



Thyroid Profile

Module 8 – Unit 1

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T₃ (Tri-iodothyronine) – The active hormone

- **Source:** Mostly produced by the conversion of T₄ to T₃ in peripheral tissues; small amount directly from the thyroid.
- **Role:** The most biologically active thyroid hormone, responsible for metabolic effects.
- **Total T₃ vs. Free T₃:**
 - **Total T₃:** Measures bound and unbound T₃. Also affected by protein levels.
 - **Free T₃ (FT₃):** Measures only the unbound, active form. **Provides direct insight into cellular metabolic activity.**
- **Normal Reference Range (Free T₃ - Typical):**
 - 2.3 – 4.2 pg/mL (or 3.2 – 6.2 pmol/L)
- **Note:** Free T₃ is often tested when TSH and Free T₄ are normal but symptoms persist, or in specific cases of hyperthyroidism.

Reverse T3

Reverse T3 (rT3):

Reverse T3 is an **inactive metabolite** of T4 (thyroxine). It's structurally similar to the active hormone T3 (triiodothyronine) but **biologically inactive**.

How is it made?

When T4 is converted in the body, it can be converted to rev T3

It tends to rise during:

- Chronic stress
- Starvation or severe caloric restriction
- Illness (e.g., critical illness, trauma, liver/kidney dysfunction)
- Hypothyroidism or euthyroid sick syndrome

Significance of Reverse T3

Why does it matter?

Elevated rT3 can compete with T3 at receptor sites, **blocking T3's action**, leading to symptoms of hypothyroidism despite normal T3/T4 levels.

This is often called **"thyroid resistance"** or **"low T3 syndrome"**.

Reverse T₄

Reverse T₄ (rT₄):

Reverse T₄ is **not a commonly recognized or clinically measured hormone**. It is sometimes confused with rT₃. There's no standard test or functional role attributed to "reverse T₄" in human physiology.

Likely confusion:

People often mistakenly refer to **rT₃** as "reverse T₄" because it's derived from T₄, but **rT₄ is not an established or meaningful term in clinical endocrinology**.

Anti-TPO (Thyroid Peroxidase Antibodies)

- Targets the **thyroid peroxidase enzyme**, which helps produce thyroid hormones.
- Most common antibody found in **autoimmune thyroid disorders**.
- Seen in:
 - **>90%** of patients with **Hashimoto's thyroiditis**
 - **70-80%** of those with **Graves' disease**
- Indicates **autoimmune destruction** of the thyroid, even before hormone levels change.
- Helps predict progression from **subclinical to overt hypothyroidism**.

Anti-Tg (Thyroglobulin Antibodies)

- Targets **thyroglobulin**, a protein used in making thyroid hormones.
- Commonly seen in **Hashimoto's thyroiditis** and sometimes in **Graves' disease**.
- Used to monitor **thyroid cancer recurrence**, especially after thyroid removal.
- Often ordered together with Anti-TPO for complete autoimmune assessment.

Free hormones Vs Total hormones



Feature	Free T3 \ Free T4	Total T3 \ Total T4
Definition	Unbound, active hormone in the bloodstream	Bound + unbound hormone (mostly bound to proteins)
Biological Activity	Biologically active and available to tissues	Inactive when bound to proteins (e.g., TBG, albumin)
Measurement Use	Reflects actual hormone available to cells	Reflects overall production, but not active levels
Affected by Binding Proteins	No (not influenced by changes in binding proteins)	Yes (altered by pregnancy, liver disease, certain drugs)
Clinical Relevance	More accurate in diagnosing thyroid dysfunction	May be misleading if binding protein levels are abnormal
Commonly Used In	Routine thyroid function testing	Used selectively when binding abnormalities are suspected

