

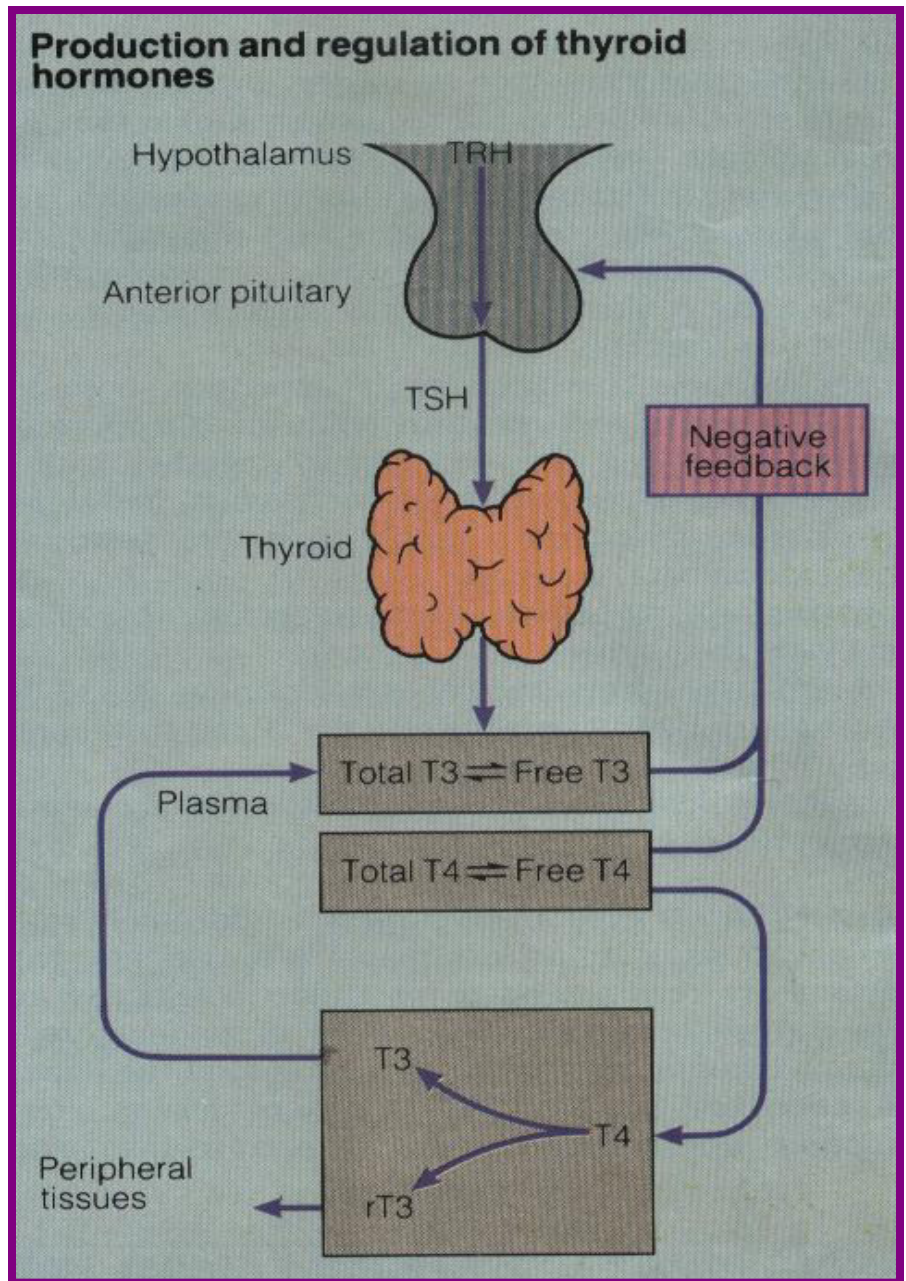
