

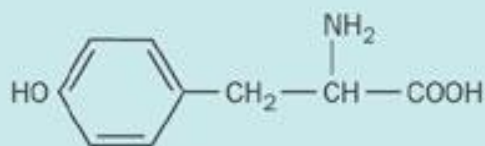
بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

**LABORATORY ASSESSMENT OF
THYROID STATUS**

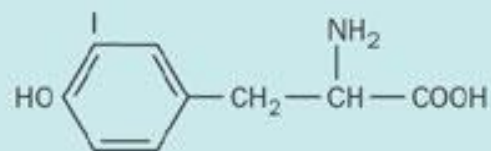
Dysfunction and anatomic abnormalities of the thyroid are among the most common diseases of the endocrine glands

*The thyroid gland produces two related hormones, **thyroxin (T₄)** and **triiodothyronine (T₃)***

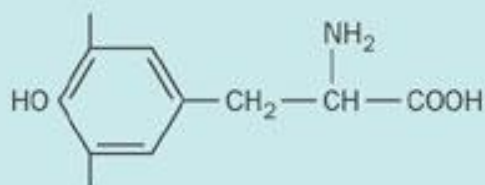
Thyroid hormones and related compounds



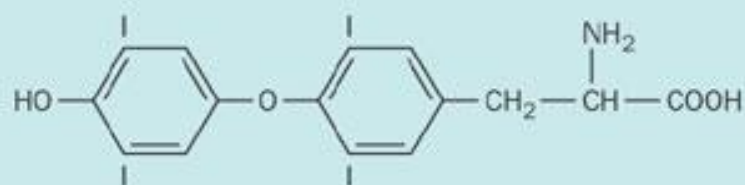
Tyrosine



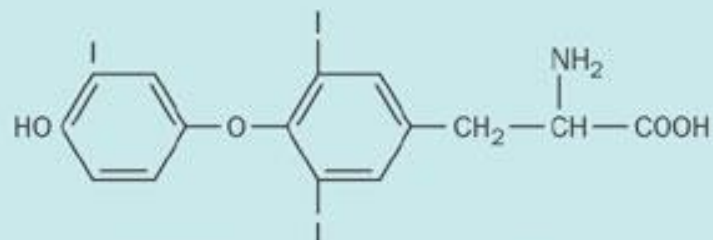
3-iodotyrosine (MIT)



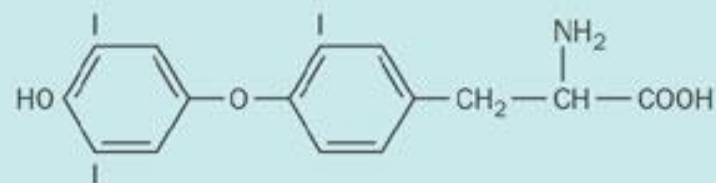
3,5-diiiodotyrosine (DIT)



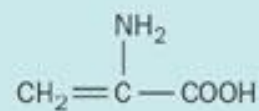
Thyroxine (T₄)



3,5,3'-triiodothyronine (T₃)



3,3',5'-triiodothyronine (reverse T₃)



Dehydroalanine (DHA)

These hormones play a critical role in cell differentiation during development and help maintain thermogenic and metabolic homeostasis in the adult

In considering the laboratory assessment of the patient with known or suspected thyroid disease, the physician should seek to arrive at both:

1. *a functional diagnosis*

2. *an anatomic diagnosis*

Laboratory determinations will confirm whether there is:

1. excess, (Hyperthyroidism)

2. normal, (Euthyroidism)

OR

3. insufficient (Hypothyroidism)

supply of thyroid hormones

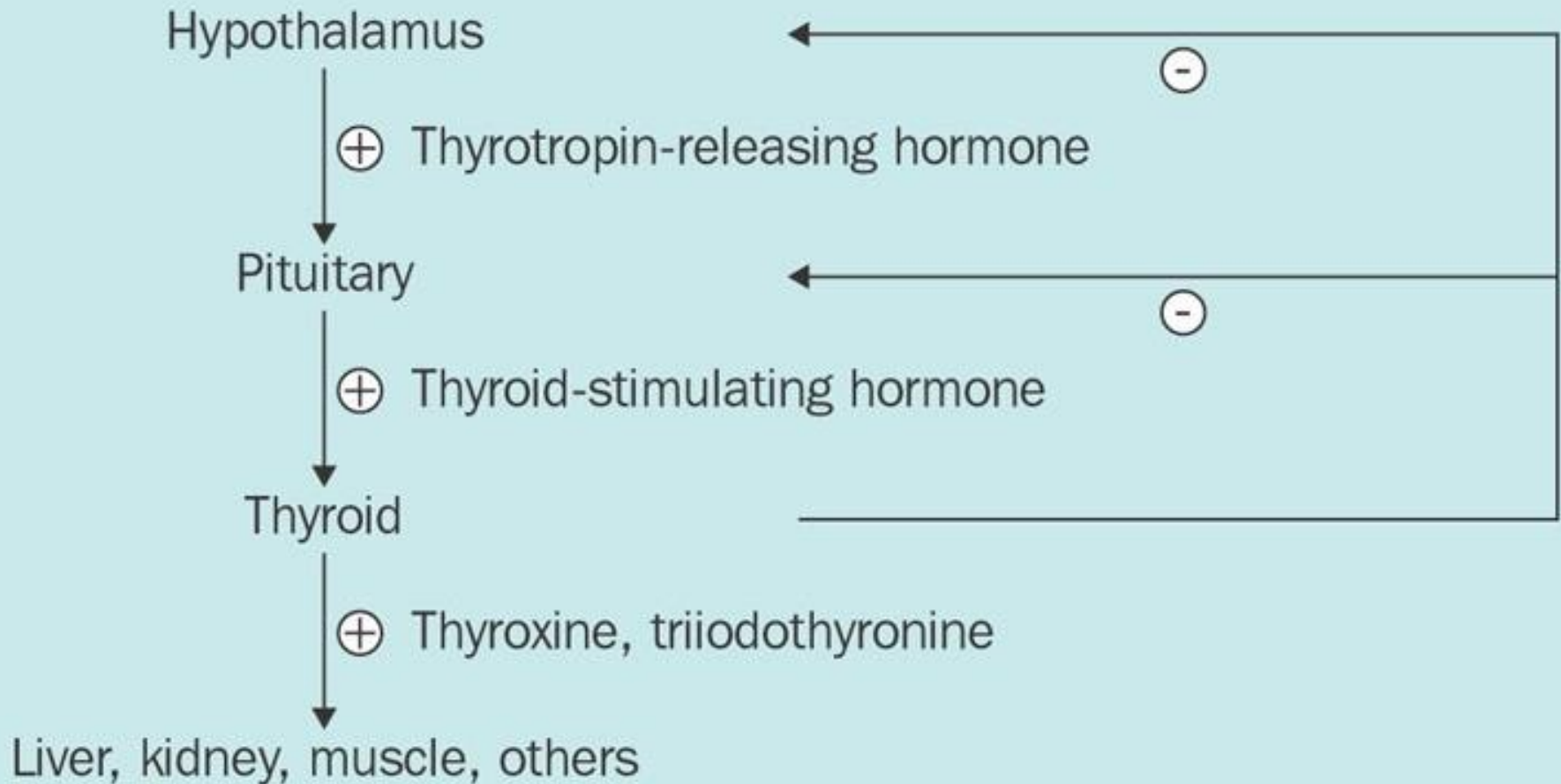
Laboratory tests can be divided

into five major categories:

- (1) those that assess the state of the hypothalamic-pituitary thyroid axis*
- (2) tests that estimate the T_4 and T_3 concentrations in the serum*
- (3) those that reflect the impact of thyroid hormone on tissues*
- (4) tests for the presence of autoimmune thyroid disease*
- (5) tests that provide information about thyroidal iodine metabolism.*

