Hyperthyroidism

Introduction

Hyperthyroidism is **increase in the functionality of the thyroid gland. It is increase 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.
- Anterior 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 that is attached to TSH receptors on the thyroid gland leading to secretion of thyroid hormones T3,T4 and TG (Thyroglobulin).

Causes of Hyperthyroidism

Grave disease

It is one of the most important causes of Hyperthyroidism.

It is called thyrotoxicosis.

Plasma cells make antibodies that attack the thyroid gland at the site of the TSH receptors. These antibodies are called Thyroid Stimulating Immunoglobulin (TSI). TSI attach themselves to the TSH receptors and stimulate the thyroid gland more than not is stimulated by TSH.

Normally, TSH stimulates thyroid gland with in the body needs, but TSI stimulates the thyroid gland more than what is needed so it leads more T3 and T4 and Hyperthyroidism.

TSI also attack the eyes, especially the tissue (fibroblasts) leading to excess production of collagen and glycosaminoglycans accumulation around the eyes leading to Exophthalmos. It is a known sign of Hyperthyroidism.

TSI also attack the skin around the tibia excess production of collagen and glycosaminoglycans accumulation leading to Tibial Myxedema.

Also, excess production of collagen and glycosaminoglycans accumulation around the fingers.

Grave disease mostly affect middle aged women (20-50 years of age).

Eg: the singer Om Kalthoum who had Grave disease and used to wear glasses to hide her eyes because of Exophthalmos.

TSI also affects the thyroid follicles by causing follicular cells enlargement and distortion and that leads to Diffuse Goiter

Toxic multi-nodular goiter. (Autonomous)

Toxic means increase in the thyroid hormones. Multi means multiple. Nodular means tumours or nodes.

In multiple areas of the thyroid gland, thyroid tissue become Autonomous which means they are affected by the TSH and they have more response than normal thyroid tissue.

It is usually associated with old age and it happens more in males especially in areas with less iodine.

These nodules are sensitive to iodine.More stimulation of these nodules means increase in T3 and T4 and that means Hyperthyroidism.

Goiter means enlargement of the thyroid gland, however in Toxic multi-nodular goiter means goiter only in the site of the nodules and not diffusely like Grave disease.

Toxic solitary goiter (Plummer disease) (Adenoma)	Toxic means increase in the thyroid hormones. Solitary means there is only one nodule (Adenoma) that secretes more T3 and T4 than the rest of the thyroid gland. It is a secretory Adenoma
Thyroiditis	Inflammation of the thyroid gland. It is usually caused by virus and not Hashimoto's. Viral thyroiditis start by thyroid hormones increasing till the thyroid tissue dies then the thyroid hormones level decreases. It causes Tender goiter, fever, and increase of T3 and T4 (Hyperthyroidism) then decrease of T3 and T4 (Hypothyroidism
Drug induced (Amiodarone, α-interferon)	Some drugs stimulates the thyroid gland to secrete more T3 and T4.
Factitious	A patient with a little bit of medical knowledge that thyroid hormones lead to increase of the metabolism. So that patient goes to the pharmacy asking for thyroid hormones. He is given Levothyroxine. That patient takes Levothyroxine for a day , 2 , a week, 2 weeks, then he find a result in weight loss. So, he continues, till he comes to the hospital with sweeting, insomnia, and other symptoms of hyperthyroidism. When they do lab investigations, and find that T4 and T3 are increased and TSH is low. It is difficult to diagnose Factitious Hyperthyroidism, less the patient confesses to taking unprescribed Levothyroxine or we do TG test . TG will be decreased as the increase in thyroid hormones T3 and T4 is external not internal. The thyroid gland is producing less hormones but more are still in the blood

Ectopic foci	A focus or number of foci out side the thyroid gland may be a tumour in the lung or some place else that secretes thyroid hormones in addition to the thyroid gland. So, there is increase in thyroid hormones T3 and T4
Thyrotropinoma (Secondary)	The main problem here is the Pituitary gland. A tumour in the cells in. The anterior pituitary that secretes TSH leading to an increase secretion of TSH and therefore, an increase in T3 and T4. Among all the tumours that happen in the pituitary, Thyrotropinoma is very rare. In this tumour, TSH is increased and T3 and T4 are increased as well

All the primary causes of hyperthyroidism usually T3 & T4 are increased and in return TSH decrease. But in secondary hyperthyroidism, TSH increase and in return it leads to a T3 and T4 increase.