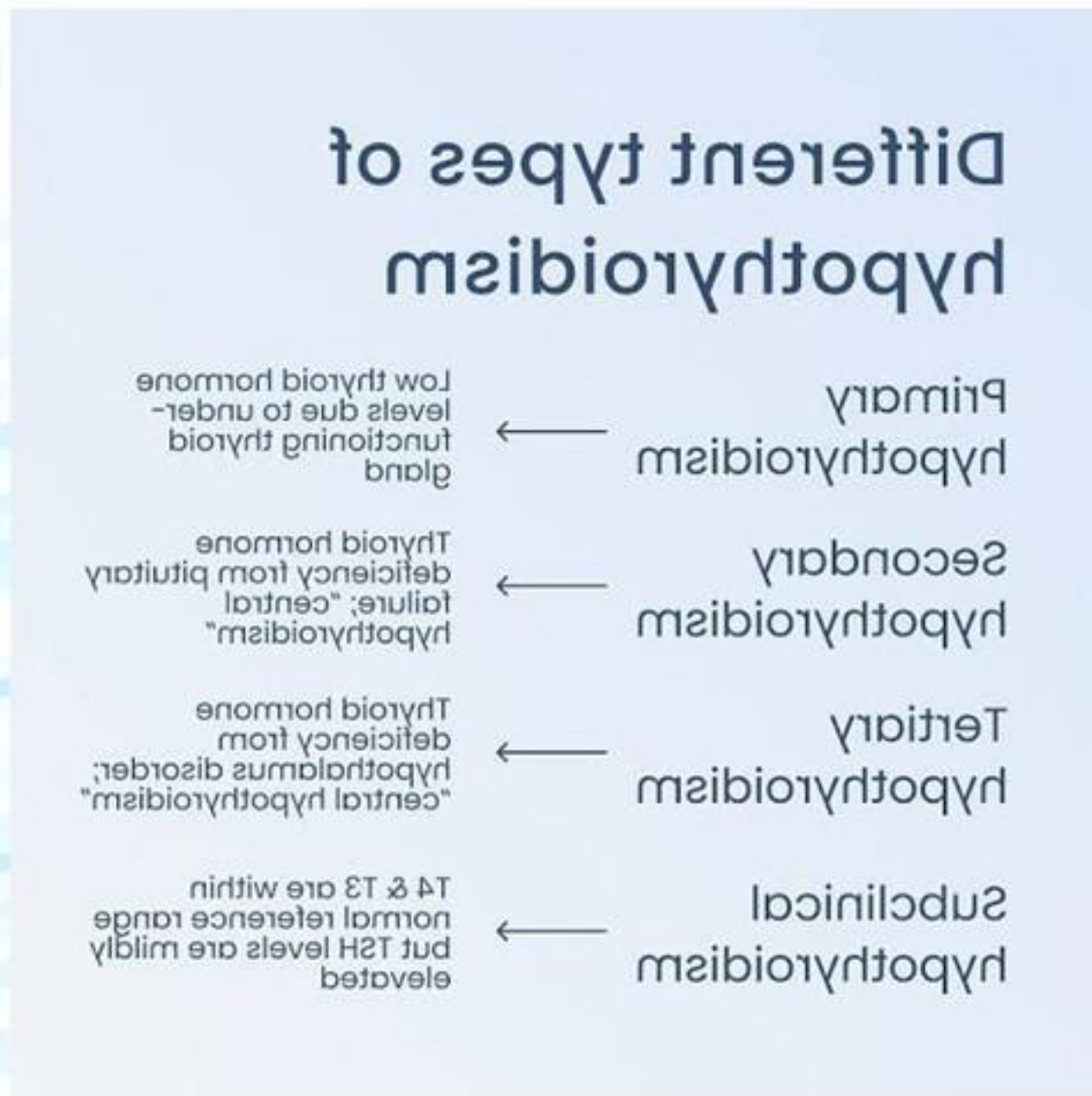
Why Free T₄ is more reliable than total T₄

Medicines to treat asthma, arthritis, skin conditions, and other health problems—can lower T₄ levels. These conditions and medicines change the amount of proteins in your blood that “bind” or attach to T₄. Bound T₄ is kept in reserve in the blood until it’s needed. “Free” T₄ is not bound to these proteins and is available to enter body tissues. Because changes in binding protein levels don’t affect free T₄ levels, many healthcare professionals prefer to measure free T₄.