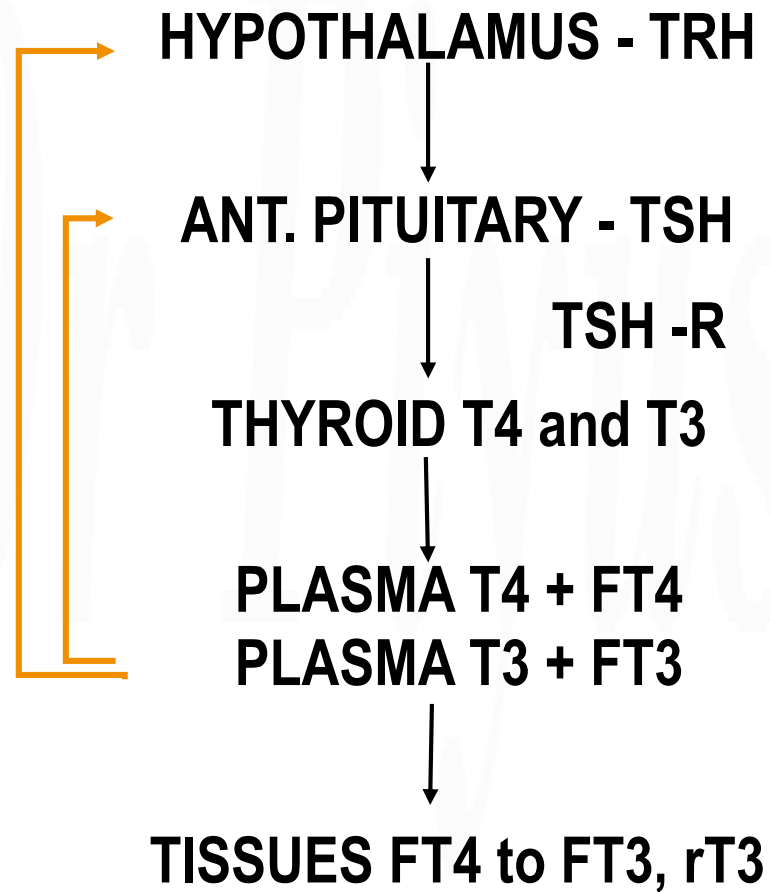
Hypothyroidism

