

Cannot Tolerate Hot Weather

Endocrine Block, PBL; Case 1



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Learning Objectives:

- 1) Discuss the anatomy and physiology of the thyroid gland.
- 2) Discuss the formation of the thyroid hormones and their physiological action.
- 3) Discuss the pathology and pathogenesis of Graves's disease.
- 4) Use basic science to interpret the symptoms, signs and investigation.
- 5) Discuss the pharmacology of drugs used in graves disease.
- 6) Discuss management goals and construct a management plans for patient with Graves's disease.

Color Guide:

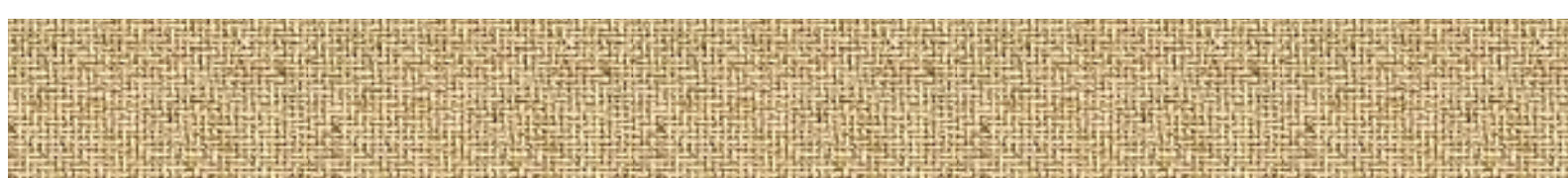
- **Red:** Relatively important & mentioned in case tutorials.
- **Black:** Questions.
- **Blue:** Answers (mentioned in case tutorials).
- **Green:** Additional answers/notes.
- **Orange:** Explanation.

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New Terms:

TERM	Definition
Accountant	A person concerned with the maintenance and audit of business accounts and the preparation of consultant reports in tax and finance.
Palpitation	Irregular, rapid beating or pulsation of the heart.
Vitiligo	Is a condition in which skin loses melanin, the pigment that determines the color of skin, hair and eyes. Vitiligo occurs when the cells that produce melanin die or no longer form melanin, causing slowly enlarging white patches of irregular shapes to appear on skin. <i>It's an autoimmune disease.</i>
Exophthalmos	When there is an increase in the volume of the tissue behind the eyes, the eyes will appear to bulge out of the face.
Lid Lagging	Is a condition in which the upper eyelid is unable to follow the rotation of the eye.
White Rim of Sclera	----
Overstretched	To stretch or extend over.
Bruit	A sound or murmur heard in auscultation, especially an abnormal one.
Thyroxin	The hormone secreted by the thyroid gland.
Tri- iodothyronin	A hormone that helps regulate growth and development helps control metabolism and body temperature, and, by a negative feedback system, acts to inhibit the secretion of thyrotropin (TSH) by the pituitary gland.
TSH	A hormone secreted by the pituitary gland that controls the release of T4 by the thyroid gland.
TSH receptors IgG antibody	<i>An antibody that binds to TSH receptor that found in the thyroid gland.</i>
Thyroid Scan	An image obtained from the thyroid gland after oral administration of radioiodine.



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Case Scenario

Key information:

- Female.
- 29 years old.
- Working as an accountant in a Bank.

Presenting problems:

1. Always feels Hot.
2. Sweats a lot.
3. Tremors in her hands.
4. Lost 6Kg in bodyweight.

History:

- 1) Feeling hot all the time even when the air condition is on and maximum.
- 2) She has excessive sweating all over her body all the time.
 - The palms of her hands are usually wet.
 - She directs sweat after taking shower.
- 3) Shaking of her hand.
- 4) Increase in her appetite, however, she lost 6 Kg in body weight over the last 2 months. (Not on diet and not doing any exercises).
- 5) Heartbeats (palpitations) → even during rest.
- 6) Her bowels open 3 to 4 times daily.
- 7) Feels tired and under stress most of the time.
- 8) Loses her temper easily.
- 9) Her menstrual periods are regular.

Past Medical History: Nothing significant.

Family History: Her mother is known to have a vitiligo for about 15 years. No family history of tremor.

Medication and Allergy: Nil.

Alcohol and Smoking: Nil.

Social history: She has been married for about 5 years. She has one child, 3 years old.

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Clinical Examination:

She looks anxious and restless.

Vital signs:

- She has ↑ pulse rate, BP, and respiratory rate.

Eye examination:

- Exophthalmos.
- Lid lagging on looking down.
- A white rim of sclera is seen above and below the cornea.

Skin and hand examination:

- Her outstretched hand show fine tremor.
- Wet and warm palms.

Neck examination:

- Swelling in front of her neck which **moves up** on swallowing.
- There is a bruit heard over the neck swelling.

Upper and lower limbs:

Muscles of the shoulders and thighs are weak compared to distal.