Thyroid disorders – General classification

Depending on the etiology or the level at which problem occurs in the HPT axis, the thyroid disorders can be classified as following:



Primary Thyroid disorders

Chapter outline

- Thyroid hormones
- Complete thyroid profile
- Interpretation of thyroid function tests
- Primary thyroid disorders
- Secondary thyroid disorders
- Subclinical Hypothyroidism
- Sample reports

Primary Hypothyroidism



- **Pathophysiology:** The thyroid gland is underactive and cannot produce enough T₃ and T₄.
- **Causes:** Hashimoto's thyroiditis (autoimmune), iodine deficiency, thyroidectomy, radioactive iodine therapy.
- **Lab Values:**
 - **TSH: HIGH** (Pituitary senses low T₃/T₄ and works harder to stimulate the thyroid).
 - **Free T₄: LOW** (Thyroid isn't producing enough).
 - **Free T₃: Often Normal or Low** (Depends on severity, but Free T₄ drops first).
- **Clinical Presentation:** Fatigue, weight gain, cold intolerance, constipation, dry skin, depression.

Primary Hyperthyroidism



- **Pathophysiology:** The thyroid gland is overactive and produces too much T₃ and T₄.
- **Causes:** Grave's disease (autoimmune), toxic nodule, thyroiditis.
- **Lab Values:**
 - **TSH: LOW \ UNDETECTABLE** (Pituitary senses high T₃/T₄ and shuts down TSH production to try to stop the thyroid).
 - **Free T₄: HIGH** (Thyroid is overproducing).
 - **Free T₃: HIGH** (Often elevated disproportionately in Grave's disease).
- **Clinical Presentation:** Weight loss, heat intolerance, palpitations, anxiety, tremor, increased appetite.

Secondary thyroid disorders

Secondary Hypothyroidism



- **Pathophysiology:** The pituitary gland (or hypothalamus) isn't producing enough TSH (or TRH), leading to under stimulation of a healthy thyroid gland.
- **Causes:** Pituitary adenoma, Sheehan's syndrome, cranial radiation, severe head trauma.
- **Lab Values:**
 - **TSH: LOW \ NORMAL (inappropriately)** (Pituitary isn't signaling enough TSH, even though T₃/T₄ are low).
 - **Free T₄: LOW** (Thyroid is not being stimulated).
 - **Free T₃: LOW**
- **Clinical Presentation:** Similar to primary hypothyroidism, but may also have symptoms related to pituitary dysfunction (e.g., visual field defects, other hormone deficiencies).

Secondary Hyperthyroidism



- **Pathophysiology:** The pituitary gland is overproducing TSH (e.g., a TSH-secreting pituitary adenoma), leading to overstimulation of a healthy thyroid gland.
- **Causes:** TSH-secreting pituitary adenoma (very rare).
- **Lab Values:**
 - **TSH: NORMAL \ HIGH (inappropriately)** (Pituitary is overproducing TSH despite high T₃/T₄).
 - **Free T₄: HIGH**
 - **Free T₃: HIGH**
- **Clinical Presentation:** Similar to primary hyperthyroidism, but may have symptoms related to pituitary mass (e.g., headaches, visual disturbances).

Subclinical Hypothyroidism



The term 'subclinical' is used when the serum concentration of TSH is persistently abnormal (however defined), while the concentrations of T₄ and T₃ remain within their reference intervals. Because results can fluctuate spontaneously, a new diagnosis of subclinical thyroid dysfunction is not warranted on basis of a single laboratory sample. The following five criteria define endogenous subclinical thyroid dysfunction:

- TSH increased above or decreased below designated limits (see below)
- Normal free T₄ concentration (and free T₃ for hyperthyroidism)
- Abnormality is not due to medication (see below)
- There is no concurrent critical illness or pituitary dysfunction.
- A sustained abnormality is demonstrated over 3-6 months.



