In The Name Of God

Neonatal Hypothyroidism Screening

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SUMS

National Newborn Hypothyroidism Screening Program

- **Education** for pregnant mothers in the third trimester
- Sampling at **3 to 5 days** of age at designated sampling centers
- Sampling of all newborns admitted to the hospital
- Sampling from the **baby's heel** on **filter paper**

- Measuring **TSH concentration** in heel blood sample on filter paper (as an **initial screening test**)
- Immediate recall of suspicious cases
- Conducting a **serum test** to **confirm** or **rule out** the disease
- Starting **replacement therapy** with **levothyroxine** tablets

Rescreening For Hypothyroidism In Newborns

- **Premature infants** (repeat heel screening at **2**, **6**, and **10** weeks of age)
- Newborns weighing **less than 2500** grams
- Newborns weighing **more than 4000** grams
- **Twins** and **multiples**
- **Hospitalized** infants or those with a **history of hospitalization**

- Infants who have had a **history of receiving** or **exchanging blood**
- Infants who have taken **certain medications**: such as **dopamine**, **Corticosteroid compounds**, etc.
- Infants whose screening test results (initial **TSH test results on filter paper**) were between **5 - 9.9**.

Evaluation And Handling Of Different Screening Results

- **At 3-7 days old**: TSH concentration **less than 5 mu/L is normal.**
  - TSH concentration of 5- 9.9 mu/L
  - TSH concentration of 10- 19.9 mu/L
  - TSH concentration ≥ 20 mu/L
- **At 8-90 days old:** TSH concentration **≤ 4 mu/L is normal.**

TSH concentration of 5- 9.9 mu/L

- **Re-screening** in the **second week** of life
  - TSH concentration **less than 5 mu/L is normal**
  - TSH concentration **≥٥ mu/L→ check T4 or free T4, TSH, T3RU**

TSH concentration of 10- 19.9 mu/L

- Performing **tests to confirm** the diagnosis **at 2 weeks of age**
  - **check T4 or free T4, TSH, T3RU**
  - If confirmatory tests are in favor of the disease, start treatment.

TSH concentration ≥ 20 mu/L

- Performing **tests to confirm** the diagnosis **at 2 weeks of age**
  - **Starting treatment at the same time as sending confirmation tests**
  - **check T4 or free T4, TSH, T3RU**
    - If confirmed: Continue treatment

Diagnosis of hypothyroidism

- A **definitive diagnosis** of neonatal hypothyroidism is made by measuring serum concentrations of **T4** (or free T4) and **TSH**.

Results of hormonal tests used to confirm the diagnosis

- **Low T4** and **high TSH concentration**
  - **In a term infant, T4 < 6.5 µg/dL and TSH ≥ 10 mU/L is considered primary hypothyroidism.**
  - **Replacement therapy with levothyroxine should be started as soon as possible.**
  - **By achieving optimal metabolic control, the prevalence of serious complications of the disease can be prevented.**

- **Normal T4 (≥6.5)** and **high TSH (≥10) concentration (Hyperthyrotriponemia)**
  - **Transient**
  - **Permanent**
- **It is more common in Down syndrome**
- **Its transient form may persist until the age of 10 y/o.**

Causes Of Hyperthyrotriponemia

- **Mild primary hypothyroidism**
- **Delay in the development of the pituitary-hypothalamic axis**
- **Iodine deficiency**
- **Excessive iodine exposure**
- **Maternal antithyroid antibodies**
- **TSH and TSH receptor disorders**
- **Thyroid hormone synthesis disorders**

Not all experts consider starting treatment necessary for these cases except:

- If the **TSH elevation (TSH ≥ 10 mU/L)** persists by the end of the infant's **second week of life**

- **If the tests are repeated 2-3 times (every 2-4 weeks)** and T4 remains normal and TSH remains high

  – initiation of replacement therapy with **levothyroxine** is recommended. (***Subclinical Primary Hypothyroidism***)

TSH ≥ 6-10 mU/L after one month of age

- **The TSH test should be repeated every 2 to 4 weeks and treatment should be initiated if it is above 10 mU/L.**