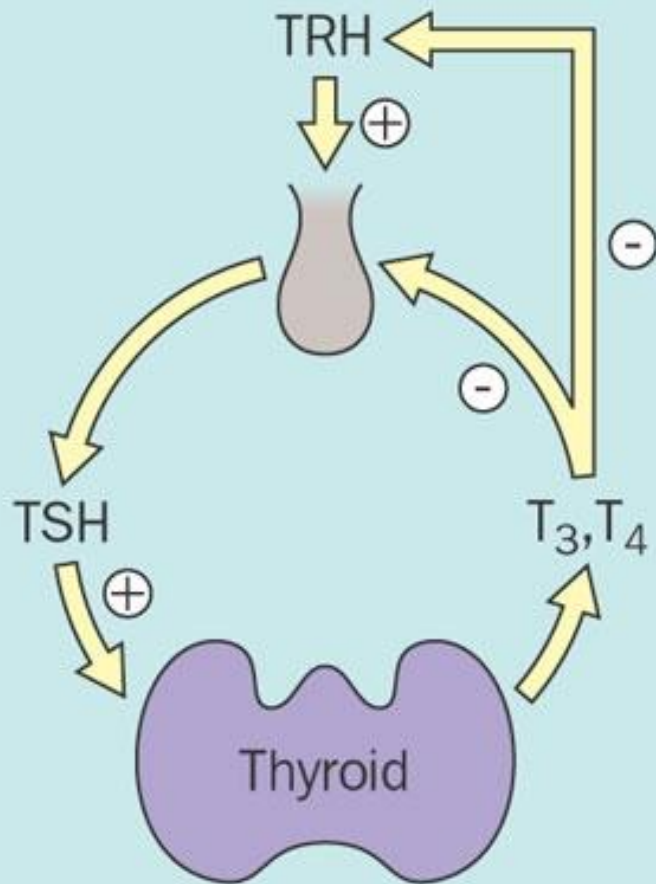
Tests of the Hypothalamic-Pituitary- Thyroid Axis