Thyroid Function Test Report

Patient Information

Name: Mrs. [REDACTED]
Age \ Sex: 38 \ Female
Date of Test: 10 June 2025

Fasting: Yes

Clinical Note: Fatigue, mild weight gain, cold intolerance

Test	Result	Reference Range	Units	Interpretation
TSH	8.8	0.4 - 4.0	µIU/mL	Elevated
Free T4 (FT4)	1.1	0.8 - 1.8	ng/dL	Normal
Free T3 (FT3)	2.9	2.3 - 4.2	pg/mL	Normal
Anti-TPO Antibodies	85	>35	IU/mL	Positive (suggests Hashimoto's)

Impression

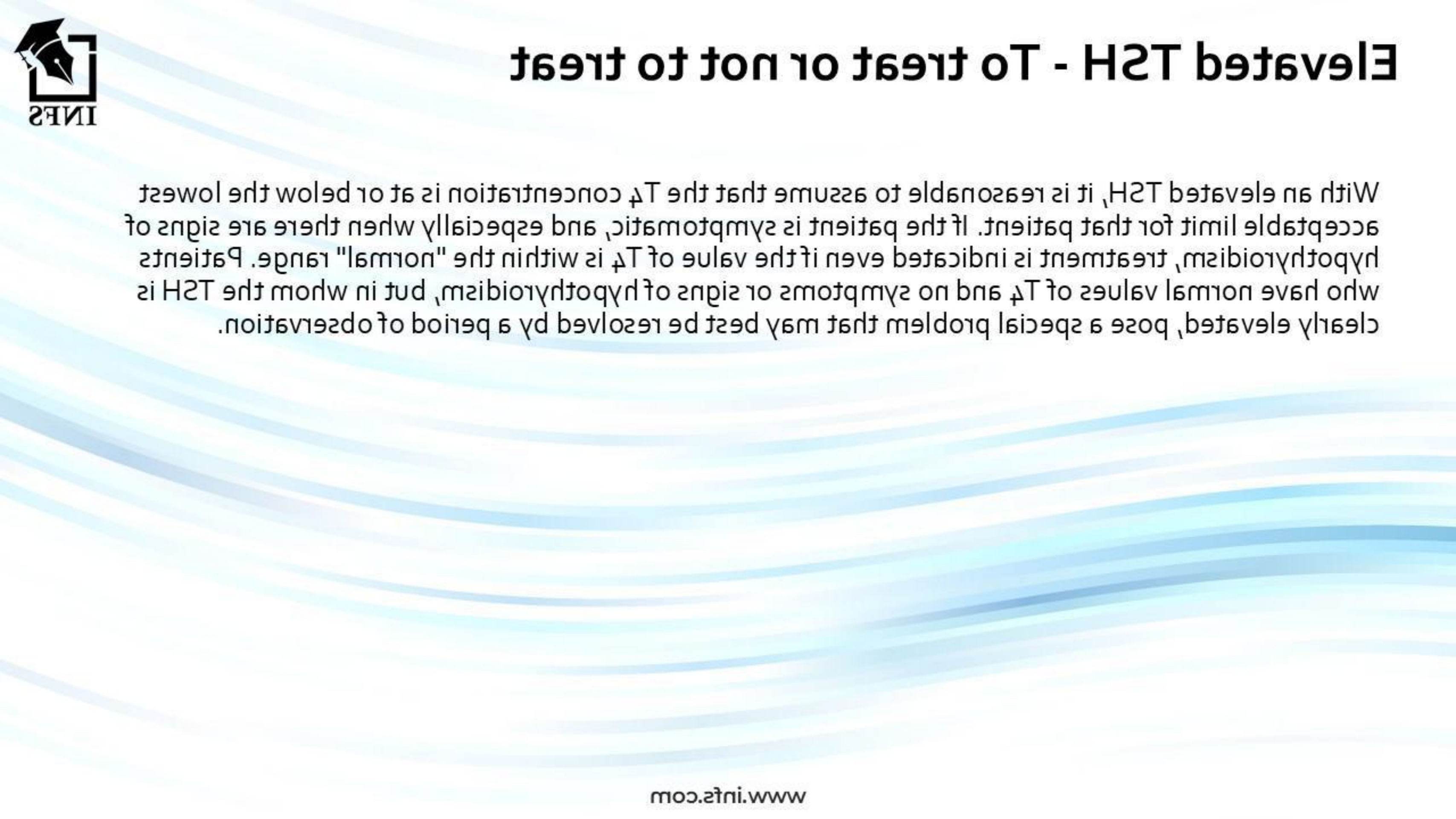
Subclinical Hypothyroidism: Elevated TSH with normal Free T4 and T3.
Positive Anti-TPO antibodies suggest autoimmune thyroiditis (Hashimoto's).
Recommend follow-up with repeat thyroid profile in 6-12 weeks. Consider endocrinology referral if symptomatic or planning pregnancy.

