

THYROID FUNCTION TEST

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Epidemiology

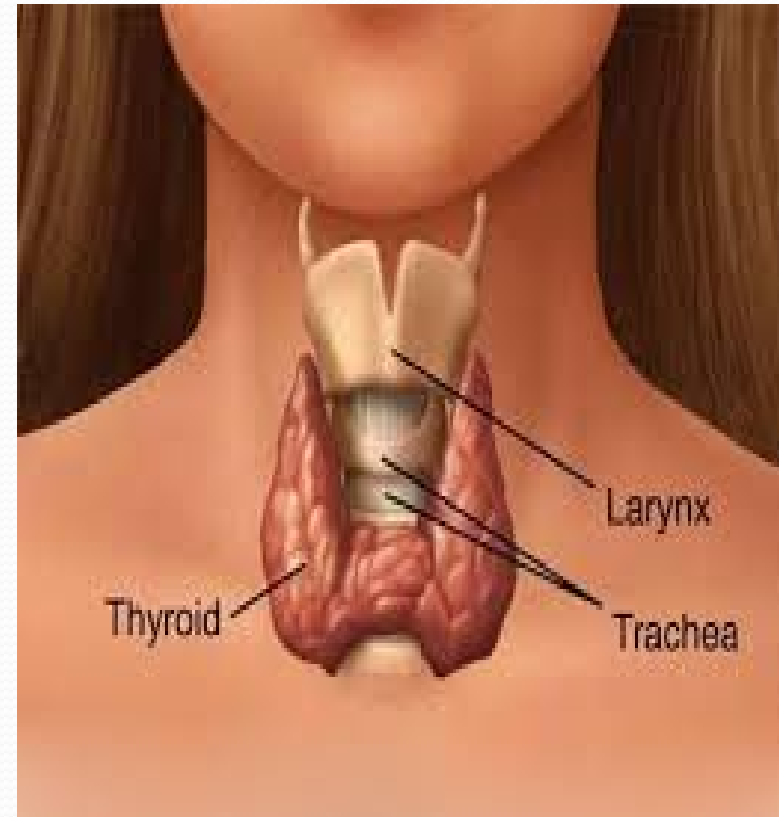
According to the Indian Thyroid Society, it is estimated that **4.2 crore people in the country** are suffering from thyroid disorders with almost **90 per cent undiagnosed**.