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Introduction

- About 42 million people in India suffer from thyroid diseases.
- Prevalence of hypothyroidism = 3.9%
- More common in females.
- Second to DM , it is most common endocrine disorder.

Thyroid Regulation

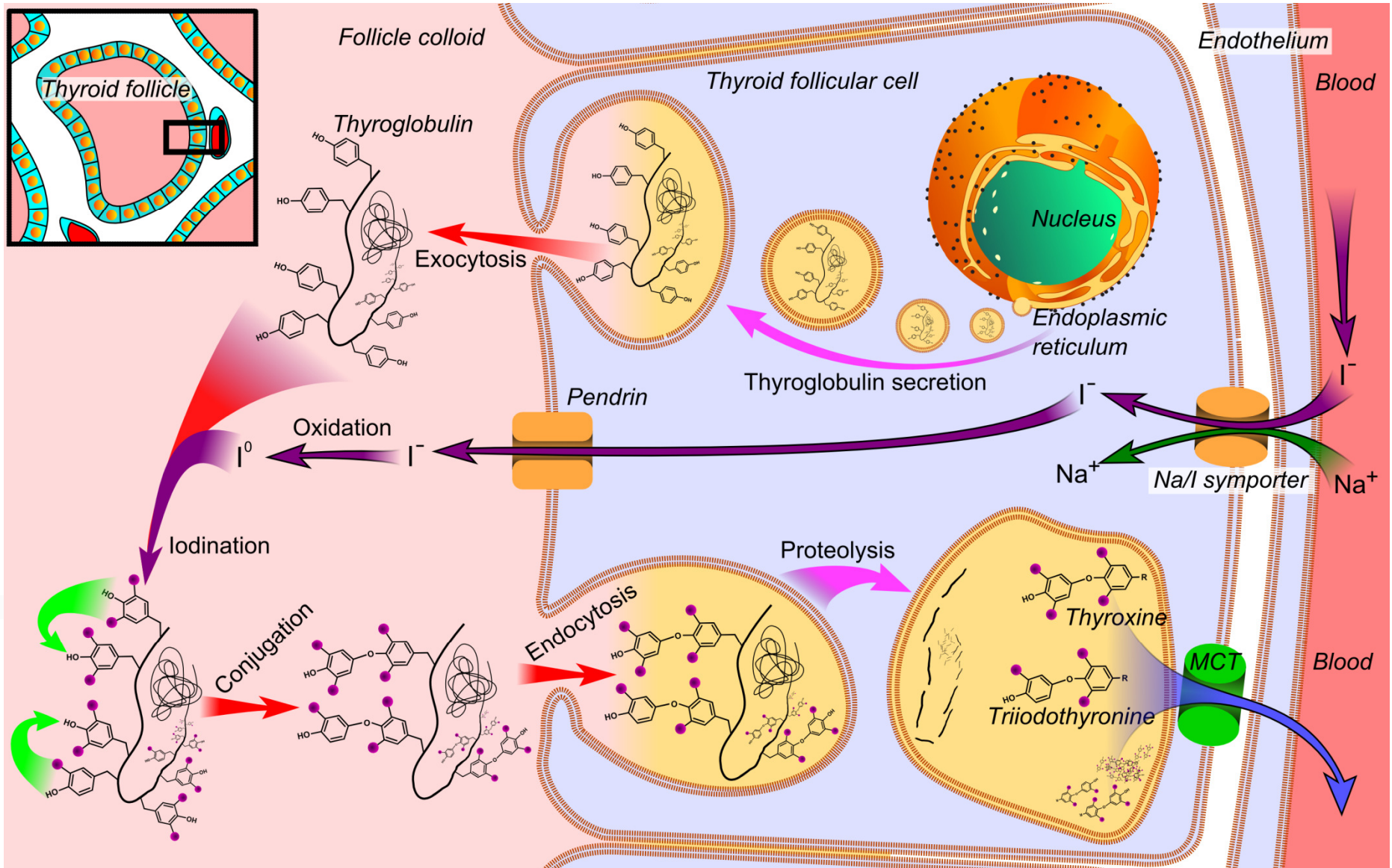


Thyroid Hormone Synthesis

There are the following 5 steps in the hormone synthesis

1. Trapping of inorganic iodine from dietary iodides
2. Activation of iodine to high valence I_2
3. Incorporation of I_2 into Tyrosine of Thyroid Globulin
4. Coupling of formed MIT and DIT to form T_4 & T_3
5. Proteolysis of Thyroglobulin to release T_4 & T_3

Thyroid Hormone Biosynthesis



The Thyronines

Mono Iodo Tyrosine	- MIT	
Di Iodo Tyrosine	- DIT	
Tri Iodo Thyronine	- T ₃	- Half life 6 hours
Tetra Iodo Thyronine	- T ₄	- Half life 7 days
Reverse T ₃	- Metabolically inactive	
Bound hormones	- Metabolically inactive	
Free T4 and Free T3	-- Metabolically Active	

The Thyroxines

Tri Iodo Thyronine – T_3

- 10% is from thyroid gland
- 90% derived from conversion of T_4 to T_3

Tetra Iodo Thyronine – T_4

- Is exclusively from thyroid gland

From the thyroid gland

- 80% of hormone secreted is T_4
- 20% of hormone secreted is T_3

Classification of Hypothyroidism

Primary hypothyroidism(90%)

- high serum thyrotropin (TSH) concentration
- low serum free thyroxine (T4) concentration.

Secondary (central) hypothyroidism

- Low T4 concentration
- low TSH concentration

Subclinical hypothyroidism

- normal free T4 concentration
- elevated TSH concentration.
- *Mild hypothyroidism, Preclinical hypothyroidism*

Transient or temporary hypothyroidism

- can be observed as a phase of subacute thyroiditis.

Consumptive hypothyroidism

- Increase inactivation by 3-iodothyronine deiodinase (D3).