When to treat Subclinical hypothyroidism

According to the American Thyroid Association (ATA) and American Association of Clinical Endocrinologists (AAE) guidelines, levothyroxine therapy would be considered for 9% of women with subclinical hypothyroidism and $TSH \geq 10 \text{ mIU/L}$

Subclinical hypothyroidism or mild thyroid failure (increased TSH, normal free T₄ estimate)

- Non-specific symptoms may improve with treatment
- Progression to overt hypothyroidism
- Independent risk factor for atherosclerosis
- Increased risk of coronary artery disease
- Increased frequency of congestive heart failure
- Adverse effects on vascular compliance
- Abnormal cardiac function may improve with treatment
- Beneficial effect of treatment on lipids
- Increased prevalence of depressive illness
- Impaired fibrinolysis



Elevated TSH - To treat or not to treat

With an elevated TSH, it is reasonable to assume that the T₄ concentration is at or below the lowest acceptable limit for that patient. If the patient is symptomatic, and especially when there are signs of hypothyroidism, treatment is indicated even if the value of T₄ is within the "normal" range. Patients who have normal values of T₄ and no symptoms or signs of hypothyroidism, but in whom the TSH is clearly elevated, pose a special problem that may best be resolved by a period of observation.



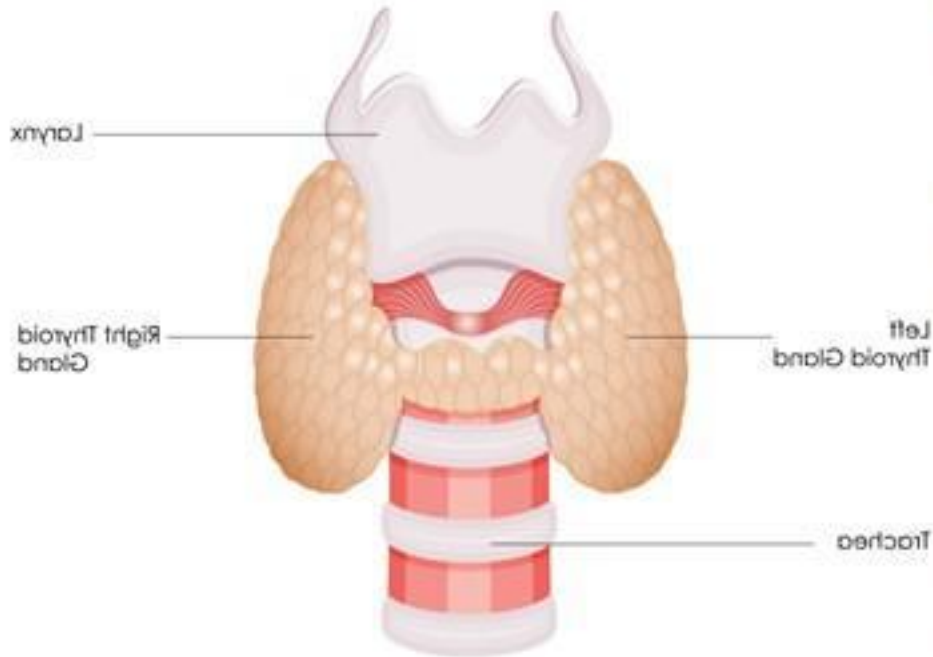
Subclinical hyperthyroidism

Subclinical hyperthyroidism (suppressed TSH, normal free T₄ and free T₃ estimates)

- Exposure to iodine may precipitate severe thyrotoxicosis
- Threefold increased risk of atrial fibrillation after 10 years
- Abnormalities of cardiac function
- Osteoporosis risk increased
- Progression to overt hyperthyroidism

Thyroid gland & its importance

- The thyroid is a small, butterfly-shaped gland located in the front of the neck.
- Despite its size, it plays a crucial role in regulating the body's metabolism through the release of thyroid hormones — primarily T₃ (triiodothyronine) and T₄ (thyroxine).
- These hormones influence nearly every organ system, controlling heart rate, energy production, body temperature, and weight.
- A healthy thyroid is essential for growth, brain development, and maintaining overall hormonal balance.
- Dysfunction of the thyroid can lead to wide-ranging health issues, including fatigue, weight changes, and mood disturbances.