Clinical features of Hyperthyroidism

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

Clinical features of Hyperthyroidism	
Insomnia, Depression, Anxiety, Weakness	Increase of T3 and T4 means increase of the metabolism and that leads to Insomnia. Couple of weeks of insomnia leads to Anxiety, Weakness and Depression
Heat intolerance, Diaphoresis	Temperature is measured from the forehead, and it is what comes after the head going down. Increase of T3 and T4 means increase of the metabolism and that leads to an increase in the body temperature, Heat intolerance, and Diaphoresis. Heat intolerance even if the weather is cold and skin is always warm
Goiter	The thyroid gland is enlarged but that mostly appears on Ultrasound only
Tachycardia, Atrial fibrillation	The thyroid hormones T3 and T4 increase will mean increase number of β1 receptors on the heart leading to increase in the effect of adrenaline on those receptors and the heart leading to increase in the heart rate (Tachycardia), and it may lead to Atrial fibrillation
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
Diarrhea, Weight loss	T3 and T4 increase will mean increase metabolism which means faster GIT movement and Diarrhea. Also, they increase the catabolism and fat breakdown leading to Weight loss. Some people use thyroid hormones like L- thyroxine to lose weight. It is good to lose weight, but the side effects like Insomnia, Tachycardia and others are noy good. It also leads to increase the appetite. The patient eats more but doesn't gain weight
Tremor	T3 and T4 increase will mean increase metabolism and increase the adrenaline effect on the receptors and muscles leading to Tremor

Clinical features of Hyperthyroidism

- Exclusive to Grave disease

Clinical features of Hyperthyroidism, exclusive to Grave disease	
Exophthalmos, Photophobia, Double vision	TSI attack the eyes, especially the tissue (fibroblasts) leading to excess production of collagen and glycosaminoglycans accumulation around the eyes leading to Exophthalmos. Exophthalmos is bulging of the eyes. Bulging of the eyes could lead to Photophobia and fear of light. It also could lead to impairment of ocular movements leading to blurred or Double vision
Dermopathy, Pretibial Myxedema	Dermopathy means affection of the skin. TSI attack the skin around the tibia excess production of collagen and glycosaminoglycans accumulation leading to Tibial Myxedema. There is a huge difference between Tibial Myxedema and myxedema coma. Myxedema coma means severe decrease in the thyroid hormones, and it is caused by Hypothyroidism. Tibial Myxedema is caused by Hyperthyroidism
Acropathy	Acropathy is excess production of collagen and glycosaminoglycans accumulation around the fingers

Investigations of the Hypothyroidism

To Investigate hyperthyroidism, there are two ways either laboratory through TSH, T3 and T4 or Scan through Radioactive Iodine Uptake Scan and Radioisotope Thyroid Scan. Remember that thyroid hormones increase lead to negative feedback on the pituitary gland leading to decrease in TSH

There are two types of Hyperthyroidism: Primary and Secondary.

In primary hyperthyroidism, T3 &T4 increase leading to negative feedback on the pituitary gland leading to decrease in TSH. And that means, in primary hyperthyroidism, T3 &T4 increase and TSH decreases.

In secondary hyperthyroidism, the problem is in the pituitary gland. It means Pituitary gland increase the secretion of TSH leading to stimulation of the thyroid gland and increasing T3 &T4. And that means, in secondary hyperthyroidism, TSH increase and T3 &T4 increase.

Example. If we set up an interview, I will be the host and I will ask the thyroid gland in the secondary hyperthyroidism why are you recreating an increased amount of T3 and T4. It will answer that it is not its fault as the pituitary is stimulating it from above

TSH

T3 &T4

Radioactive Iodine Uptake Scan/ Radioisotope Thyroid Scan(99Tc)

- Grave disease, TMG, Toxic adenoma, Thyroiditis, Factitious, Drug induced
- It is a scan Radioactive Iodine that determine the amount of the thyroid gland absorption of Iodine and it shows the areas of defect. The normal thyroid gland takes up Radioactive Iodine in a small amount. ^{99}Tc is Technetium-99 a Radioisotope absorbed by the thyroid gland through Sodium- Iodine channel same as Radioactive Iodine except that ^{99}Tc is safer than Iodine. Radioactive Iodine Uptake Scan could cause cancer and takes longer time to be done 24 hours. So ^{99}Tc replaced Radioactive Iodine Uptake Scan now.These nodules in the thyroid gland appear on scans as either Hot nodule or cold nodule. Hot nodules take more Radioactive substance, but Cold nodules take less Radioactive substance. Cold nodules are more dangerous as they as they can be cancerous, so you need to take a biopsy to confirm. Hot nodule is most likely to be Toxic adenoma.
- Abnormal thyroid gland on Radioactive Iodine Uptake Scan/ Radioisotope Thyroid Scan(^{99}Tc) shows:
  - In Grave disease, the thyroid takes more Radioactive substance diffusely in every part of it.
  - In TMG. The toxic multiple nodules take up more Radioactive substance than the rest of the thyroid gland (healthy tissue).
  - In Toxic adenoma, The toxic single nodule takes up more Radioactive substance than the rest of the thyroid gland (healthy tissue).
  - In Thyroiditis, the Radioactive substance uptake will be very little as the thyroid gland is destroyed.
  - In Factitious, the thyroid gland Radioactive substance uptake is normal as the patient is just taking Thyroid hormone externally.
  - In Drug induced, the thyroid gland Radioactive substance uptake is normal as the patient is just taking Amiodarone or Lithium drugs.
- It is very important to differentiate every type of Hyperthyroidism on Radioactive scan
- If you suspected that a patient has Grave disease especially from the history. The patient comes complaining of Exophthalmos, Dermopathy, and Pretibial Myxedema, you should ask the patient to take TSI test. Also, check if the patient has other autoimmune diseases like DM, Pernicious anemia or others