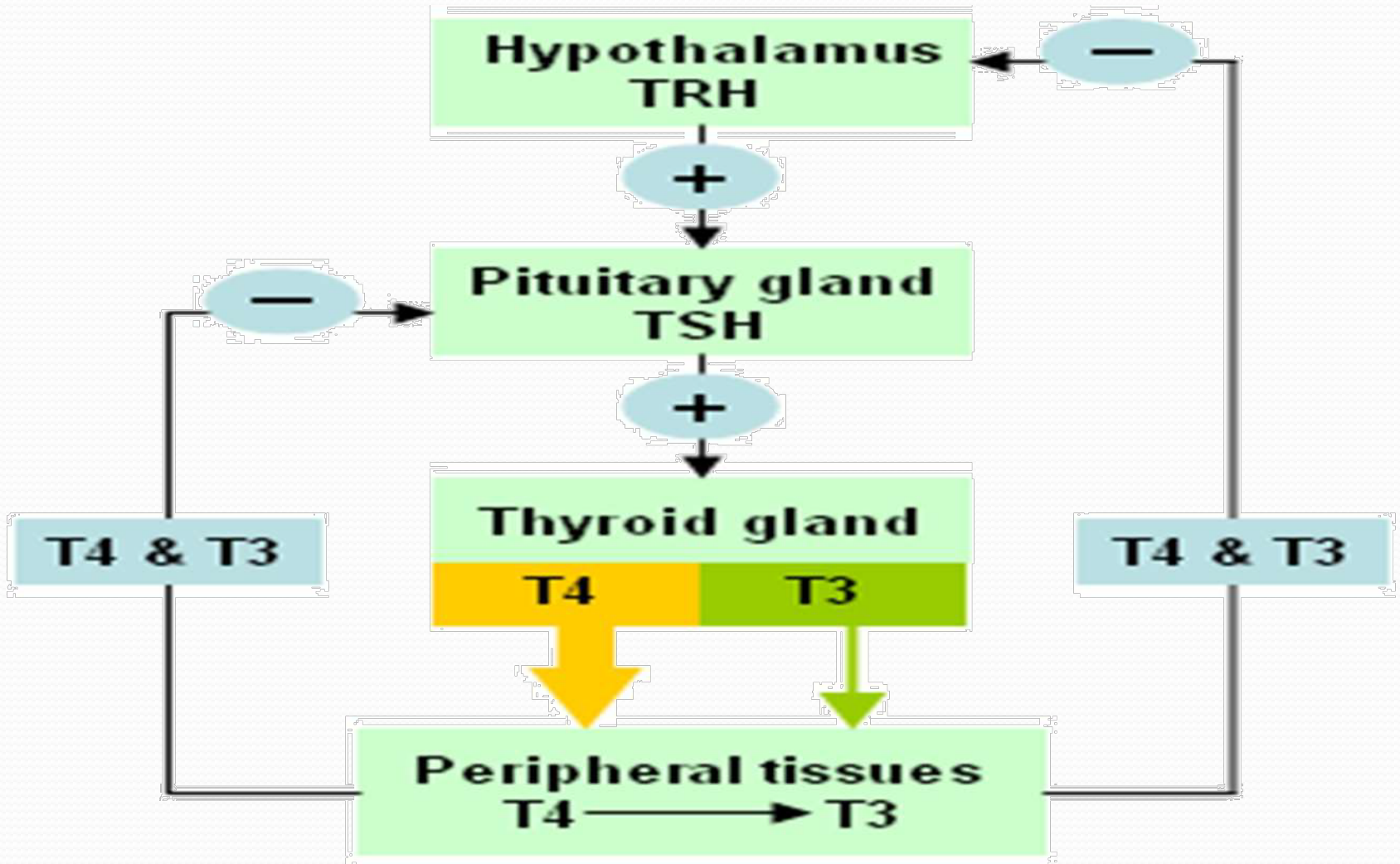


Anatomy of Thyroid gland

The thyroid gland is a butterfly-shaped endocrine gland that is normally located anterior side of the neck lying in front & around the larynx & trachea just below the laryngeal prominence.

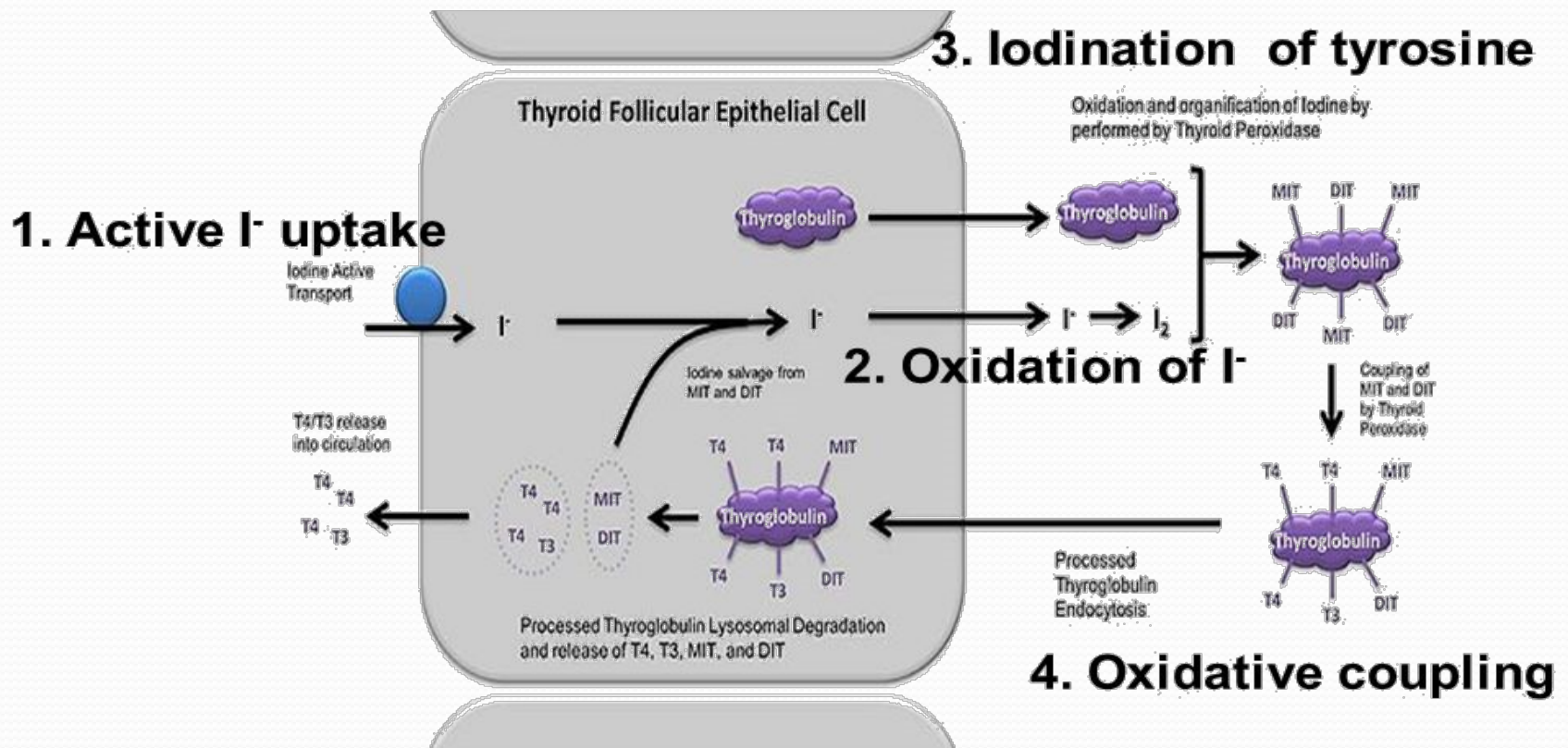
(Adam's apple)