Low T4 (more than 2SD below the mean for age or often < 10 µg/dl) and normal TSH

- 3-5% of all newborns
- 12% of **premature** babies (Especially **under 30 weeks**), (From **a few days to a few weeks**: 8 weeks)
- Ill neonates (Non-thyroidal illness)
- **Central hypothyroidism**

- Infants with **primary hypothyroidism** and **delayed TSH rise**
- Taking TSH-inhibitory medications: **Dopamine** and **high-dose corticosteroids**
- **TBG deficiency** (**NL TSH** & **Free T4** with **↑T3RU**) (No need for replacement therapy)

Delayed TSH Elevation

The prevalence of **delayed TSH elevation** is high in **premature**, **VLBW**, **LBW**, and **critically ill** (term and premature) infants, infants **admitted to the NICU**, and those with **cardiac abnormalities**.

It is essential to follow these infants with **TSH** testing at **2** and **6 weeks**.

In premature infants, heel screening is recommended at 2, ٤, and ١٠ weeks of age due to the phenomenon of delayed TSH elevation.

Symptoms In Favor Of Central Hypothyroidism

- **Hypothyroxinemia (↓T4) plus**
  - **Hypoglycemia** (caused by GH and ACTH deficiency)
  - **Polyuria** (due to ADH deficiency)
  - **Midline facial abnormalities**
  - **Microphallus** (Caused by gonadotropin deficiency)
  - **Congenital nystagmus** and **visual impairments**

Clinical Signs & Symptoms Of Neonatal Hypothyroidism

- Prolonged jaundice
- Feeding disorders
- Puffiness of the face and body
- Gestational age less than 37 or more than 42 weeks
- Constipation
- Large posterior fontanel
- Drowsiness

- Birth weight less than 2500 or more than 4000 grams
- Enlarged tongue
- Palor
- Hypothermia (often below 35 degrees)
- Inactivity and slow movements
- Abdominal distension
- Respiratory disorders (apnea and nasal congestion)

Clinical Signs And Symptoms At The End Of One Month

- Peripheral and extremity mottling
- Edema of the external genitalia
- Failure to gain weight and poor sucking
- Constipation
- Abdominal distension
- Bradycardia
- Decreased activity
- Drowsiness
- Respiratory distress due to enlarged tongue

Newborn With Hypothyroidism

Newborn with hypothyroidism (before and after treatment)

Hypothyroidism Treatment

- Thyroid hormone plays a very important role in all stages of **central nervous system development.**
- To achieve a **normal IQ**, **adequate** amounts of **thyroid hormone** are needed at least until the **age of 3**.
- It is ideal to **start treatment** about **2 to 3 weeks** after birth.

Factors Affecting Success In Preventing Serious And Irreversible Complications Of Hypothyroidism

- The **Timing Of Treatment Initiation**
- The **Quality Of Metabolic Control** Of The Disease

The Best Time Frame To Achieve Optimal Metabolic Control

- Normalization of serum **T4** concentration **within 2 weeks**
- Normalization of serum **TSH** concentration **within one month**

- The treatment of choice for neonatal hypothyroidism is **levothyroxine** tablets.
- Dosage: **10-15** mcg/kg/day
- The most important factor in dose **adjustment** of levothyroxine is the **T4** concentration.

- During treatment,

serum T4 concentrations should be in the **Upper Half Of The Normal Range** and

serum TSH concentrations should be in the **Lower Half Of The Normal Range**.

The optimal range of serum TSH concentration during treatment in infants <3 years of age is 0.5-2 mU/L

How To Take Levothyroxine Tablets

- It should be taken once a day at least 30 minutes before a meal.
- It is safe to take levothyroxine tablets during breastfeeding.
- The tablets can be crushed and dissolved in breast milk or water.

- The tablets should not be taken with soy based formula or with iron supplements.
- It should be taken at least 4 hours apart from calcium-containing compounds.
- It should be taken at least 1-2 hours apart from iron-containing compounds.
- Dissolving the tablet and storing it for another day is not recommended at all.