Other considerations



- **Non-Thyroidal Illness (Sick Euthyroid Syndrome):** Acute illness can affect thyroid hormone levels (often low T_3 , sometimes low T_4 , TSH variable).
- **Medications:** Many drugs can affect thyroid tests (e.g., biotin, amiodarone, corticosteroids, estrogen).
- **Pregnancy:** TSH reference ranges change during pregnancy.
- **Thyroid Antibodies**
 - TPO Ab (Thyroid Peroxidase Antibodies): Common in Hashimoto's.
 - Tg Ab (Thyroglobulin Antibodies): Also in Hashimoto's, some thyroid cancers.
 - TSI (Thyroid-Stimulating Immunoglobulin): Specific for Grave's disease.

Summary – Key values

Condition	TSH	Free T4	Free T3
Normal (Euthyroid)	Normal	Normal	Normal
Primary Hypothyroidism	High	Low	Normal/Low
Primary Hyperthyroidism	Low/Undetect	High	High
Secondary Hypothyroidism	Low/High. Normal	Low	Low
Secondary Hyperthyroidism	Normal/High	High	High



- TSH is the cornerstone for screening thyroid function.
- Free T₄ and Free T₃ provide crucial confirmation and detail.
- The HPT axis feedback loop explains the reciprocal relationship between TSH and thyroid hormones in primary disorders.
- Secondary disorders present a different pattern, indicating a central problem.
- Always integrate lab results with clinical symptoms for accurate diagnosis and management.