Biosynthesis of thyroid hormones

Biosynthesis of T3 and T4



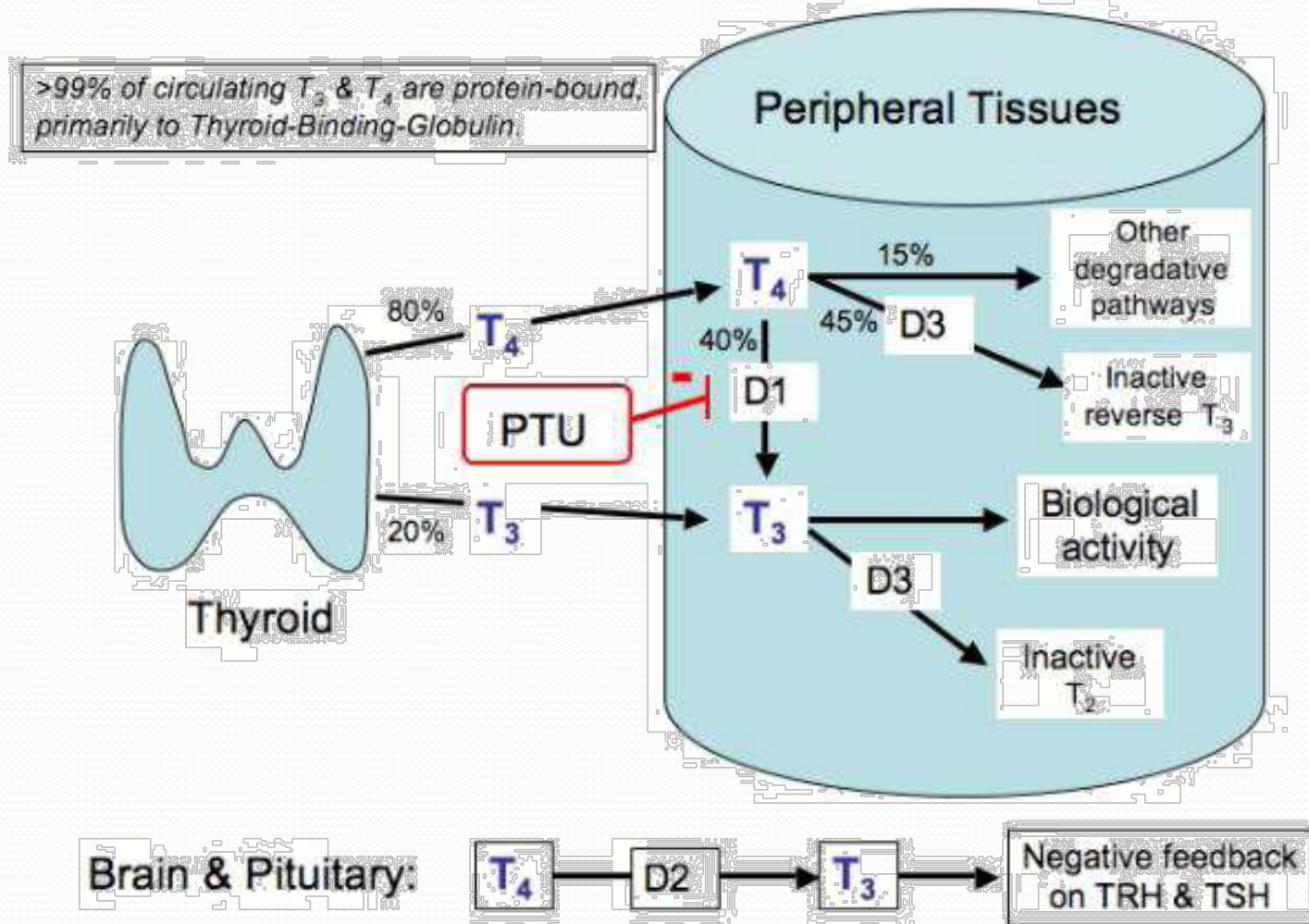
Steps:

