism, the metabolism is weak. So, there will be hair loss and dry and thick skin
Neuropsychiatric, Depression, Poor memory, Fatigue	Below the hair, there is the brain, Neuropsychiatric, Depression, Poor memory, and Fatigue happen as the metabolism is weak. T3 and T4 is responsible for the metabolism, so less or no T3 and T4 will lead to decreased metabolism
Cold intolerance	After that, if you put your hand over the patient forehead or skin you feel cold, as the patient can't tolerate cold. We can't say that it is hypothermia as the drop in temperature is not massive, but the patient feels cold. There may be a decrease in temperature. It will be explained later. Goiter could occur in hypothyroidism, but not in many cases. It can happen in Hashimoto's
Bradycardia	The thyroid hormones are important for the heart. There is no metabolism, T3 and T4 are important in stimulating the receptors on the heart (Beta 1 receptors on the heart). That leads to bradycardia (decease in the number of heart beats. The respiration will not be affected, but there may be decrease in the respiratory rate due to decrease in the metabolism
Constipation	More metabolism means faster movement of the intestine. So, with slower metabolism, that lead to slower movement of the intestine. That could lead to constipation
Weight gain	There is less metabolism, so they patient can't burn throw the food consumed. So, fats accumulate in the body leading to weight gain
Macroglossia	Macroglossia means enlargement of the tongue. Accumulation of some portentous substances on the tongue leading to Macroglossia and there isn't an enzyme that can break down these substances, so they accumulate
Menorrhagia	In women, Hypothyroidism causes menorrhagia. Menorrhagia means less bleeding
Myxedema Coma (Hypothermia, Seizure, Respiratory Depression)	if a trauma or an infection occurs, it leads to severe decrease in the thyroid hormones and functions. Severe hypothyroidism is Myxedema Coma. Symptoms like Hypothermia, Seizure, and Respiratory Depression happen ink addition to the other hypothyroidism symptoms discussed above. There is severe decrease in T3 and T4. It is very dangerous

Investigations of the Hypothyroidism

To recap, TSH from the pituitary gland stimulates T3 &t4 secretion from the Thyroid gland. To review the normal values of the hormones, Total T3&T4 can be measured but the most important and more accurate is T3& T4.

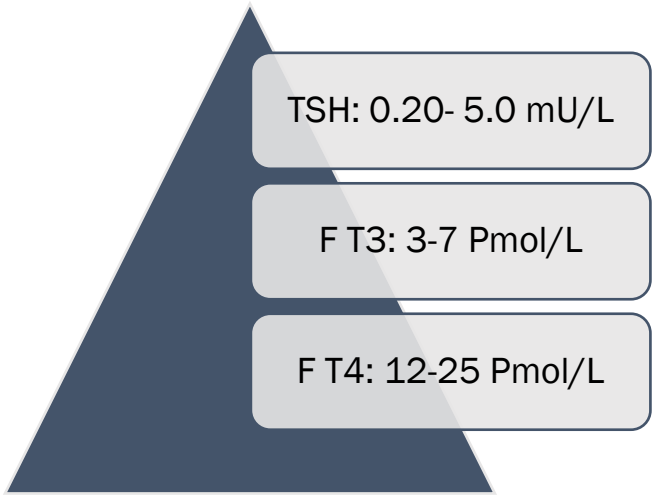
There are Primary , Secondary and Sub clinical hypothyroidism. In Primary hypothyroidism, the problem is in the thyroid gland. In Secondary hypothyroidism, the problem is in the pituitary gland. Sub clinical hypothyroidism will be discussed later.

In Primary hypothyroidism, the main problem is in the thyroid gland so labs look like this T3 &T4 are low so The pituitary gland stimulates the thyroid more leading to increase in the TSH.

In Secondary hypothyroidism, the main problem is in the pituitary gland, so labs look like this TSH is low so The pituitary gland cannot stimulate the thyroid enough leading to a decrease in the T3 &T4.

In cases of Subclinical thyroiditis, only parts of the thyroid gland but parts are still healthy. So, first T3&T4 decrease due to less secretion from the defective thyroid tissue and that leads to increase of the TSH hormone from the pituitary gland. Increased TDH will stimulate the healthy thyroid tissue more, so the healthy thyroid parts secrete more T3 &T4. As, a result it means T3& T4 levels return to normal, but TSH hormone is still increased. In long lasting case, TSH is increases while T3 &T4 is normal. Symptoms are not apparent yet.

The difference between Primary hypothyroidism and Subclinical thyroiditis is that in Primary hypothyroidism, the whole thyroid gland is dead, so no matter how much TSH increases both T3 & T4 are still decreased; however, in Subclinical thyroiditis, half the thyroid gland is still functional so an increase in TSH leads to increase in the functionality of these healthy parts to compensate for the decrease in T3 &T4, therefore T3 &T4 levels are normal. In some cases, especially in Hashimoto's thyroiditis it starts of as Subclinical thyroiditis, then turn into Primary hypothyroidism. In Secondary hypothyroidism, the defect is in the pituitary, so patient could be given TRH and see the result, if there is an increase in T3 &T4, it means the pituitary gland is functional. So, the most sensitive test for hypothyroidism is TSH.