Regulation of thyroid hormones secretion

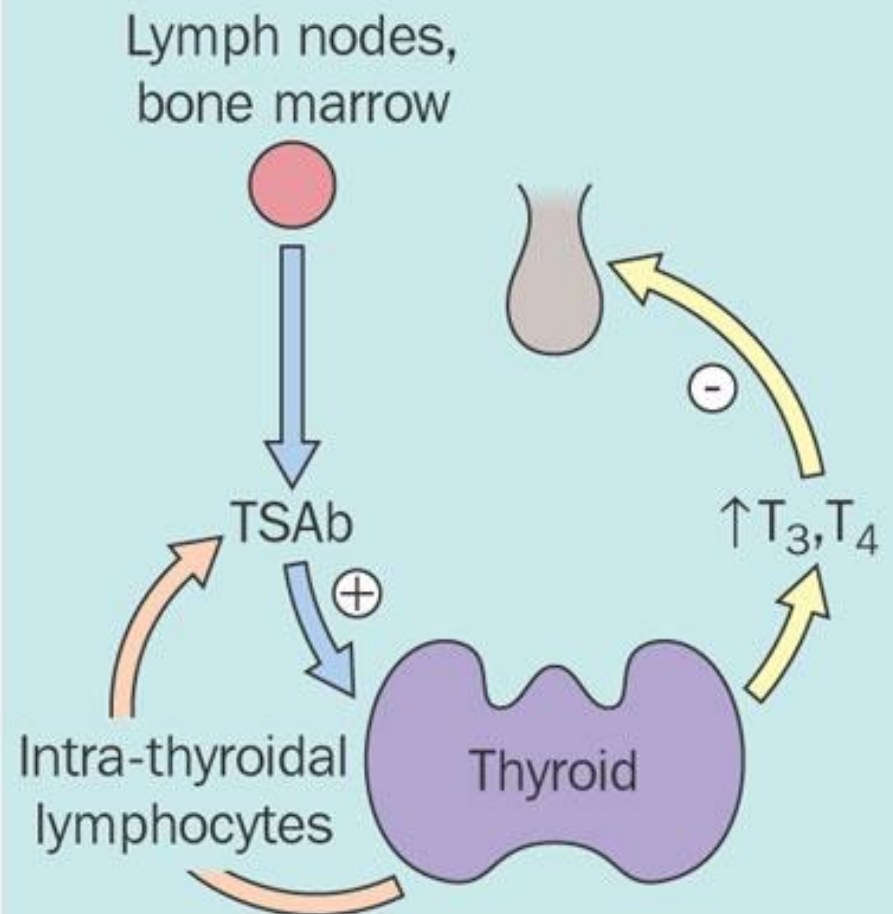


Disruption of the hypothalamic–pituitary–thyroid axis in Graves' disease

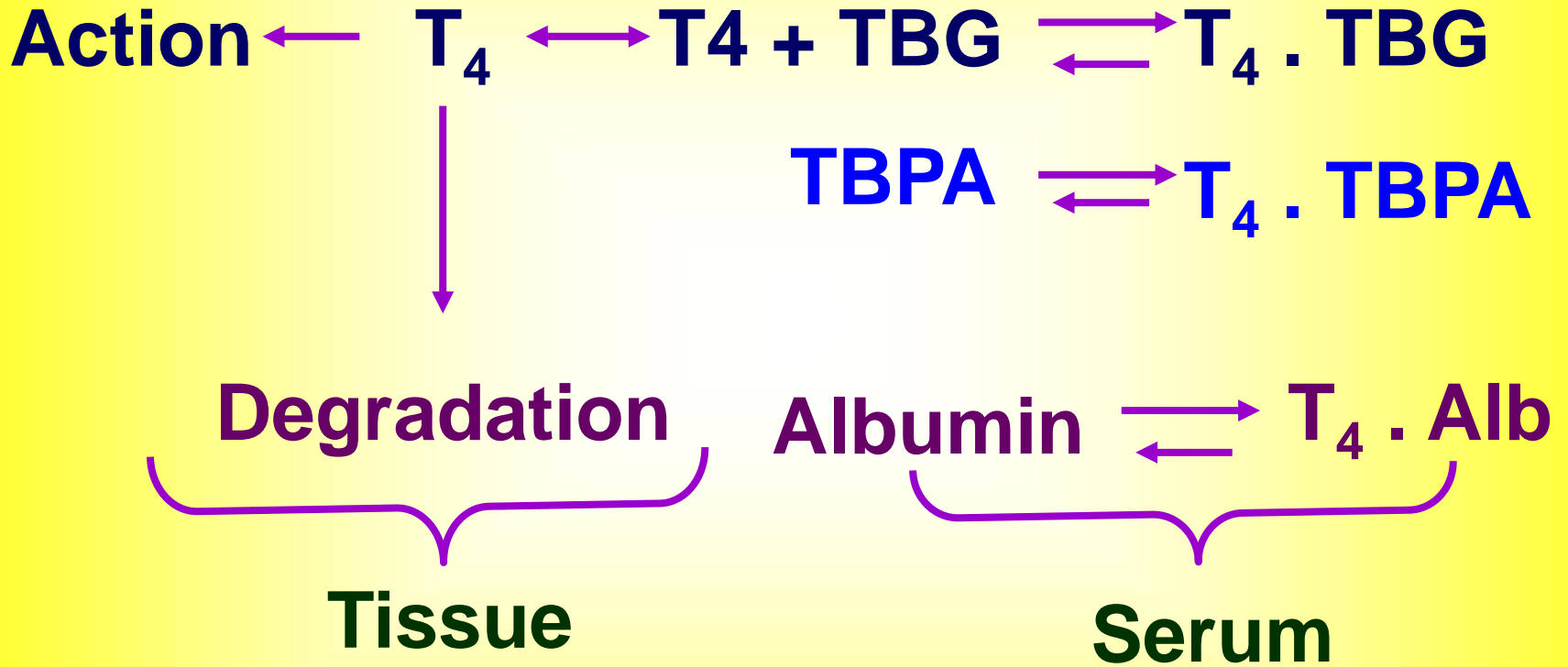
Normal relationship



Graves' disease



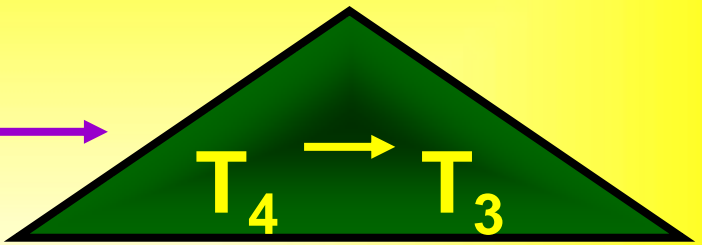
Thyroid



Thyroid

liver

T₃ + T₄



Action ← **T₃** ↔ **T₃ + TBG** ↔ **T₃ . TBG**

TBPA ↔ **T₃ . TBPA**

Degradation

⏟

Albumin ↔ **T₃ . Albumin**

⏟

Tissue

Serum

Circumstances Associated with Alterations in Binding of T4 by TBG

Increased Binding

Pregnancy

Neonatal state

Estrogens and hyperestrogenemic states

Tamoxifen

Oral contraceptives

Acute intermittent porphyria

Infectious and chronic active hepatitis

Biliary cirrhosis

Genetic determination

Perphenazine

HIV infection

Decreased Binding

Androgenic or anabolic steroids

Large doses of glucocorticoids

Active acromegaly

Nephrotic syndrome

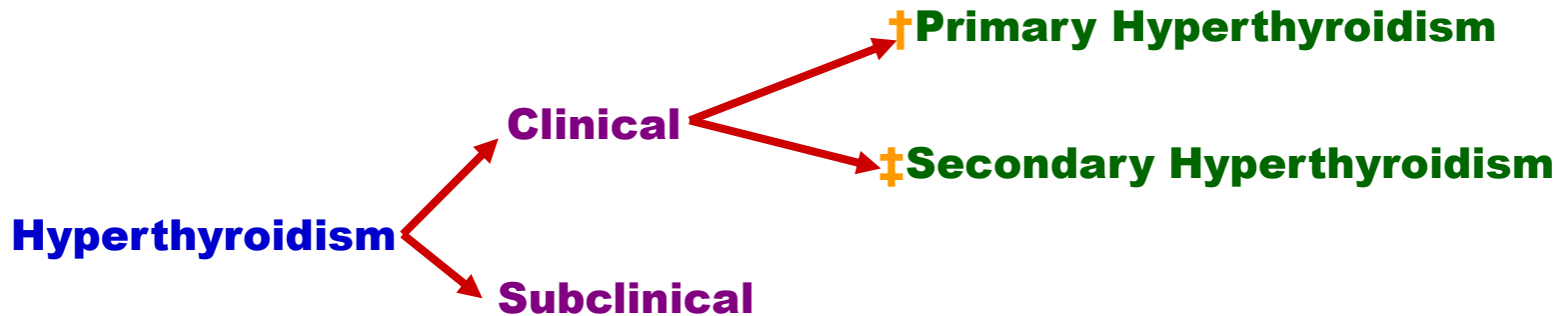
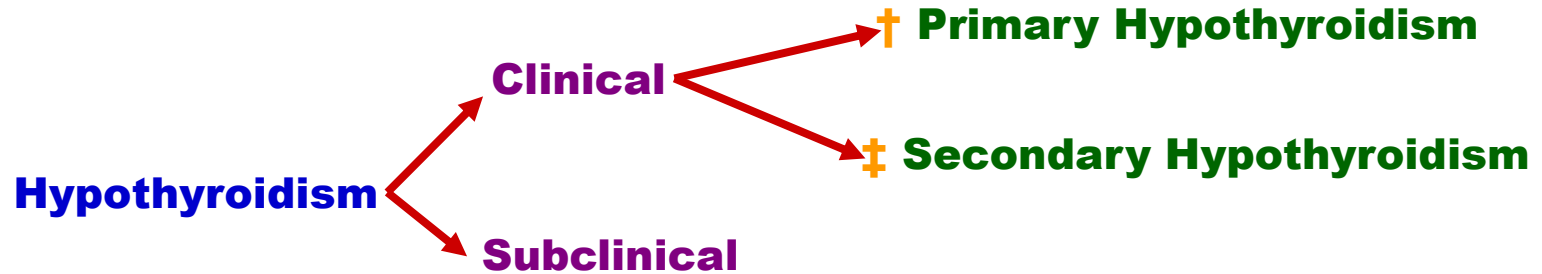
Major systemic illness

Genetic determination

Asparaginase

Patterns of Thyroid Function

Euthyroidism



† → Normal HP Axis → Thyroid dysfunction

‡ → Abnormal HP Axis → Thyroid dysfunction. Secondary to abnormal TSH Secretion

Clinical Utility of Thyroid-Related Laboratory Tests

NAME OF TEST	ABBREVIATION	CLINICAL UTILITY
Tests for Evaluation of Thyroid Status		
Thyrotropin (by asensitive IA) (by conventional RIA)	sTSH TSH	Best general test; should be phased out
Free thyroxine (by appropriate method)	FT₄	Second-best general test
Free (3,5,3') triiodothyronine	FT₃	Adjunct test, diagnosis of T ₃ toxicosis, rare forms of hyperthyroidism
Total (3, 5, 3' -) triiodothyronine	T₃	Used in lieu of FT ₃
Total thyroxine	T₄	Inadequate as general test
Thyroglobulin	Tg	Valuable in follow-up of thyroid cancer
TSH response to TRH	TRH	Largely superseded by sTSH
Reverse (3,3'5' -) triiodothyronine	rT₃	Not used routinely
Free T ₄ index:	FT₄I/FTI	
T ₄ × T ₃ -BR		Should be replaced by FT ₄
T ₄ × T ₄ -BR		Need further evaluation
T ₄ /TBG ratio	T₄/TBG	Should be replaced by FT ₄
Free T ₃ index (T ₃ × THBR)	FT₃I	Obsolete

Thyroid-Stimulating Hormone (TSH)

tests that assess the state of the hypothalamic-pituitary-thyroid axis play a critical role in the diagnosis of thyroid disease.

TSH in Patients with Thyroid Dysfunction

Patients with hyperthyroidism or thyrotoxicosis always have a subnormal TSH. The values fall into two general categories:

- 1) those between the lower limit of normal and 0.1 mU/L,*
- 2) (subclinical hyperthyroidism), and those less than 0.1 mU/L. symptomatic thyrotoxicosis*

TSH in Patients with Thyroid Dysfunction

Patients with primary hypothyroidism have serum TSH concentrations that range from minimally elevated to 1000 mU/L. Patients with serum TSH values in the range of 5 to 15 mU/L have few if any symptoms, Such individuals with modest TSH elevation are said to have subclinical hypothyroidism if the serum free T_4 is in the normal range.

TSH in Patients with Thyroid Dysfunction

An elevation in both serum TSH and free T_4 is unusual and indicates either autonomous TSH production, as with a TSH secreting pituitary tumor (TSH-oma) or resistance to thyroid hormone (RTH)

Clinical Utility and Limitations of TSH Immunometric Assays *Limitations.*

A subnormal sTSH is not entirely specific for, or diagnostic of, hyperthyroidism. A misleading, subnormal sTSH may be recorded in

- (1) hypopituitary or hypothalamic disease,**
- (2) in the first trimester of pregnancy,**
- (3) in patients with NTI and/or under treatment with dopamine, glucocorticoids, and certain other drugs, and**
- (4) in acute psychiatric illness.**

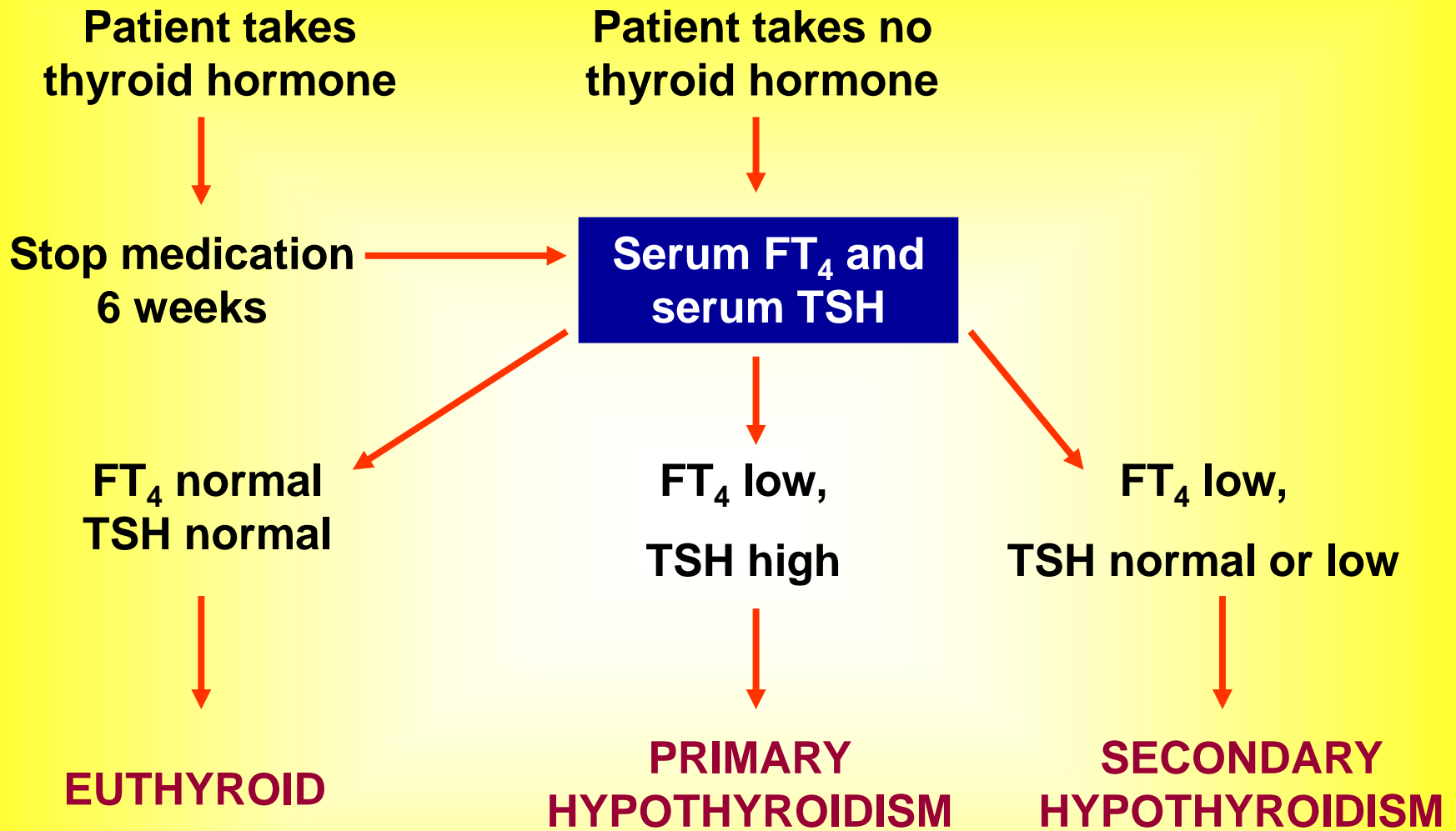
Elevated sTSH levels are not always a sign of hypothyroidism.