- 1. Iodide (I⁻) enters the thyroid cell via sodium iodide symporter
- 2. It enters the colloid through pendrin receptor
- 3. It is oxidized into Iodine (I₀) by peroxidase enzyme
- 4. Then it is organified into MIT and DIT (mono and di iodo thyronine)
- 5. Then after coupling it forms T₃ (Tri iodo thyronine) and T₄ (Thyroxine)
- 6. T₃ and T₄ conjugate with TBG (thyroid binding globulin)
- 7. conjugated TBG is stored in colloid till required
- 8. While releasing into blood stream, it is first endocytosed into thyroid cell and then de - coupled to form, T₃ and T₄ with MIT and DIT
- 9. MIT and DIT can be reutilized for coupling

• 10. T₃ and T₄ are released into the blood stream



What happens to thyroid hormones after release



D2 catalyzes production of T_3 for negative feedback

Concept of FT₃ and FT₄

- 1. Out of the total T₃ and T₄ in circulation, most of it remains bound to thyroid binding globulin *, prealbumin and albumin. (*note :this is not thyroglobulin)
- 2. Only about 0.05% of each T₃ and T₄ remains free in circulation. This is FT₃ and FT₄.
- 3. **These are better indicators for thyroid function than total T₃ and Total T₄.** (total=bound+free)
- 4. For example in pregnancy, level of thyroid binding globulin rises; hence though total T₃ and total T₄ remains same, level of FT₃ and FT₄ decreases.



CLASSIFICATION OF THYROID DISEASE

HYPO
THYROIDISM-
MOST
COMMON

HYPER
THYROIDISM

SUB CLINICAL
CASES-
1.HYPO
2.HYPER
(ASYMPTO-
MATIC
CASES)



Hypothyroidism

Causes:

Primary Hypothyroidism (High TSH, low T₃ and T₄)

1. Iodine deficiency
2. Goitrogens (excess amount interfere in iodine uptake)
 - SOY products
 - strawberry,
 - Sweet potatoes
 - cabbage, cauliflower, spinach
 - Broccoli
 - Millet etc.
3. Hashimoto's
 - (anti microsomal antibodies)
4. Iatrogenic – surgery
 - Anti thyroid drugs,
 - Radiation



Secondary hypothyroidism (Low TSH with normal TRH)

- i.e. pituitary problem
- diseases of pituitary

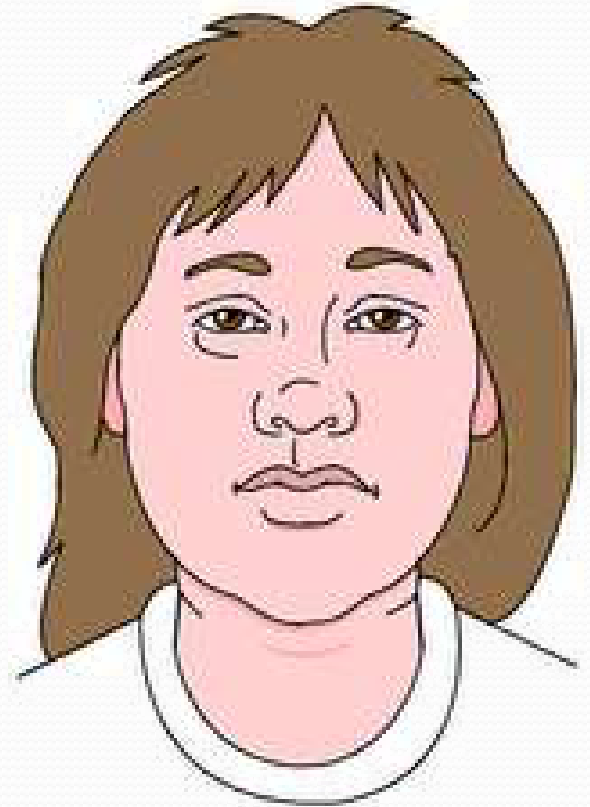
Tertiary hypothyroidism (LOW TSH, Low TRH)