TSH

T3 &T4

Anti- TPO & Anti- TG

- Antibodies that attack the thyroid gland, it is present in Hashimoto's thyroiditis.
- It not a test that is routinely done

Cholesterols, LDL

- Cholesterols and LDL both increase because the decrease in T3 & T4 less metabolism of LDL so more LDL and more Cholesterol

Creatine kinase

- Creatine kinase increases due to some muscular atrophy

Hyperprolactinemia

- Increase of TSH could stimulate lactophil cells that secrete prolactin hormone leading to Hyperprolactinemia

SHBG

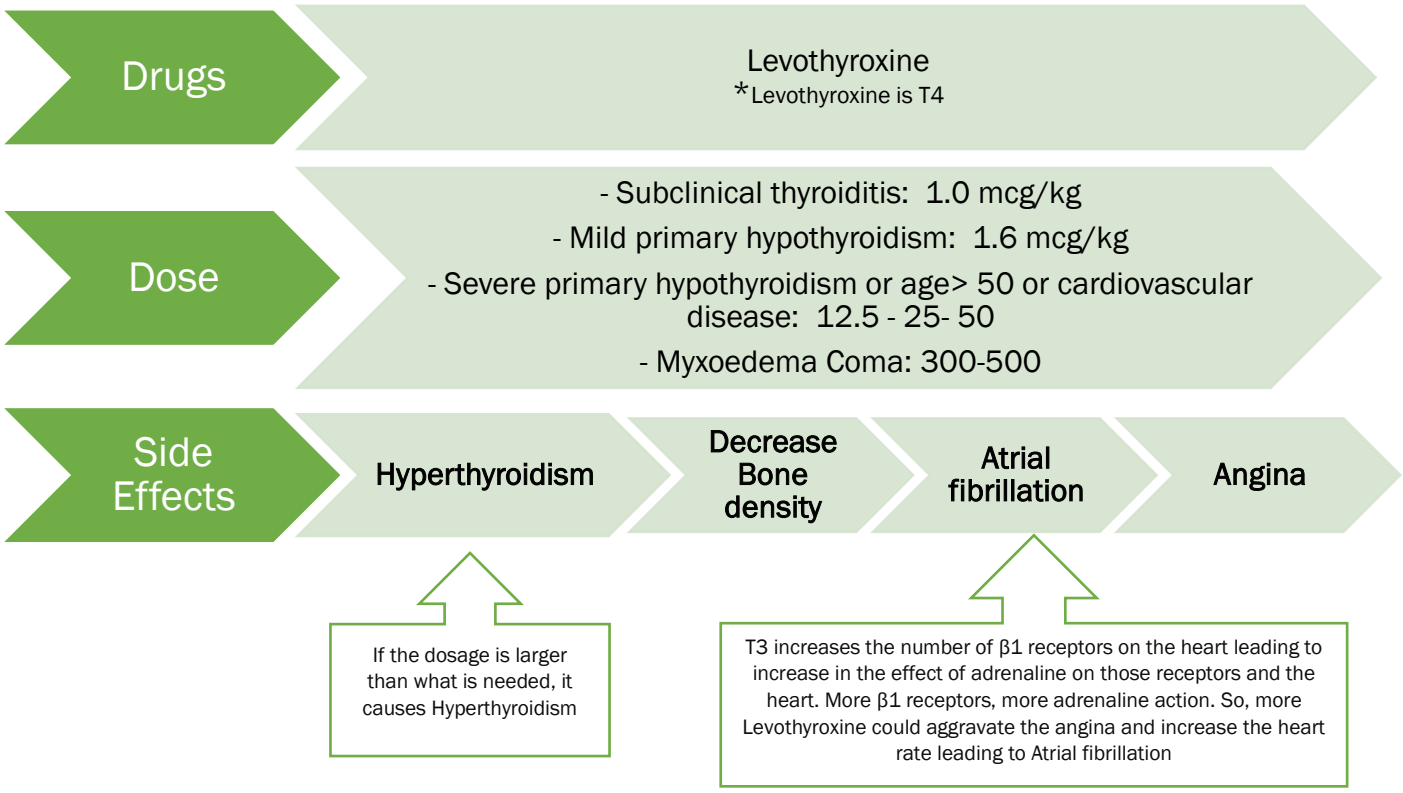
- Sex hormones binding globulin (SHBG) decreases. Leading to more free testosterone that may cause physical changes on the patient.

MCV

- Mean Corpuscular Volume (MCV). Normally the red blood cell volume is 80-100 F/L but in hypothyroidism, the metabolism decreases so RBC enlarge leading to Macrocytic anemia that is called non-megaloblastic Macrocytic anemia. The size increase but the number is decreased.

Pharmacology and Treatment of Hypothyroidism

Hypothyroidism means decrease in the thyroid hormones, so there is a need to give the patients' supplements to compensate for the thyroid hormones that are decreased. There was a lot of discussion about whether to give the patient T3 of T4 and there was a fear form giving the patients the active form T3 as the body might not need all this amount and could lead to hyperactivity of the thyroid gland. So, the patient is given T4 and let the body use the amount it needs and convert it to active T3.



Drugs that hinder the absorption of Levothyroxine:

These drugs reduce the absorption of Levothyroxine and its activity

Calcium	Iron	Proton pump inhibitors	Amiodarone	Rifampicin