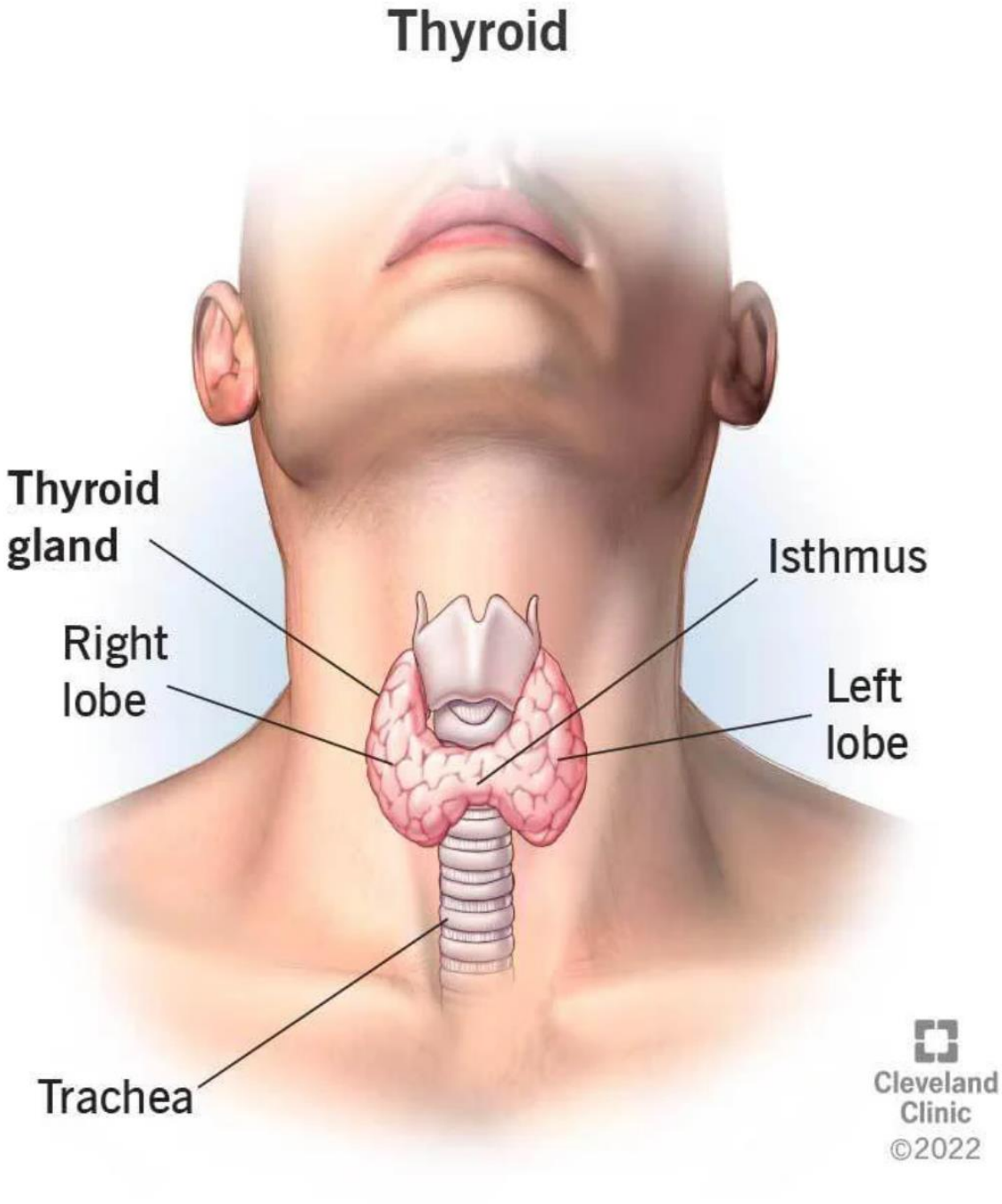
Hypothroidism

Dr.Afsane Nazari

Pediatric Endocrinologist


Thyroid
Thyroid gland
Right lobe
Isthmus
Left lobe
Trachea
Cleveland Clinic
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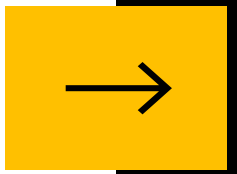
Types of Hypothyroidism

1. Congenital:

If symptoms appear in the first weeks or months of birth

2. Acquired:

If symptoms appear after 2 years.