Conducting Follow-up Serum Thyroid Tests

- **2 to 4 weeks** after starting treatment
- **Every 2 months** in the **first 6 months** of life
- **Every 3 months** between the ages of **6 and 36 months**
- **Every 3 to 6 months** from **36 months** of age (if the disease is permanent)

Investigating whether hypothyroidism is transient or permanent in patients undergoing treatment after the age of three

- ✓ **Discontinue levothyroxine** tablets and perform serum **T4** and **TSH** tests **after 4 weeks.**
- ✓ **Reduce** the dose of **levothyroxine** tablets **to half** the usual dose and test serum **T4** and **TSH** after **4 weeks**.

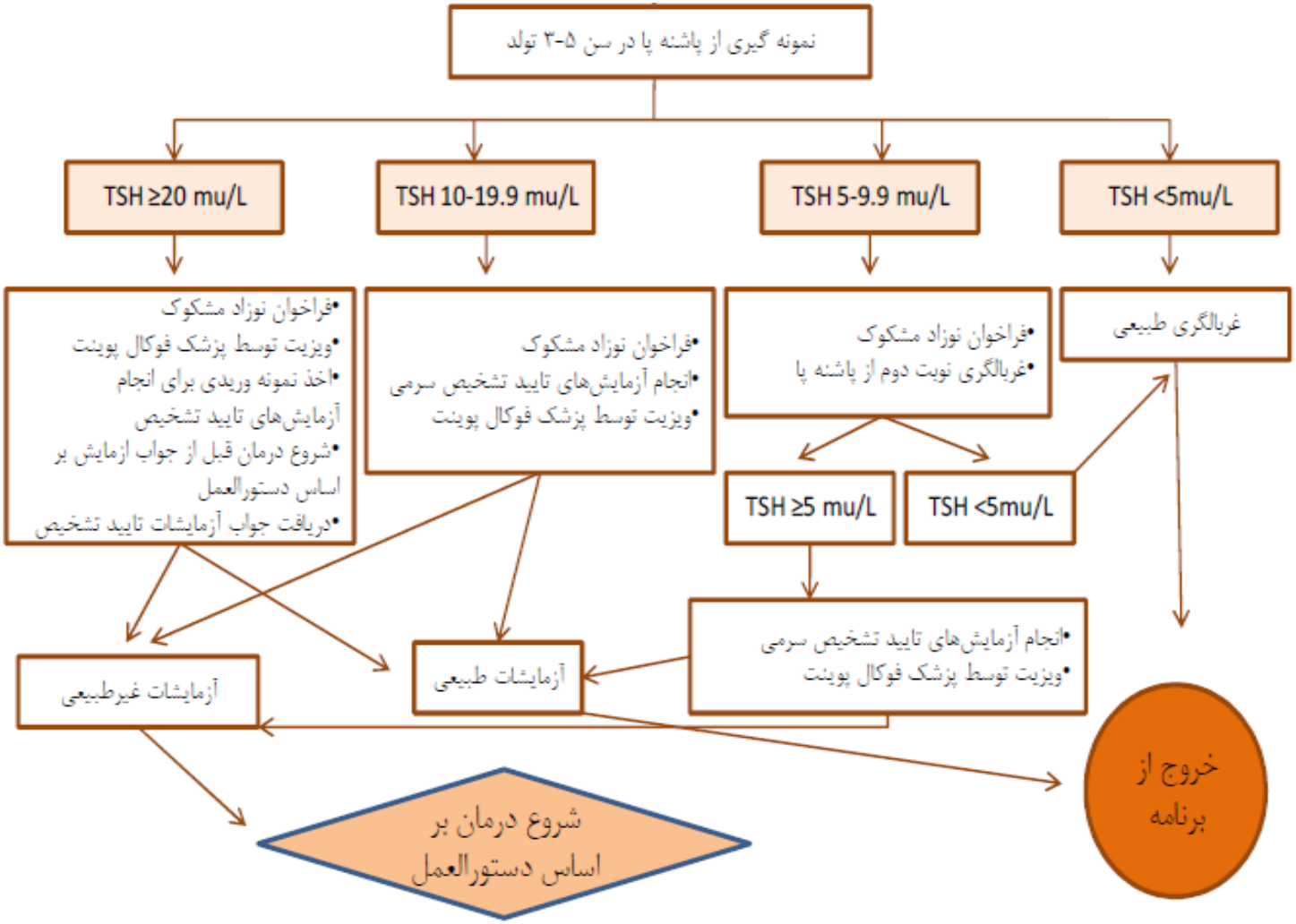
Normal Levels Of Thyroid Hormones In Premature And Term Infants