Type & Etiology of Hypothyroidism

- Primary hypothyroidism
- Secondary hypothyroidism
- Tertiary hypothyroidism
- Iatrogenic hypothyroidism
- Congenital hypothyroidism
- Autoimmune hypothyroidism

PRIMARY HYPOTHYROIDISM

- Idiopathic hypothyroidism
- Hashimoto's thyroiditis
- Irradiation of thyroid
- Surgical removal
- Iodine deficiency
- Selenium deficiency
- Drug therapy induce
 - e.g. Amiodarone, Lithium, Interferon,
 - Long term Iodine excess (**Wolff-Chaikoff effect**)
- Infiltrative Diseases:
 - Amyloidosis
 - Hemochromatosis

SECONDARY HYPOTHYROIDISM

- Pituitary or hypothalamic neoplasm.
- Congenital hypopituitarism.
- Pituitary necrosis (Sheehan's syndrome)

TERTIARY HYPOTHYROIDISM

- Hypothalamus related pathology

IATROGENIC HYPOTHYROIDISM

- After 3–4 months radioiodine treatment
- After Subtotal thyroidectomy

GOITROGENS

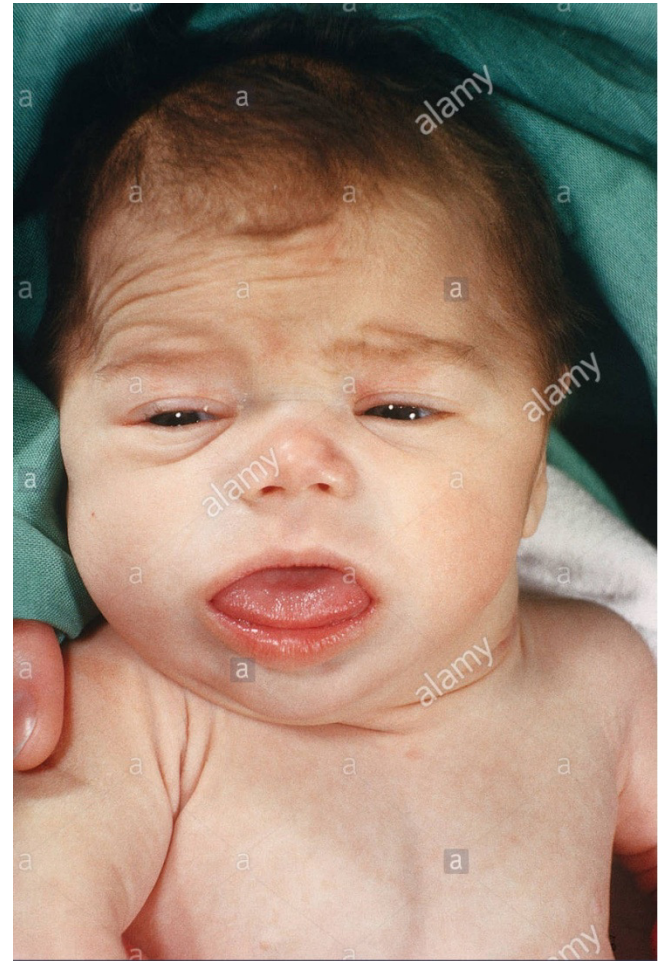
- **DRUGS** = Sulfonamides , Lithium , Oral Hypoglycemic drugs
- **FOOD** = Soybeans , Cabbage

CONGENITAL HYPOTHYROIDISM (CRETINISM)

- Infants appear normal at birth
- Delayed Milestone
- Delayed bone maturation
- Permanent neurologic damage = if treatment is delayed.
- Hypotonia
- Prolonged jaundice
- Feeding problems
- Umbilical hernia
- Enlarged tongue
- Congenital Cardiac malformations are 4 times more common.

Cretinism Face

- Dry & Thin Hair
- Short & Low nasal bridge
- Periorbital puffiness
- Large Head
- Short Forehead
- Big & Hypertrophy tongue
- Big Lips



AUTOIMMUNE HYPOTHYROIDISM

- Subclinical hypothyroidism

Hashimoto's thyroiditis

- **Anti TPO antibody & Anti TG antibody**
- lymphocytic infiltration of the thyroid
- Mild to moderate fibrosis.
- Atrophy of the thyroid follicles

Atrophic thyroiditis

- Fibrosis is much more extensive
- Represents end stage of Hashimoto's thyroiditis

Modifying Environmental Factor :

- Chronic exposure to high iodine diet

Associated conditions

➤ Other Autoimmune disorders: (Most Common)

- ❖ Type 1 Diabetes mellitus
- ❖ Addison's disease
- ❖ Pernicious anemia
- ❖ Vitiligo
- ❖ Celiac disease
- ❖ Rheumatoid Arthritis
- ❖ Systemic Lupus Erythematosus

CLINICAL MANIFESTATIONS

A generalized slowing of metabolic processes.