Causes of a low or undetectable TSH level

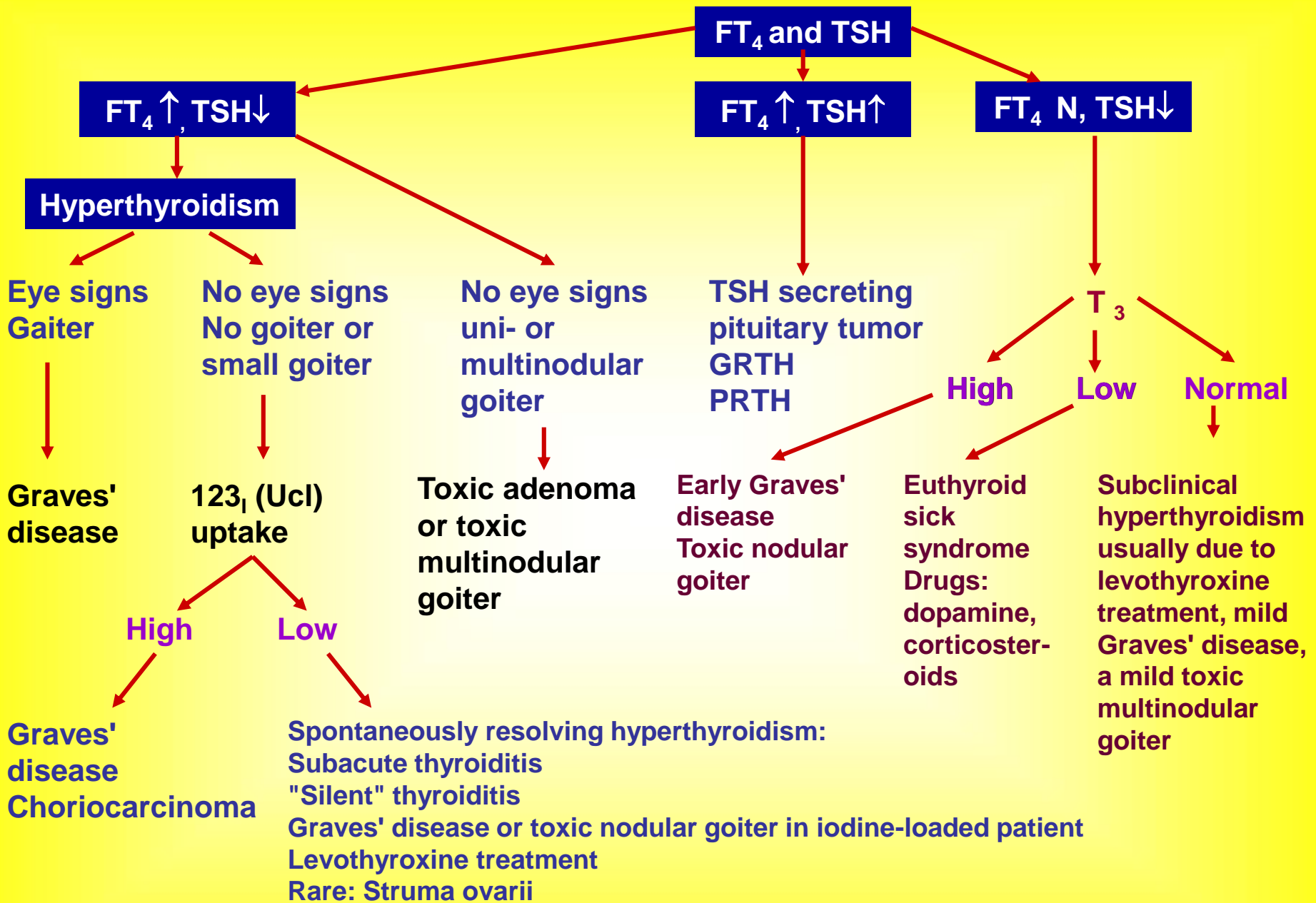
Lowered TSH

Free thyroid hormone levels

Overt thyrotoxicosis	↑
Subclinical thyrotoxicosis	N
Recently treated hyperthyroidism	N
Thyroid-associated ophthalmopathy without Graves' disease	N
Excessive thyroxine treatment	N or ↑
Nonthyroid illness (sick euthyroid syndrome)	↓ or N
First trimester of pregnancy	N or ↑
Pituitary or hypothalamic disease	N or ↓
Anorexia nervosa	N or ↓
Dopamine, somatostatin (acute effect)	N
Glucocorticoids	N

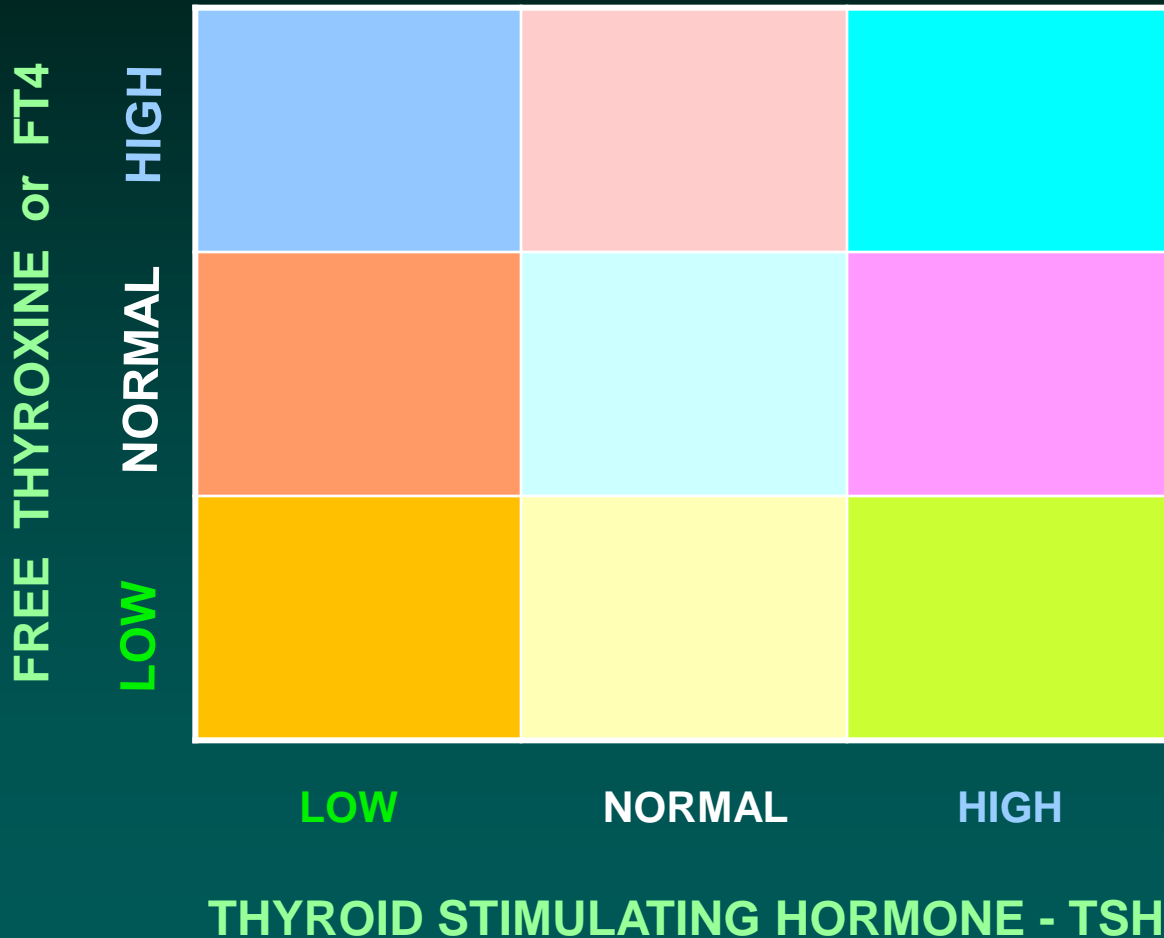


Diagnosis of hypothyroidism



Laboratory tests useful in the differential diagnosis of hyperthyroidism (see text for details)