Tendon reflexes: bilaterally symmetrical and brisk.

Investigations:

1. **Blood Tests:** ↑T₄, ↑T₃, ↓TSH.
2. **Thyroid autoantibodies:** ↑ TSH receptor IgG antibodies (TRAb).
3. **Thyroid scan:** Thyroid scan shows homogenous increased uptake of the radioactive iodine.

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Questions

Before answering the questions below, please read tutorials 1 and 2.

1) Describe the levels of the following in Graves' disease: TSH, free T4, total T3 (tT3), and radioiodine uptake.

- TSH → very low serum.
- Free T4 → elevated.
- Total T3 → elevated
- Radioiodine uptake → homogenous increased uptake.

2) What is the most important laboratory test of the thyroid?
Serum TSH.

3) What is the most common cause of hyperthyroidism?
Graves disease.

4) Precipitating factors leading to Graves's disease?

- Depleted iodine supply.
- Infection.
- Stressful life events.
- Genetic predisposition.

5) Graves disease is caused by an autoimmune production of?
Antibodies against the TSH receptor that elevates T4.

6) What's the mechanism of Grave's Disease?

Thyroid receptor antibodies attach to the thyroid follicular cells and cause increased production and release T3/T4.

7) Why do patients with Grave's have hand tremors?
Over-action of the sympathetic system.

8) What is the laboratory testing for Grave's disease?

Serum T4, Serum T3, Antithyroid antibodies, Sensitive serum TSH test.

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9) What is the triad that indicates Grave's disease?

- Thyrotoxicosis.
- Ophthalmopathy.
- Dermopathy.

10) How is Grave's an autoimmune disorder?

Antibodies are developed to TSH receptors leading to thyrotoxicosis and progressing to destruction of thyroid tissue causing hypothyroidism.

11) What is a Grave's specific clinical manifestation of hyperthyroidism ?

Exophthalmos.

12) What are some cardiovascular manifestations of hyperthyroidism (Grave's disease)?

Bruit over thyroid gland, systolic hypertension, increased cardiac output.

13) The name of Bulging eyes in Graves Disease?

Graves Ophthalmopathy.

14) List 3 possible ways by which a patient with Graves' disease can develop hypothyroidism?

- Thyroid ablation by surgery or ^{131}I radiation .
- Autoimmune thyroiditis, leading to Thyroid destruction.
- Development of antibodies that block TSH stimulating.

15) How can we confirm the diagnosis of Graves' disease?

By blood tests and the nuclear scanning of the thyroid gland.

16) What are the management options in this case?

1. Medical treatment. "We start with the medical treatment before surgery"
2. Surgical removal of the thyroid gland.
3. Destroying the active cells of the thyroid by radioactive iodine.

17) Which one of beta blockers is recommended in this case and why?

Propranolol, because it will ameliorate the symptoms that mimic over stimulation of sympathetic nervous system. "palpitation, tremor and anxiety".

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18) Why we would use Carbimazole in this case?

To block the synthesis and secretion of thyroxine from the thyroid gland.

19) What are the possible side effects of these medications?

Sever allergic reactions. "skin rash, fever or sore throat".

20) What does the IgG antibody do when it binds to TSH receptor?

It mimics the action of TSH, stimulating adenylcyclase with resultant increased release of thyroid hormones.

21) Why there is decreased level of TSH in our patient's blood ?

Because there is increased level of thyroid hormones in the circulation which will send negative feed back to the pituitary and hypothalamus.

22) How do you interpret the investigation results?

Interpretation of investigations

Item	Change	Hypotheses/interpretation
Thyroxin level (T4)	Increased	Excessive secretion of T4 from the thyroid gland. The process is autonomous and can not be stopped via negative feedback mechanism.
Tri-iodothyronin level (T3)	Increased	Excessive secretion of T4 from the thyroid gland. The process is autonomous and cannot be stopped via negative feedback mechanism.
TSH	Low	Because of the increased T3, T4 as part of the negative feedback at the hypothalamus and thyroid levels. There is no problem in the hypothalamus.
TSH receptor IgG antibody	Increased	Support that the defect in the thyroid gland is autoimmune.
Thyroid scan	Increased uptake of radioactive iodine. The uptake is homogeneous.	These investigations together with the increased uptake and exophthalmos are consistent with Graves disease

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General Information

- ✓ **Thyroid gland is a small gland in front of the neck.**
- ✓ **Secrets the hormone thyroxin.**
- ✓ **Controlled by the anterior pituitary hormone (TSH) which is already controlled by the hypothalamic hormone (TRH).**
- ✓ **Increased and decreased levels of thyroid hormones cause pathological conditions " Hypo and Hyperthyroidism " which will be either primary if the problem was in the thyroid gland itself or secondary if the problem was in the anterior pituitary or the hypothalamus.**
- ✓ **Graves' disease is an autoimmune disorder in which there is autoantibodies against the TSH receptors.**