- Cold intolerance
- Constipation
- Weight gain
- Fatigue
- Slow movement
- Slow speech

Accumulation of Matrix Glycosaminoglycans (GAG)

- Myxedema
- Coarse hair and skin
- Puffy facies
- Enlargement of the tongue
- Hoarseness.

Common signs and symptoms

Symptoms

Decrease Appetite

Cold Intolerance

Horseness of Voice

Weight Gain

Eyelid edema

Constipation

Forgetfulness

Slow speech

Weakness

Decrease Sweating

Signs

Bradycardia

Myxedema

Goiter

Depression

Facial edema

Cold Skin

Dry & Coarse skin

Pallor

CLINICAL MANIFESTATIONS

- **General**

- Weight Gain
- Goiter
- Cold Intolerance

- **Skin & Subcutaneous issue**

- Coarse & Dry Skin
- Puffiness of face
- Myxoedema
- Minimum sweating
- Alopecia
- Non Pitting Edema

- **Cardiac**

- Bradycardia
- Cardiomyopathy
- Cardiac Failure
- Pericardial & Pleural effusion

- **Neuromuscular**

- Carpal Tunnel Syndrome
- Slurred speech
- Hoarseness of voice
- Ataxia
- Muscle Cramp
- Myopathy

- **Respiratory**

- Shortness of Breath
- Sleep apnea

- **Hematological**

- Iron deficiency anemia
- Pernicious anemia

CLINICAL MANIFESTATIONS

- **G.I.T.**

- Constipation
- Ascites

- **Reproductive System**

- Menorrhagia
- Infertility
- Decrease Libido

- **Psychiatric**

- Depression
- Dementia
- Psychosis

- **Developmental**

- Growth retardation
- Delayed Puberty
- Mental retardation

- **Metabolic**

- Hyponatremia
- Hypercholesterolemia
- Hypertriglyceridemia

- **Miscellaneous**

- Hoarseness of voice because of vocal cord thickening
- Hyperlipidemia
- Xanthomas