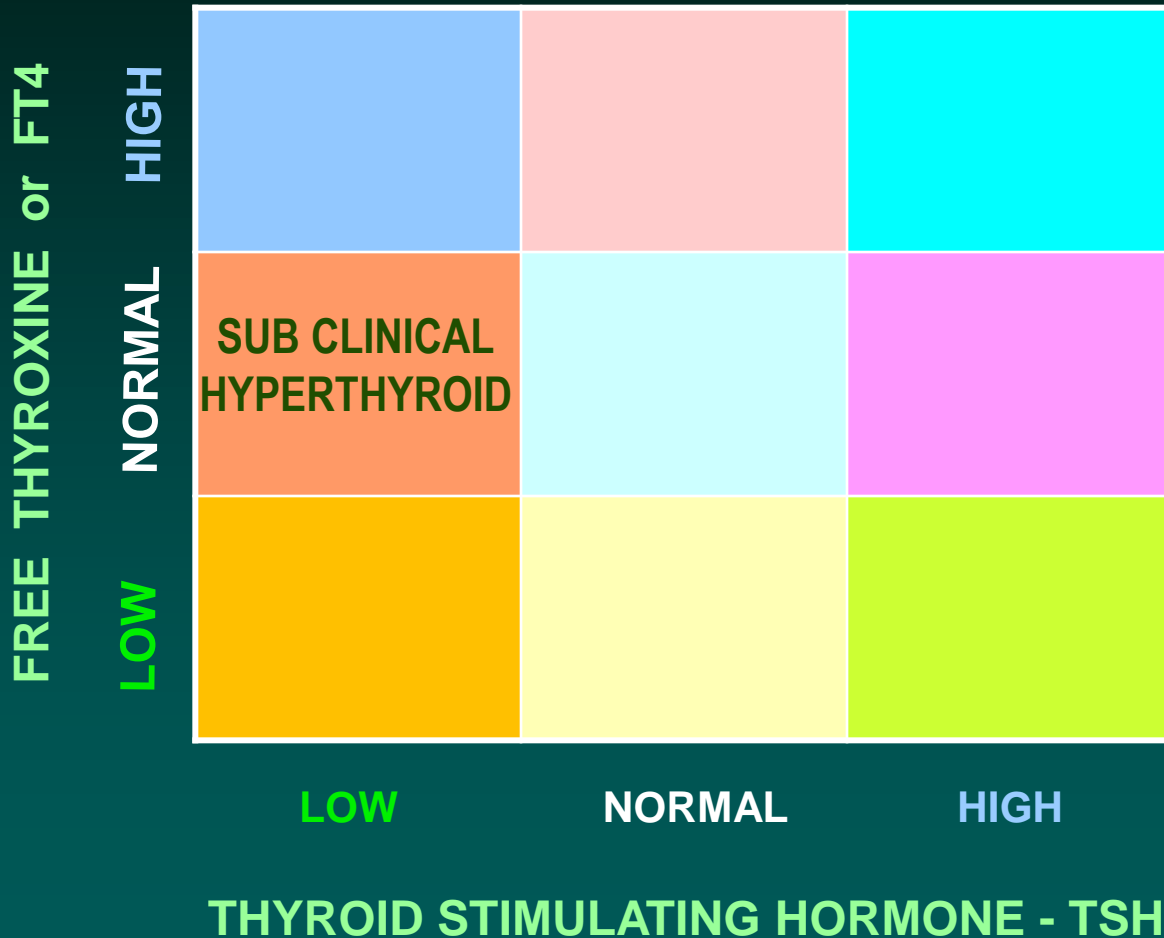
Nine Square Approach



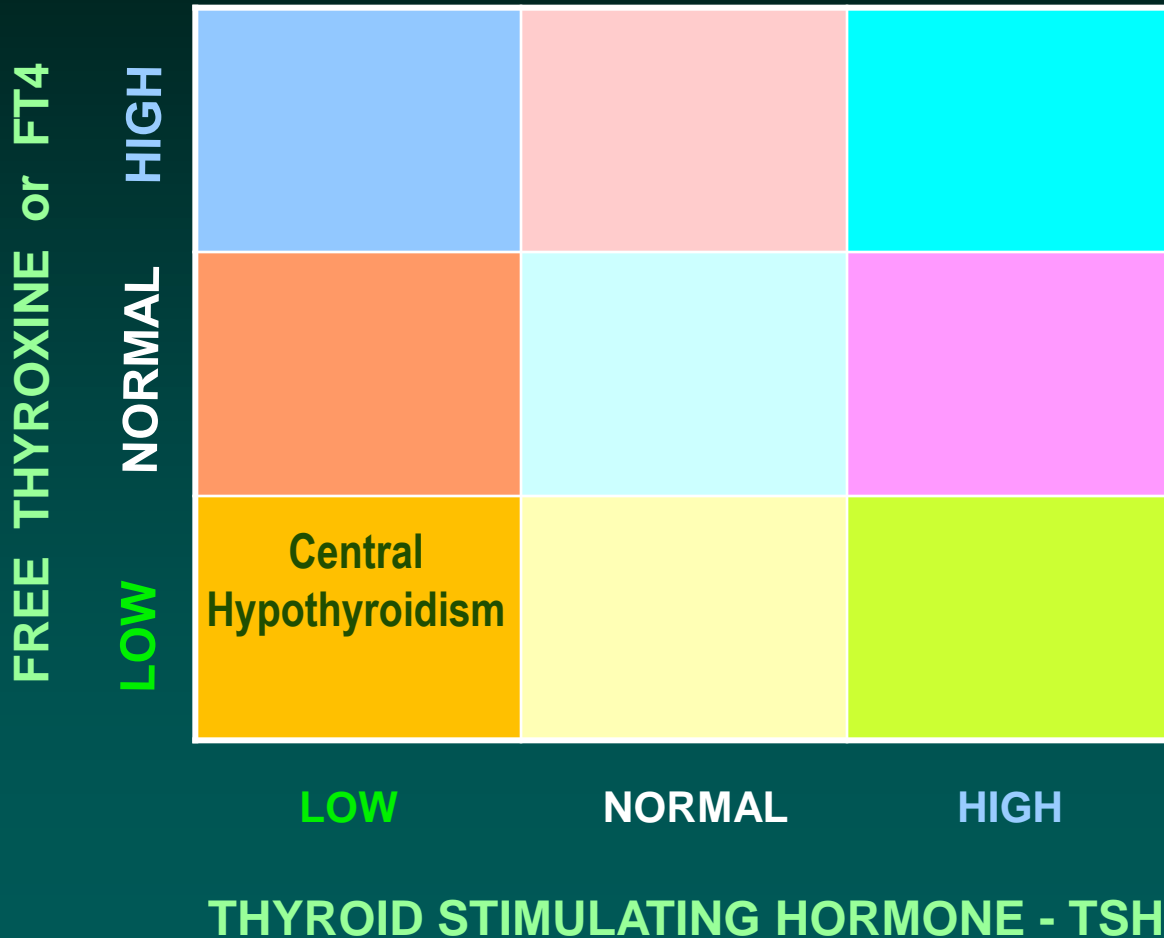
Nine Square Approach

FREE THYROXINE or FT4	HIGH	PRIMARY HYPERTHYROID		
	NORMAL			
	LOW			
		LOW	NORMAL	HIGH
		THYROID STIMULATING HORMONE - TSH		