- i.e. hypothalamic problem
- 1. diseases of the hypothalamus
- Exaggerated response to TSH RH stimulation
- Rise and Delayed response to TSH-RH stimulation



Common Signs and Symptoms of Hypothyroidism

- Dry skin
- Brittle and lustreless hair
- Weight gain
- Tiredness
- Constipation
- Muscle aches
- Bradycardia
- Cold intolerance
- Depression
- Memory Loss
- Menstrual abnormality



Lab abnormalities in hypothyroidism

- Hyper lipidemia
- Anemia (macrocytic-due to vit B12 def)
- High LDH
- High CPK
- Hyper prolactemia
- Hypo natremia



Hyperthyroidism Causes:

Primary hyperthyroidism Low TSH, High T₄	Secondary Hyperthyroidism High TSH, High T₄ Pituitary/Para neoplastic syndrome	Factitious Hyperthyroidism
<ol style="list-style-type: none">1. Grave's disease2. Toxicity in Multi nodular goitre3. toxicity in adenoma4. Sub acute thyroiditis	<ol style="list-style-type: none">1. TSH secreting pituitary adenoma2. Tropho blastic tumours that secrete TSH (chorio carcinoma, H. mole)	Exogenous ingestion of large dose of thyroid hormone.



Common Signs and Symptoms of Hyperthyroidism

- **Warm moist skin**
- **Hair loss**
- **Weight loss**
- **Nervousness**
- **Increased bowel movements**
- **Muscle weakness**
- **Tachycardia**
- **Heat intolerance**
- **insomnia**
- **Difficulty in concentrating**
- **Light or Absent periods**



Laboratory findings in Hyperthyroidism

- TSH nearly undetectable
- Elevated FT₄ or FT₃
- Mild leuko penia
- N/N anemia
- ESR elevated
- ↑ed hepato cellular enzymes
- Mild ↑ Ca⁺⁺
- ↓ Albumin
- ↓ Cholesterol



TRH Stimulation test

Indication:

- To rule out secondary or tertiary hypo/hyper thyroidism

Baseline sample collected for estimation of basal serum TSH levels



Inject TRH (200 to 500 ug i.v)



Measure TSH at 20 & 60 mins



	Baseline TSH	20 min TSH	60 min TSH	interpretation
	Normal	Rise of >2mU/L	Small decline	normal
Hypothyroidism	Elevated	Further rise	Small decline	Primary hypothyroidism
	Low	No rise		Secondary hypothyroidism (pituitary)
	Low	rise	Further rise (delayed)	Hypothalamic hypothyroidism
Hyperthyroidism	elevated	rise		Thyroid hormone resistance
	elevated	No rise		Pituitary adenoma/ para neoplastic

THYROID FUNCTION TEST

INDICATION

- Suspicion of thyroid disease based on clinical signs and symptoms.
- Screening for thyroid disease.
- Evaluation of treatment for thyroid disease.



Thyroid Disease – Who Is At Risk ?

- All new borns (neonatal screening)
- Personal history of thyroid disease
- Strong family history of thyroid disease
- Have an autoimmune disease, such as Type 1 Diabetes
- Some genetic conditions (e.g. Down, Turner syndromes)
- Past history of neck irradiation
- Drug therapies such as lithium and amio darone



- **Women over age 35**
- **Elderly patients**
- **Pregnant women during the first trimester**
- **Women 6 weeks to 6 months post-partum**
- **Have elevated lipid levels**



BLOOD test to evaluate thyroid disease:

TSH ,T₄ ,T₃

FT₄ , FT₃: Free hormone(Active metabolite)

rT₃ :(inactive metabolite)high in NTI , newborn, hyperthyroidism

Thyro globulin mesurement

Thyroid antibodies: AntiTPO antibodies, (microsomal)
TSH receptor Abs
Anti TG antibodies

Urinary iodine mesurement

Thyroxine binding globulin:



METHODS USED TO MEASURE THYROID HORMONES

RIA

- Radioimmunoassay

ELISA

- Enzyme-linked immunosorbant assay

CLIA

- Chemiluminescent immunoassay

FIA

- Fluorescent immunoassay

Principle of FT₄ measurement by immunoassay method.