Laboratory Evaluation

Thyroid Function Tests

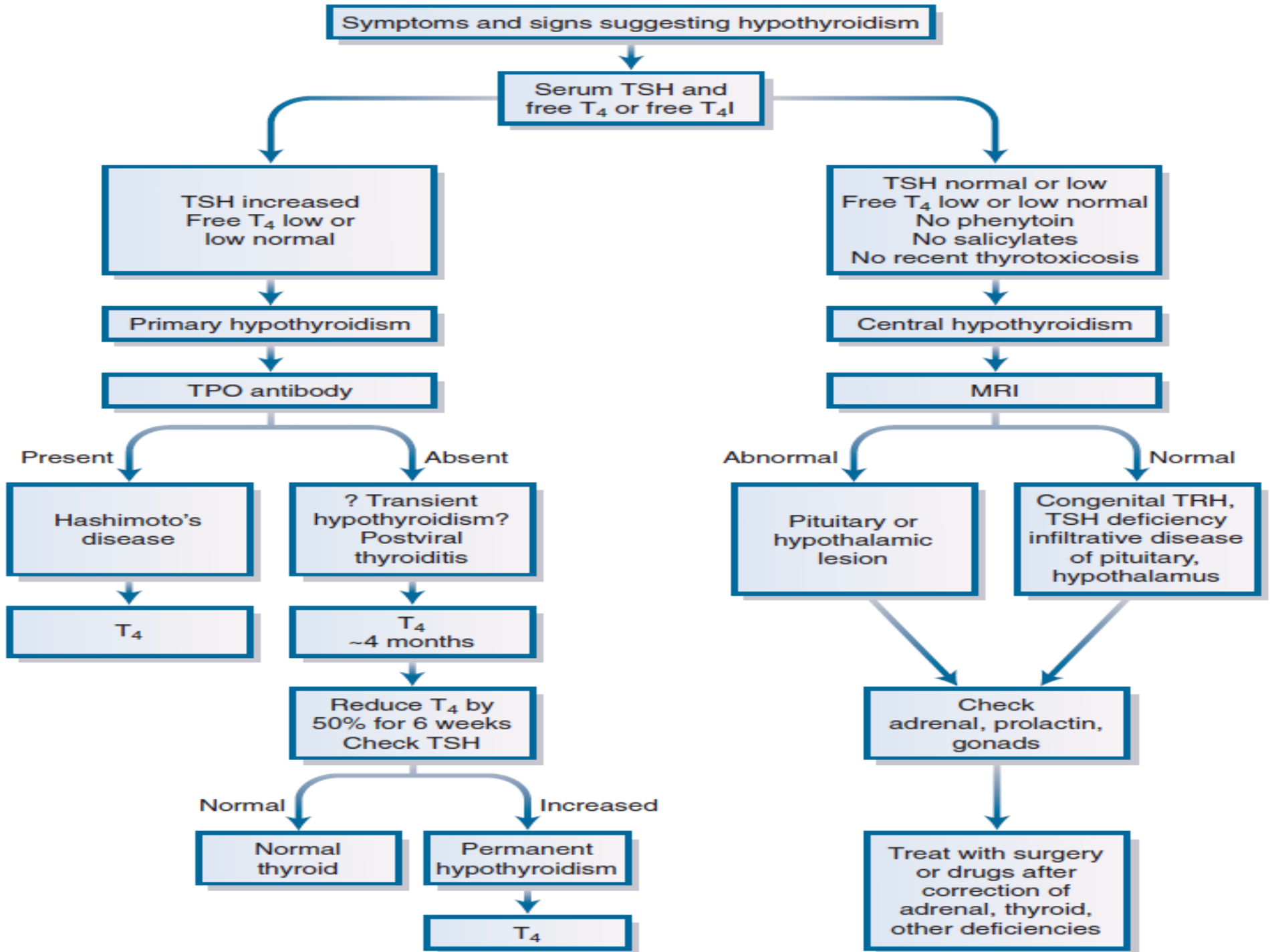
- Total T4 (thyroxine), Total T3 (triiodothyronine)
- Free T4 , Free T3
- TSH
- Iodine Uptake Test
- Anti-Thyroid Antibodies
- Anti TPO Antibody
- FNAC of nodule

Thyroid Antibodies

- Anti Microsomal (TM) Antibodies
 - Anti Thyroglobulin (TG) Antibodies
 - Anti Thyroperoxidase (TPO) Antibodies
 - Anti Thyroxine Antibodies
 - Thyroid Stimulating (TSA) Antibodies
-
- High TPO Ab = Hashimoto's thyroiditis
 - High Anti thyroxine Ab = Peripheral resistance to Thyroxine
 - High TSA (TSI) = Graves' Hyperthyroidism

Tests of Thyroid Function

Test	Reference Ranges*
TSH	0.3- 4.0 mU/ L
T4	4- 11 μ g/ dL
Free T4	0.7- 2.1 ng/ dL
T3	75- 175 ng/ dl
Free T3	0.300 – 0.7 ng / dl



Treatment

- Treatment of choice is **Thyroxine**
- TSH measured = 6 to 8 weeks interval
- Adults = 1.7 microgm/kg/day (100 microgram/day)
- Elderly = 1.0 microgm/kg/day (50 - 75 microgram/day)
- Children may need up to 4 microgm /kg/day
- Increase in increments of 25 microgm every four weeks until TSH returns to normal.
- If Serum albumin low
 - Decrease dose by 20%.

Over - and Under- Dose Replacement Risks

➤ **Over-replacement Risks**

- Reduced bone density/osteoporosis
- Tachycardia, arrhythmia : Atrial fibrillation
- In elderly or patients with heart disease, angina, arrhythmia, or myocardial infarction

➤ **Under-replacement Risks**

- Continued hypothyroid state
- Long-term end-organ effects of hypothyroidism
- Increased risk of hyperlipidemia

Recovery after L-Thyroxine





2010

After 2 years on
Eltroxin (T4) only



2014

After 3 years on
T4 and T3