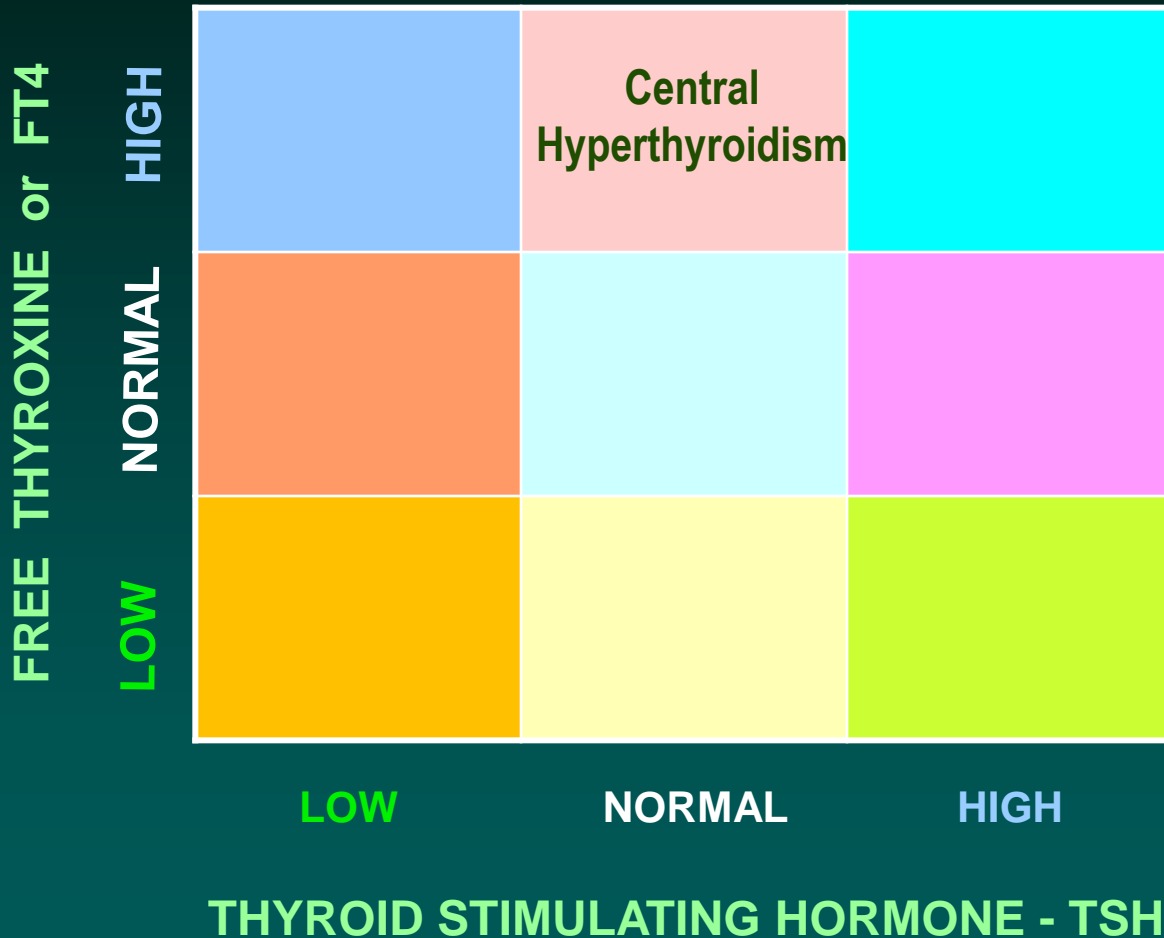
Nine Square Approach



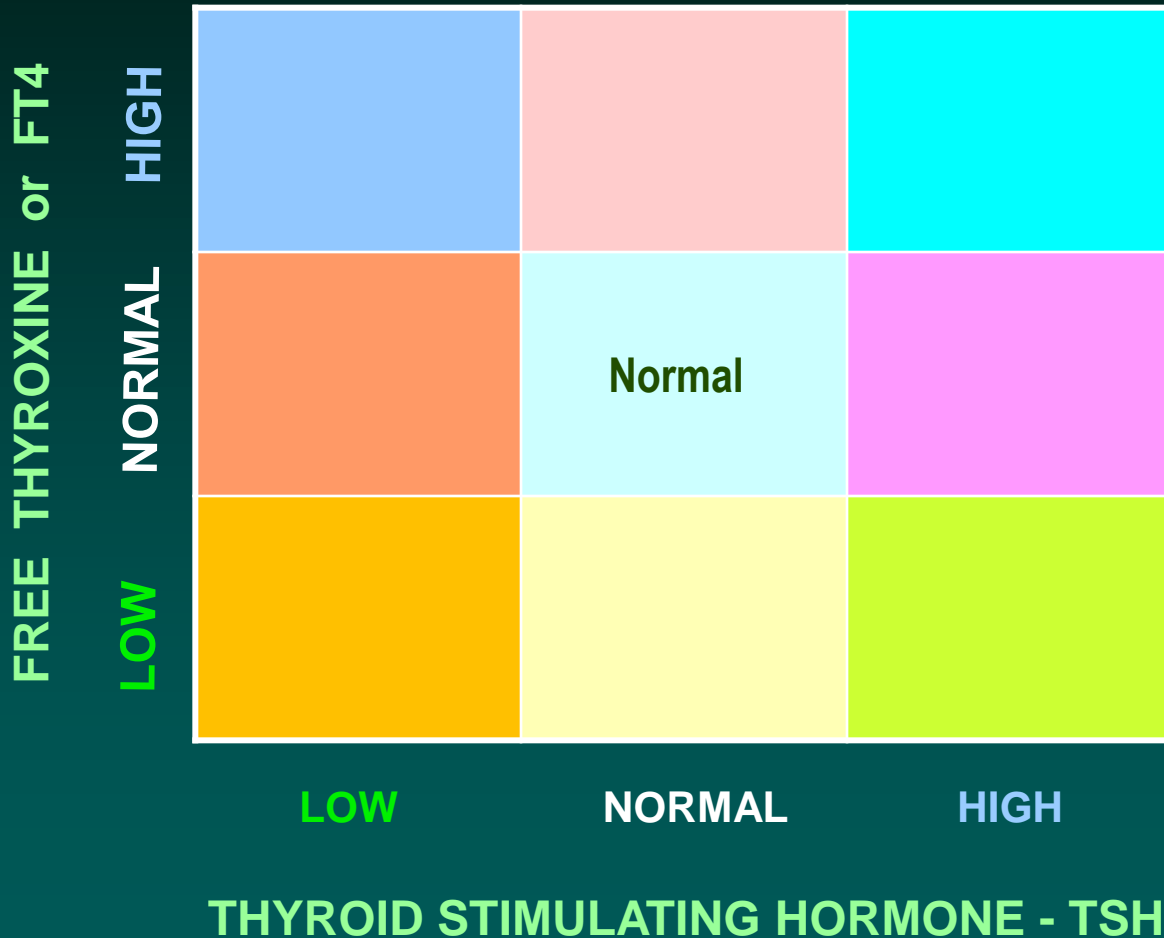
Nine Square Approach



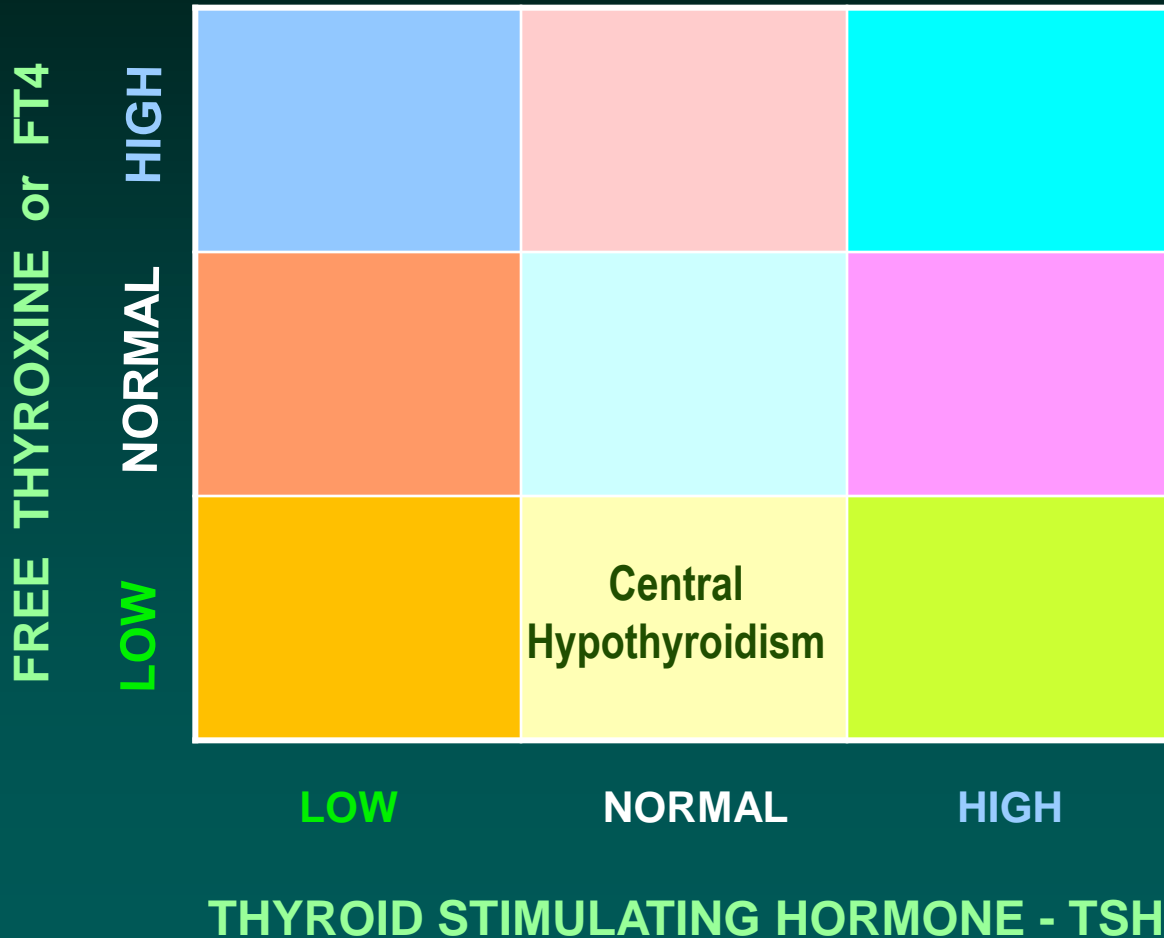
Nine Square Approach



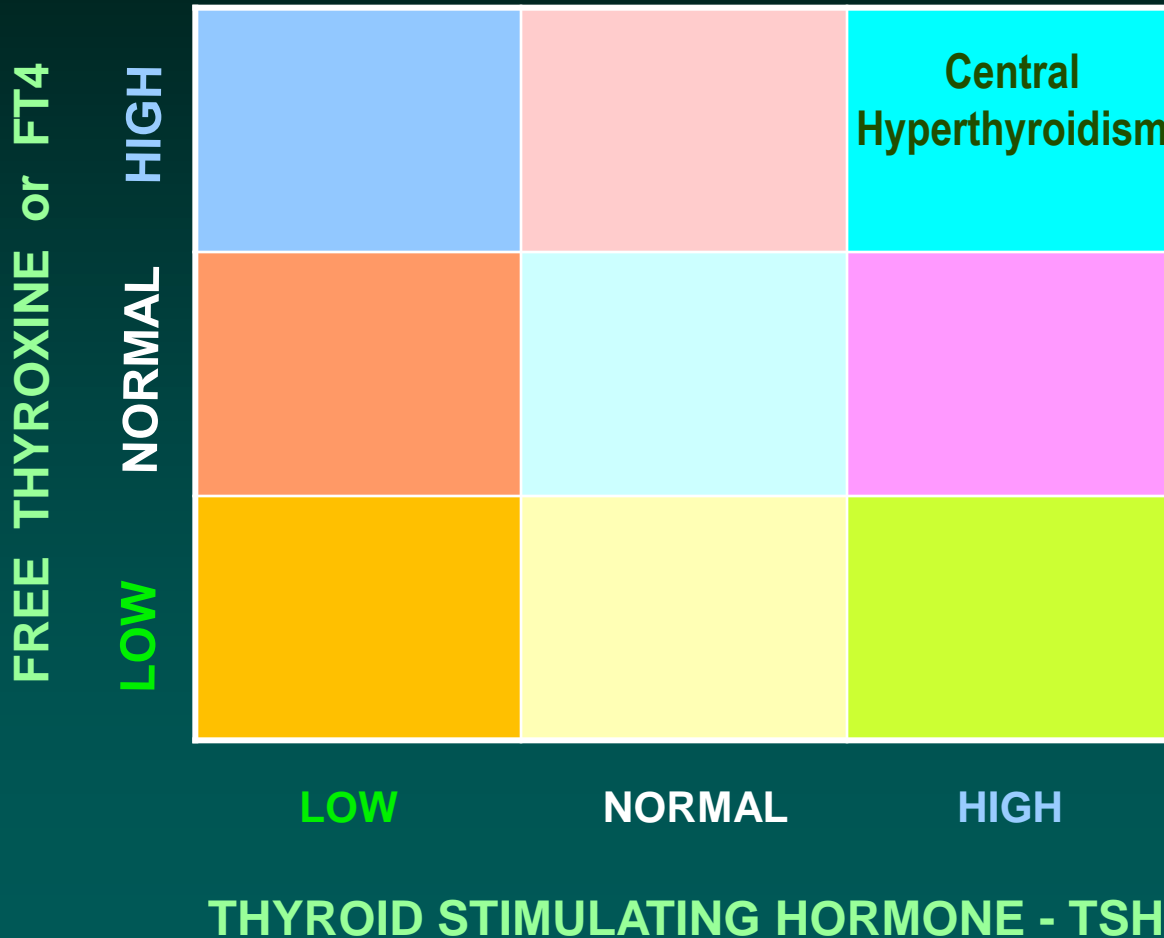
Nine Square Approach



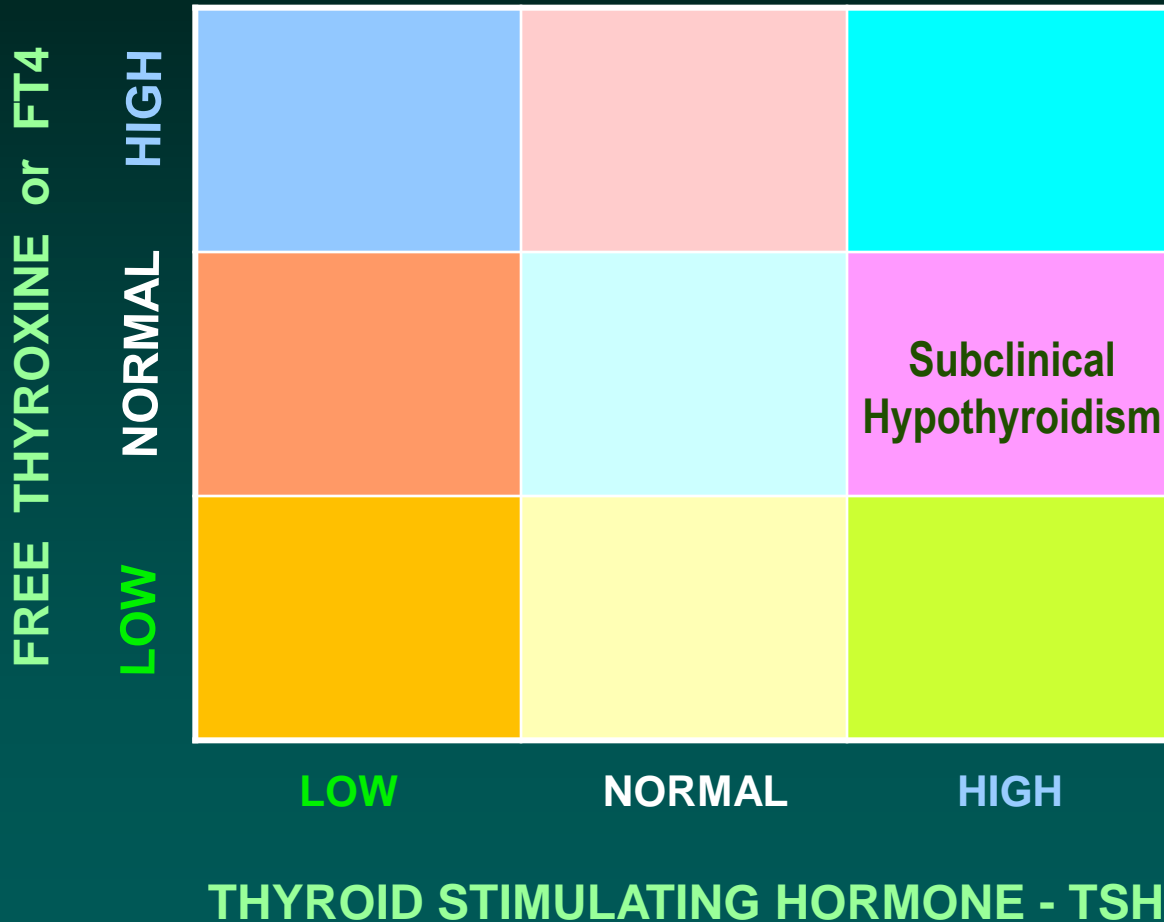
Nine Square Approach



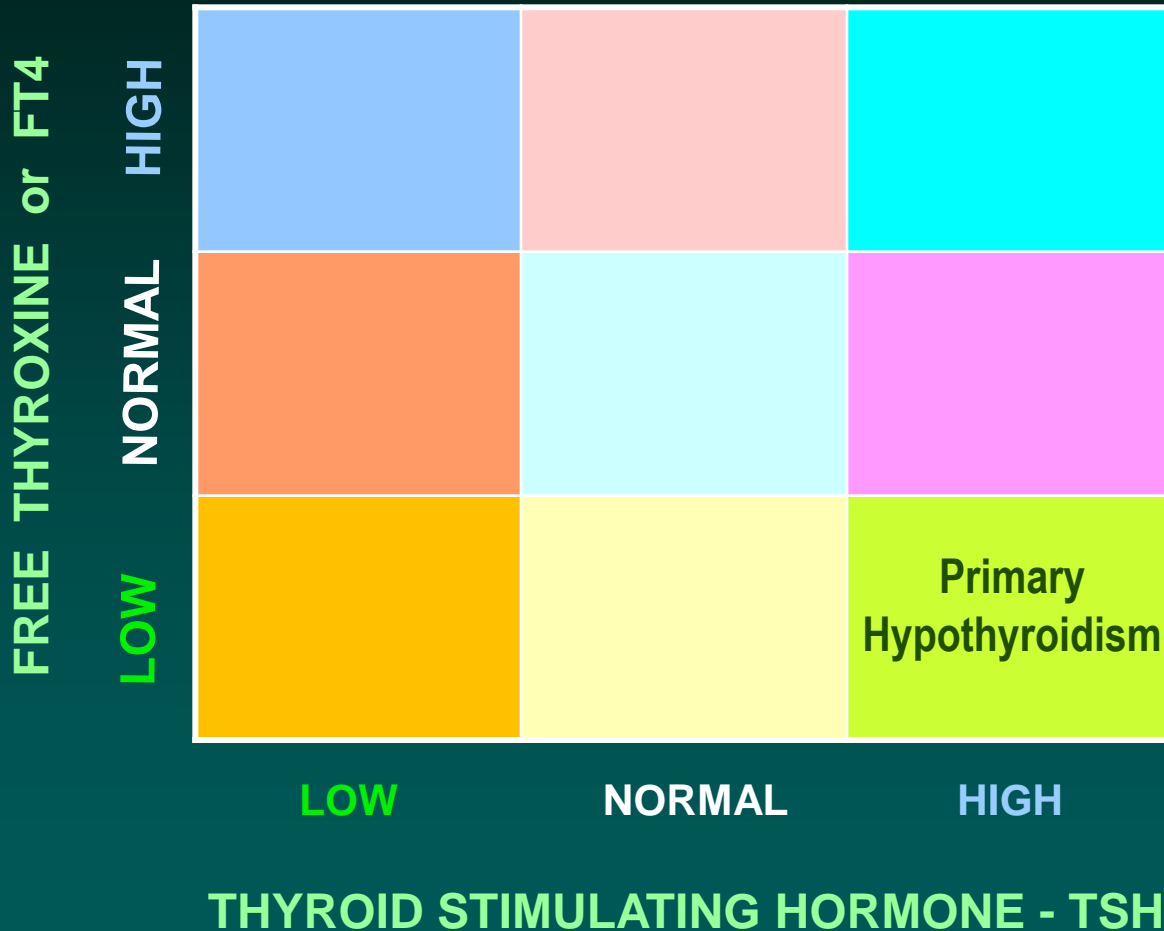
Nine Square Approach



Nine Square Approach



Nine Square Approach



Nine Square Approach

FREE THYROXINE or FT4	HIGH	PRIMARY HYPERTHYROID	Central Hyperthyroidism	Central Hyperthyroidism
	NORMAL	SUB CLINICAL HYPERTHYROID	Normal	Subclinical Hypothyroidism
	LOW	Central Hypothyroidism	Central Hypothyroidism	Primary Hypothyroidism
		LOW	NORMAL	HIGH
		THYROID STIMULATING HORMONE - TSH		

Case 1

35 y/o woman

- Asymptomatic L thyroid nodule, 3.5 cm
- P 80, negative PE otherwise
- eyes negative
- TSH = 0.04 mIU/L (0.3-5.0)
- FT₄ = 1.4 μg/dL (0.8-1.8)
- T₃ normal
- TPO antibodies negative

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- TSH = 0.04 mIU/L (0.3-5.0)
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- TPO antibodies negative

Case 1

Which is most likely to explain this curiosity?

- A. Functioning (i.e. "hot") thyroid nodule
- B. Subclinical Hypothyroidism
- C. Thyroid hormone resistance
- D. TSH secreting pituitary tumor
- E. Thyroxine autoantibodies

Case 2

54 y/o woman, GME

- mild fatigue, cold intolerance
- negative PE
- thyroid normal size and texture
- TSH = 11.0 mIU/L (0.3-5.0)
- FT₄ = 1.1 µg/dL (0.8-1.8)