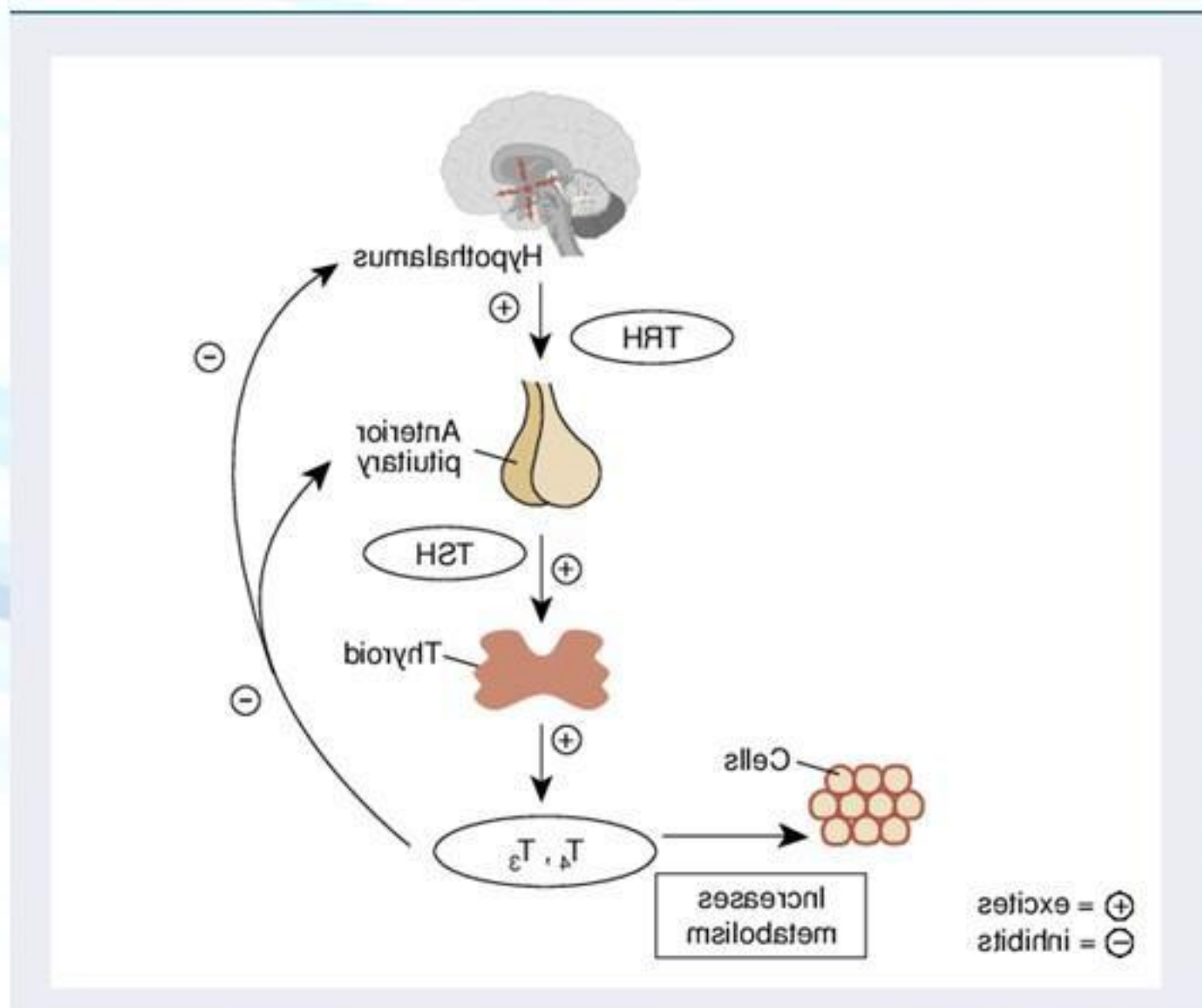


Thankyou

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Hypothalamo – Pituitary Axis



- The HPT axis is a vital hormonal feedback system that regulates thyroid function.
- Disruptions in any part of this axis can lead to thyroid disorders such as hypothyroidism or hyperthyroidism.

Understanding the Thyroid Trio

The "Thyroid Trio" refers to the three key hormones commonly measured to assess thyroid function:

- TSH (Thyroid-Stimulating Hormone)
- Free T₃ (Triiodothyronine) and
- Free T₄ (Thyroxine).

Evaluating all three together provides a comprehensive picture of thyroid health and helps in diagnosing conditions like hypothyroidism, hyperthyroidism, or central (secondary) thyroid disorders.

TSH – The pituitary messenger

Produced by the anterior pituitary gland.

The primary "signal" to the thyroid gland to produce T₃ and T₄.

- **Clinical Significance:**
 - Often the **first and most sensitive indicator** of thyroid dysfunction.
 - Reflects the pituitary's attempt to regulate thyroid hormone levels.
- **Normal Reference Range (Typical, ranges may vary slightly by lab):**
 - 0.4 – 4.0 mIU/L (or 0.4 – 2.5 mIU/L for optimal health/pregnancy planning)



Ultra-sensitive TSH or not?

- Ultra-sensitive TSH refers to a third-generation assay that can detect very low levels of TSH (as low as 0.01 mIU/L).
- It's not a different hormone—just a more sensitive testing method.
- Often labeled simply as “TSH” in modern lab reports because ultra-sensitive assays are now **standard practice** in most labs.

Why is Ultrasensitive TSH is better than TSH?

- It can **accurately detect subclinical hyperthyroidism** (when TSH is low but T₃ & T₄ are normal).
- Useful in monitoring **thyroid cancer patients**, where even tiny TSH changes are important.
- Helps in **fine-tuning thyroid medication** dosing in hypothyroid patients.

T₄ (Thyroxine) – The main prohormone

- Produced by the thyroid gland (approx. 80% of thyroid hormone output).
- **Role:**
 - Less biologically active than T₃.
 - Acts as a **prohormone**, converting to T₃ in peripheral tissues (liver, kidney, muscle, brain).
- **Total T₄ vs. Free T₄:**
 - **Total T₄:** Measures both bound (to proteins like TBG) and unbound T₄. Influenced by protein levels (e.g., pregnancy, certain medications).
 - **Free T₄ (FT₄):** Measures only the metabolically active, unbound form of T₄. **More accurate reflection of thyroid function.**
- **Normal Reference Range (Free T₄ - Typical):**
 - 0.8 – 1.8 ng/dL (or 10.3 – 23.2 pmol/L)