Pharmacology and Treatment of Hyperthyroidism

There are 3 choices to treat Hyperthyroidism Medication, Ablation by I 131, and surgery

- Anti- Thyroid drugs

Methimazole (thyroid peroxidase inhibitor)

Side effects: Agranulocytosis 1%, Congenital Hypothyroidism

Thyroid peroxidase is an important enzyme in synthesis of thyroid hormones. Methimazole work as thyroid peroxidase inhibitor. It also has a dangerous side effect that is Agranulocytosis, but fortunately, it is very rare. It only happens in 1% and it can be discoed through a CBC analysis. It means decrease in number of WBCs especially Neutrophils, which could lead to being very liable to having an infection. In some case, Antibiotics like Cephalosporins are given as prophylactic measures.

This drug crosses the placenta and reach the fetus. It causes Congenital Hypothyroidism, so that drug is unsafe in pregnancy. Congenital Hypothyroidism means that the child will have Macroglossia, Underdevelopment of the brain, big in weight as that child will have a decrease in the Thyroid glands T3 and T4. The main cause that this drug is unsafe in pregnancy is that most of it is in free form not bound to proteins. Methimazole is the drug of choice in treatment of Hyperthyroidism

Propylthiouracil (PTU)
(thyroid peroxidase inhibitor & 5 deiodinase inhibitors) (Safe in pregnancy)

The main cause that this drug is safe in pregnancy is that most of it is bound to proteins nearly 80-90% of its concentration, so o only a small amount crosses the placenta

- Radioactive Iodine Ablation

Iodine 131 (Euthyroid- hypothyroidism 80%)

Contraindications: Pregnancy- Breast feeding- Thyroid eye

Iodine 131 lead to Ablation of the thyroid gland. At first it causes Euthyroid state, but then it causes hypothyroidism in 80% of people who took it.
It is contraindicated in Pregnancy and Breast feeding. If the patient has Grave disease (Thyroid eye), Iodine 131 is contraindicated as it aggregates the disease

- Surgery

Total thyroidectomy

It is usually used in cancer cases

Subtotal thyroidectomy

Surgery is very important to treat compression syndrome due to thyroid enlargement

❖ Complications of the surgery

Hypothyroidism

- Hypothyroidism due to removal of the thyroid gland

Hypoparathyroidism (Decrease in Calcium)

- Hypoparathyroidism due to removal of the parathyroid glands leading to Decrease in Calcium level

Recurrent Laryngeal Nerve palsy (Hoarseness of the voice)

- Hoarseness of the voice due to Recurrent Laryngeal Nerve injury during surgery as it lie very close to the Thyroid gland

Beta- Blocker (Propranolol)

The most dangerous symptom of Hyperthyroidism is Tachycardia. So, we use Beta- Blocker to reduce the heart rate. But Propranolol is the drug of choice as it can inhibit the conversion of T4 to T3 in peripheral tissues (Anti-thyroid effect) beside its Beta- Blocker effect. Sometimes, the patient is very symptomatic that he cannot handle surgery right away, so we start with medical treatments first.

Methimazole

Methimazole is the drug of choice in treating Hyperthyroidism. But, if the patient suffered from Agranulocytosis, we shift the patient to Propylthiouracil. Or, if the Patient is pregnant, we use Propylthiouracil. If there is any of these contraindications (Pregnancy- Breast feeding- Grave diseases), we cannot use Radioactive Iodine Ablation.

Surgery

In surgery, Total thyroidectomy causes more complication than Subtotal thyroidectomy. so, it is mainly used in cases of cancer. Subtotal thyroidectomy still has complication but in a lesser severity tan that of the Total thyroidectomy as only part of the thyroid gland is removed. Subtotal thyroidectomy could be useful in patient that can't undergo Radioactive Iodine Ablation.

Thyroid storm

Excessive increase in the thyroid gland hormones T3 and T4. The symptoms are Excessive Insomnia, Diaphoresis, Tachycardia, Atrial fibrillation, and Diarrhea

Potassium Iodine (wolff-chaikoff effect) (10 days) (escape)	• Potassium Iodine is used in treatment of the Thyroid storm through wolff-chaikoff effect by overloading the thyroid with Iodine and that leads to decrease in in the thyroid function temporarily for almost 10 days. It is not a permanent treatment as after 10 days, the thyroid ignore the excess iodine and escape its effect. So, thyroid functions become high again
Anti-Thyroid medication	• Using medications like Methimazole could help the condition
Beta-Blocker	• Using medications like Beta-Blocker like propranolol or even other could help the condition and reduce the heart rate as its the most dangerous problem
Corticosteroid (Hydrocortisone)	• Using Corticosteroid like Hydrocortisone is very useful as thyroid hormones work in catabolism and distorting natural cortisol and Hydrocortisone is replacing it
Supportive	• Supportive measures like IV fluids, Paracetamols should be given to help decrease the temperature and replenish the fluids loss