- TPO antibodies negative

Case 2

54 y/o woman, GME

- mild fatigue, cold intolerance
- negative PE
- thyroid normal size and texture
- TSH = 11.0 mIU/L (0.3-5.0)
- FT₄ = 1.1 µg/dL (0.8-1.8)
- TPO antibodies negative

Case 2

Which is most likely to explain this curiosity?

- A. Functioning (i.e. "hot") thyroid nodule
- B. Subclinical Hypothyroidism
- C. Thyroid hormone resistance
- D. TSH secreting pituitary tumor
- E. TSH autoantibodies

Case 3

25 y/o woman

- Anxiety and weight loss
- Normal PE at time of annual gyne exam
- No meds except OCP's
- TSH = 2.2 mIU/L (0.3-5.0)
- TT4 = 14.0 μ g/dL(5 - 12.5)

Case 3

25 y/o woman

- Anxiety and weight loss
- Normal PE at time of annual gyne exam
- No meds except OCP's
- TSH = 2.2 mIU/L (0.3-5.0)
- TT4 = 14.0 μ g/dL(5 - 12.5)

Case 3

Which of the following could not explain the laboratory findings?

- A.** Functioning (i.e. "hot") thyroid nodule
- B.** Increased Thyroxine Binding Globulin (TBG)
- C.** Thyroid hormone resistance
- D.** TSH secreting pituitary tumor
- E.** TSH autoantibodies

Case 4

48 y/o man

- fatigue and cold intolerance
- decreased libido and erectile function
- thyroid not enlarged

- TSH = 2.2 mIU/L (0.3-5.0)
- FT₄ = 0.6 μg/dL (0.8-1.8)

Case 4

48 y/o man

- fatigue and cold intolerance
- decreased libido and erectile function
- thyroid not enlarged

- TSH = 2.2 mIU/L (0.3-5.0)
- FT₄ = 0.6 µg/dL (0.8-1.8)

Case 4

Which of the following is the most likely

explanation for this?

- A. Functioning (i.e. "hot") thyroid nodule