The prevalence of hypothyroidism is 1 in 2000

Risk factors of Congenital hypothyroid :

1.birth defect
2. female gender
3. Maternal DM
4.Twin
5. preterm
6. mother age >40y
7. Iodine deficiency
8. Excess iodine
9. GA >40w
10. Birth weight <2 kg and >4.5 kg
11. preecalampsia
12. Sexually transmitted diseases in pregnancy
13. Receiving ammiodarone, PTU, methimazole , expectorant ….by the mother
14. Environmental factors and environmental pollutants such as insecticides
15. ethinic composition Asian
16. Genetics

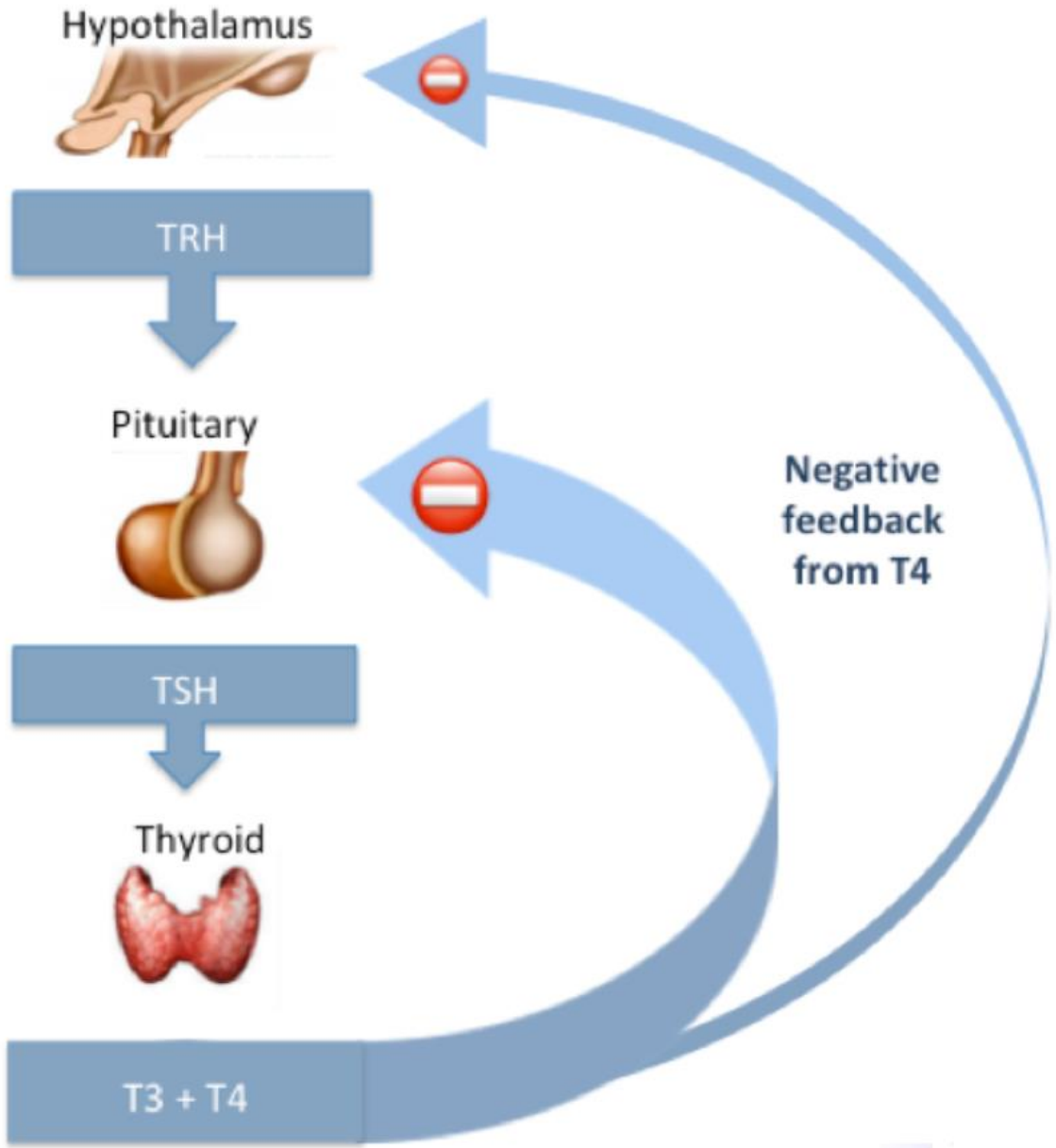
Screening:

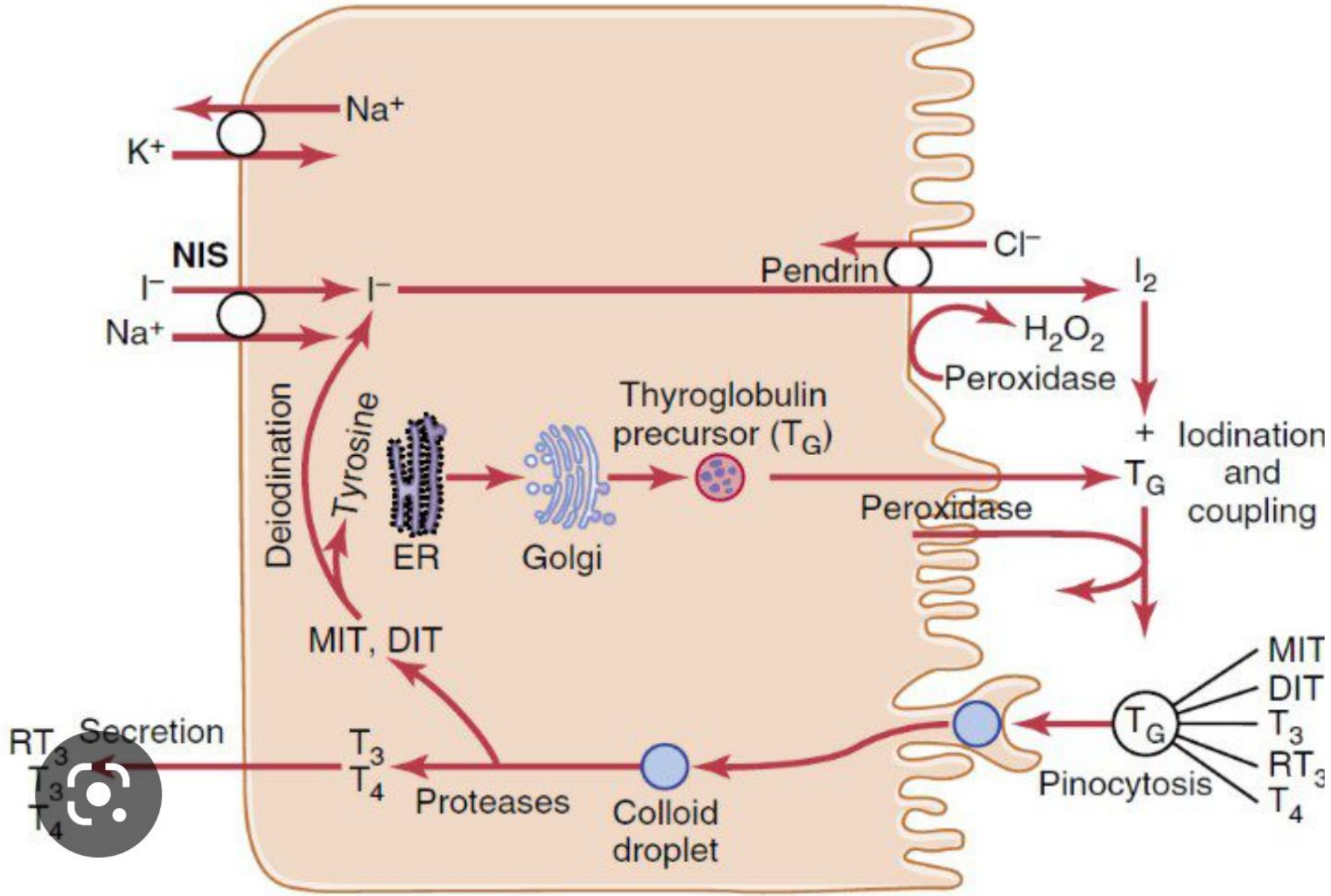
Screening is done on the 3 to 5th day of birth from the soles of the feet

Who needs re-screening?

1) **Premature neonates**
2) **Birth weight <2 - 2.5 kg**
3) **GA <37 weeks**
4) **Weight >4.5 kg and GA >40 weeks**
5) **Hospitalization in NICU**
6) **non-thyroidal illness**
7) **Receiving drugs such as dopamine and dexa**
8) **History of receiving or exchanging the blood**

Hypothalamic-Pituitary-Thyroid Axis




Na+
K+
NIS
I−
Na+
I−
Cl−
Pendrin
I2
H2O2
Peroxidase
+ Iodination and coupling
TG
Peroxidase
Thyroglobulin precursor (TG)
Deiodination
Tyrosine
ER
Golgi
MIT, DIT
MIT
DIT
T3
RT3
T4
TG
Pinocytosis
RT3
T3
T4
Secretion
T3
T4
Proteases
Colloid droplet

- ✓ T3 has a lower serum concentration than T4
- ✓ T3 is more potent than T4 and is the active thyroid hormone
- ✓ T3 has a shorter half life
- ✓ The majority of circulating T3 is derived from peripheral conversion of T4 to T3