- High affinity hormone Abs measure free hormone as a fraction of binding site occupancy. Means (unoccupied Abs sites are **inversely** proportional to free hormone.)
- Hormone labeled tracer quantified free hormone level & passing signals which are converted to concentration using calibrators.



Factors limit the validity of free T₄ IMMUNO ASSAY method

- **1. Dilution effects & protein dependence:** dissociation of bound ligand occurs with sample dilution
- **2. Anomalous protein binding of tracer:** Certain tracer used in FT₄ assay have high binding capacity to protein (albumin) → so in serum less tracer available for free Abs binding site → false high FT₄; while (in dialysis pts, low protein → more tracer bind to Abs → False Low FT₄.)
- **3. Heparin effect:** Heparin induce sample → ↑ed lipase activity (if TG is high, Albumin is low, temp is prolong at 37C → high non esterified fatty acid → inhibit binding of T₄ to serum protein in vitro only → false high FT₄.)
- **4. Dysalbuminemic hyper thyroxinemia** pts have abnormal proteins which bind T₄, so spurious result of FT₄ varies depending on labs.
- **Most accurate methods are:** Equilibrium dialysis (time consumable), Ultra filtration (avoid dilution effect), mass spectroscopy. When FT₄ is not correlate persistently with other parameter, method should be change.



Thyro globulin measurement

- Thyroglobulin: One kind of organ specific protein.
- Increased in Thyroid mass , injury , inflammation , TSH stimulation.

Indication in practice:

- 1.congenital hypothyroidism(thyroiddysgenesis(low)/
dyshormonogenesis (high))
- 2.endemic goiter area, to monitor iodine supplementation.
- 3.Differentiated thyroid cancer cases ,after Sx to monitor recurrence
- 4.Thyrotoxicosis factitia: endogenous thyrotoxicosis(\uparrow TG),
exogenous ingestion of thyroid hormone(\downarrow TG)



Drugs alter thyroid function test

Alter secretion of T ₃ ,T ₄	↑ TBG	↓ TBG	Competition with binding protein	Induction of metabolism	Activation from T ₄ to T ₃	Central TSH suppression
Thionamide	Estrogen	Androgen	Aspirin	Phenytoin	Amiodarone	Dopamine
Ethionamide	Narcotics	Danazol	Heparin	Carbamazepine	Propylthiouracil	Dobutamine
Lithium	5-FU	Nicotinic acid	Furosemide (high dose)	Phenobarbitone	Dexamethasone	Octreotide
	Clofibrate	L-asparaginase		Rifampicin	Radio-graphic agent	
				Oxcarbazepine		



Normal range of TFT in infant & children

Age	FT ₄ (ng/dl)	T ₄ (ug/dl)	FT ₃ (pg/dl)	T ₃ (ng/ml)	TSH(mu/L)	TBG(mg/dl)
Cord blood	0.9-2.2	7.4-13.0		15-75	1.0-17.4	2.5-5.1
1-4 days	2.2-5.3↑	14.0-28.4↑	180-760	100-740↑	1.0-39.0↑	
2-20 weeks	0.9-2.3↓	7.2-15.7↓	185-770	105-245↓	1.7-9.1↓	2.1-6.0
5-24 months	0.8-1.8↓	7.2-15.7	215-770	105-269	0.8-8.2	
2-7 years	1.0-2.1↑	6.0-14.2	215-700	94-241	0.7-5.7↓	2.0-5.3
8-20 yrs	0.8-1.9	4.7-12.4↓	230-650	80-210	0.7-5.7	1.8-4.2
1-45 years	0.9-2.5	5.3-10.5↓	210-440	70-204	0.4-4.2	1.8-4.2



PRE TERM BABIES

- Preterm term baby has their own unique set of thyroid function tests & its directly co relate with gestation age & birth weight.
- Usually preterm babies have” **low T₄-non elevated TSH** “ result in screening programe.

Because

- 1.discontinuation of maternal T₄.
- 2.immaturity of hypothalamic-pitutary stimulation(low TSH surge).
- 3.immaturity in thyroid hormone production.
- 4.low iodine intake(due to i.v fluids).
- **repeat test is indicated in most cases.**





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YOU*

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