- B. Increased Thyroxine Binding Globulin (TBG)
- C. Thyroid hormone resistance
- D. TSH deficiency
- E. TSH autoantibodies

Case 5

25 y/o woman

- anxiety and tachycardia
- family history of hyperthyroidism and ^{131}I Rx
- HR=100
- 40 gm diffuse goiter
- eyes negative

- $\text{FT}_4 = 3.2 \mu\text{g/dL}$ (0.8-1.8)
- $\text{TSH} = 3.5 \text{ mIU/L}$ (0.3-5.0)

Case 5

25 y/o woman

- anxiety and tachycardia
- family history of hyperthyroidism and ^{131}I Rx
- HR=100
- 40 gm diffuse goiter
- eyes negative

- $\text{FT}_4 = 3.2 \mu\text{g/dL}$ (0.8-1.8)
- $\text{TSH} = 3.5 \text{ mIU/L}$ (0.3-5.0)

Case 5

Which of the following is the not a cause of inappropriate TSH secretion?

- A. Generalized Resistance to Thyroid Hormones (GRTH).
- B. Exogenous Thyroid Hormone Poisoning
- C. Acute Mania
- D. TSH Secreting Pituitary Tumor
- E. D- T_4 therapy

هر یک از نتایج آزمونهای عملکرد تیروئید را با تشخیص مناسب ارائه شده مطابقت (Match) دهید:

	Free T4 ng/dL (N: 0.8 – 1.9)	TSH mIU/L (N: 0.4 – 4.2)
1	4.6	5.2
2	0.4	10
3	1.4	12
4	5.7	0.06
5	1.6	0.09
6	0.6	0.2
7	2.2	5.5
8	3.6	42

الف - Amiodarone use (400 mg/day of 4 weeks duration)

ب - Bexarotene for T-cell Lymphoma

ج - Subclinical thyrotoxicosis

ه - Graves Hyperthyroidism

و - Subclinical Hyperthyroidism

ز - Central Hypothyroidism

ح - TSHoma

ط - Artifactual TSH elevation



Diagnostic Utility of the Free Thyroxine Index Values

	Total T ₄	T ₃ U	FT ₄ Index
Euthyroid	N	N	N
Hyperthyroid	↑	↑	↑
Hypothyroid	↓	↓	↓
Increased TBG	↑	↓	N
Decreased TBG	↓	↑	N