Congenital Hypothyroidism

1. **Transient (35 percent)**
2. **Permanent (65 percent)**

Causes of transient hypothyroidism:

1. **Transfer of anti-thyroid drugs from mother to fetus**
2. **Maternal TRB antibody (TSH blocking antibody)**
3. **Excessive iodine exposure**
4. **Iodine deficiency**
5. **Large hepatic hemangioma**

Causes of permanent hypothyroidism

1- Defect of thyroid development : agenesis

Hypoplasia

Thyroid ectopy

2- Mutation of genes that play a role in thyroid development (PAX8, TTF2, NKX2, GLIS3, JAG1)

3- Resistance to TSH: Defect in TSH responsiveness, due to mutation of its receptor.

4- Defect in thyroid hormone synthesis(dyshormonogenesis): defect in the transfer of iodine into follicular cells (NIS mutation)

5- Defect in iodine transport from follicular cell into colloid: penderd syndrome

6- Defect in iodide organification: thyroid peroxidase (TPO) defect

hydrogen peroxidase (DUOX2) defect

7- Defect in thyroglobulin production(TG) synthesis

8- Deiodination defect: iodotyrosine deiodinase (IYD) defect

9- Thyroid hormone transport defect : mutation in monocarboxylate transporter8(MCT8)

10- Thyroid hormone resistance: mutations in alpha or beta thyroid hormone receptor gene(Resistance at the pituitary or systemic resistance)

11- Central hypothyroidism: hypothalamus or pituitary problems

Changes in TSH at birth:

Normally, at birth, TSH increases suddenly due to changes in the environmental conditions

It reaches to 100 half an hour after birth, and this increase in TSH leads to increases T3 to 300 and T4 to 16 about 4 hours after birth.

Then 24 hours later, a sharp drop in TSH occurs. Within 5 to 7 days, its value reaches less than 10 (TSH more than 10 after 2 week is considered high)

T3 concentration reaches its normal level at the end of the first week (less than 200). T4 concentration will take about 2 weeks to reach its normal level of about 10 to 12. In premature neonates, there is a sudden increase in TSH and the subsequent increase in T3 and T4 at birth, but it is less and more delayed than in term neonates.

T4 concentration in Umbilical cord is directly related to gestational age and birth weight (premature neonates have temporary hypothyroxenemia).

❑ Hypothyroidism symptoms:

can be symptomatic or asymptomatic.

In most cases, it is asymptomatic at birth.

The birth weight and height are normal, but the head circumference is slightly increased due to mixedema.

❑ In symptomatic cases, the symptoms include the following:

1. coarse crying
2. Feeding problems
3. wide fontanel
4. Hypotonia
5. Hypothermia
6. Dry skin
7. Reduction of sweating
8. prolonged jaundice
9. Nasal obstruction
10. Apnea
11. Loud breathing
12. Umblical hernia
13. Constipation
14. Edema in exterimitis
15. Low pulse
16. Heart murmur
17. Cardiomegaly
18. Pericardial effusion without symptoms
19. Narrow palpebral fissure
20. Swollen eyelid
21. Open mouth
22. Big tongue
23. far down the hairline on the forehead
24. Epiphyseal dysgenesis

B

C

The method of dealing with screening results based on the results of the primary TSH test on filter paper

01

TSH<5: normal

02

TSH 5-10: second screening from the heel on the filter paper.

03

TSH 10-20: we will do blood sampling in 2 weeks
If in the second test TSH>10 we will start treatment.

04

TSH>20: we take blood sampling, but in these cases, we do not wait for the test results , and start the treatment.

Confirmatory tests from blood:
T4 or Ft4
TSH
T3RU

T4 is low , TSH is high:

primary hypothyroidism

T4 is normal , TSH is high: subclinical hypothyroidism

if TSH is between 5 -10: the tests are repeated 2 to 4 times at intervals of 2 to 4 weeks(f/u for 3months), and the treatment was done for the following cases:

1. TSH remains more than 7.5

2. Rising TSH in follow up testing

3. The patient has symptoms of hypothyroidism

4. The patient has goiter

5. In syndromic cases such as Down syndrome

If the TSH 10-20: the test is repeated in 2 weeks old , and if TSH is still >10, we started treatment

If TSH>20: immediate treatment

T4 is low , TSH is normal:

1. TBG reduction: 1 in 10000 births in boys,xlinked, decrease t4 but normal freet4 and tsh. increase T3RU. does not require treatment

2. ill neonates

3. taking drugs such as dopamine or Dexa

4. premature neonates (hypotyroxinemia)

5. Central hypothyroidism

6. primary hypothyroidism with a delayed increase in TSH

T4 is low ,TSH is low:

central hypothyroidism

treatment unless the neonate is premature or has a non-thyroidal illness.

treatment:

Levothyroxine : 10 - 15 micro /kg/ day

If T4 <5 : 15 micro /kg/ day

Levothyroxine should be taken on an empty stomach and nothing should be eaten for 30 to 60 minutes afterwards.

vomiting less than 30 minutes after taking: the medicine must be repeated.

Levothyroxine should not be taken with:

1. soya based formula

2. Iron or calcium supplements, which should be at least 4 hours apart.

3.Colic drops like simethicone

Treatment goal: Keeping T4 and free T4 in the upper limit of NL range and TSH in the lower limit of NL range.

Ftee t4(1/4-2/3),t4(10-14),tsh(0/5-2/5)

Treatment monitoring intervals: 0-6 months: Every month

6-12 months: Every two months

1 - 3 years old :every 3 months

>3 years old: every 3 - 6 months

Tests should be repeated every 4 - 6 weeks after changing the drug dose.

To monitor the treatment at the age of 3 years, the treatment is temporarily stopped for 1 month:

if T4 is low and TSH is high, this is permanent hypothyroidism and levothyroxine should be continued.

If the tests are normal, it is probably transient and follow-up will be done.

In cases of thyroid developmental defects such as agenesis, hypoplasia or thyroid ectopy, or in cases where TSH is still high despite treatment with levothyroxine in the first year of treatment, there is no need to stop the drug at 3 years of age , Because these cases are permanent and must be treated for the rest of their lives

Prognosis

diagnosis and treatment of congenital hypothyroidism in the first few weeks of life is necessary to prevent irreversible brain damage and will cause normal growth and development.

In cases of severe involvement and low T4, severe skeletal delay, or in cases that treatment is started late, despite treatment, some degrees of IQ reduction and neuro-cognitive deficits such as hypotonia, attention deficit and speech problems may remain.

10% of cases have sensorineural hearing loss.

follow up: Audiologists, echocardiography, Kidney ultrasound, Dental examination, Examination of growth and development ,Neurological examination is necessary for follow-up.

Aquired hypothyroidism

Prevalance:
0/1- 0/2%

Cause of acquired hypothyroidism:

- **Hashimoto's thyroiditis**
- **APS syndroms**
- **Iodine deficiency (endemic goiter)**
- **Medicines (such as lithium, aminodarone,…)**
- **Consumption of goitrogenic foods for a long time**
- **Infiltration in thyroid gland (amyloidosis and sarcoidosis and …)**
- **After thyroid surgery or iodine therapy**
- **Transient hypothyroidism(post partum thyroiditis, subacute thyroiditis**

Hashimoto thyroiditis:

Autoimmune thyroiditis
the thyroid gland is diffusely large and nodular, with infiltration of lymphocytes.
Firm,nontender and diffuse goiter
Female predominance
Positive family history in 25-35%
Rare before 3 years of age
The age of onset is most commonly after 6 years old
assossiation with other autoimmune disease like diabet mellitus type 1,addisone
hypoparathyroidism,mucocutaneus candidiasis(autoimmune polyglandular syndrome)
Common in syndroms like Down and terner

Symptoms of Hashimoto's thyroiditis:

- ✓ Puffy appearance, Edema of limbs
- ✓ Pale and cool skin (due to reduced blood supply to the skin)
- ✓ Hypercarotenemia
- ✓ skin dryness
- ✓ Slow wound healing
- ✓ Easy bruising due to increased capillary inferagelity
- ✓ Dry and brittle hair and hair loss, Brittle nails
- ✓ Increased sensitivity to cold
- ✓ constipation
- ✓ sleep apnea
- ✓ depression, Memory and concentration disorders
- ✓ hearing loss
- ✓ numbness

- ✓ Delayed puberty and ovulation
- ✓ Delay bone age
- ✓ Ovulation disorders
- ✓ Decreased libido
- ✓ Fertility reduction
- ✓ Increase in spontaneous abortion
- ✓ Increase in premature births

Metablic changes:

Macrocytic anemia

Hypercholestrolemia

Hyperprolactinemia

Elevated CPK

Diagnosis:

Elevated TSH level, positive Anti TPO and Anti Tg
Sonography: thyroid gland is diffusely large with micronodular pattern ,hypoechoic and heterogeneous echotexture
No need to biopsy or scan for diagnosis

Treatment:

levothyroxine
Follow up: every 6-12 months

THANK YOU FOR YOUR ATTENTION