سن بارداری (هفته)	سن نمونه	Free T4 (ng/dl)	T4 (µg/dl)	T3 (ng/dl)	TSH (miu/L)
۲۳- ۲۷ هفته	بند ناف	۱ .۲۸ ± ۰ .۴	۵ .۴ ± ۲ .۰	۲۰ ± ۱۵	۶ .۸ ± ۲ .۹
	۷ روزگی	۱ .۴۷ ± ۰ .۶	۴ .۰ ± ۱ .۸	۳۳ ± ۲۰	۳ .۵ ± ۲ .۶
	۱۴ روزگی	۱ .۴۵ ± ۰ .۵	۴ .۷ ± ۲ .۶	۴۱ ± ۲۵	۳ .۹ ± ۲ .۷
	۲۸ روزگی	۱ .۵۰ ± ۰ .۴	۶ .۱ ± ۲ .۳	۶۳ ± ۲۷	۳ .۸ ± ۴ .۷
۲۸-۳۰ هفته	بند ناف	۱ .۴۵ ± ۰ .۴	۶ .۳ ± ۲ .۰	۲۹ ± ۲۱	۷ .۰ ± ۳ .۷
	۷ روزگی	۱ .۸۲ ± ۰ .۷	۶ .۳ ± ۲ .۱	۵۶ ± ۲۴	۳ .۶ ± ۲ .۵
	۱۴ روزگی	۱ .۶۵ ± ۰ .۴	۶ .۶ ± ۲ .۳	۷۲ ± ۲۸	۴ .۹ ± ۱۱ .۲
	۲۸ روزگی	۱ .۷۱ ± ۰ .۴	۷ .۵ ± ۲ .۳	۸۷ ± ۳۱	۳ .۶ ± ۲ .۵
۳۱-۳۴ هفته	بند ناف	۱ .۴۹ ± ۰ .۳	۷ .۶ ± ۲ .۳	۳۵ ± ۲۳	۷ .۹ ± ۵ .۲
	۷ روزگی	۲ .۱۴ ± ۰ .۶	۹ .۴ ± ۳ .۴	۹۲ ± ۳۶	۳ .۶ ± ۴ .۸
	۱۴ روزگی	۱ .۹۸ ± ۰ .۴	۹ .۱ ± ۳ .۶	۱۱۰ ± ۴۱	۳ .۸ ± ۹ .۳
	۲۸ روزگی	۱ .۸۸ ± ۰ .۵	۸ .۹ ± ۳ .۰	۱۲۰ ± ۴۰	۳ .۵ ± ۳ .۴
۳۷ هفته و بیش تر	بند ناف	۱ .۴۱ ± ۰ .۳	۹ .۲ ± ۱ .۹	۶۰ ± ۳۵	۶ .۷ ± ۴ .۸
	۷ روزگی	۲ .۷۰ ± ۰ .۶	۱۲ .۷ ± ۲ .۹	۱۴۸ ± ۵۰	۲ .۶ ± ۱ .۸
	۱۴ روزگی	۲ .۰۳ ± ۰ .۳	۱۰ .۷ ± ۱ .۴	۱۶۷ ± ۳۱	۲ .۵ ± ۲ .۰
	۲۸ روزگی	۱ .۶۵ ± ۰ .۳	۹ .۷ ± ۲ .۲	۱۷۶ ± ۳۲	۱ .۸ ± ۰ .۹

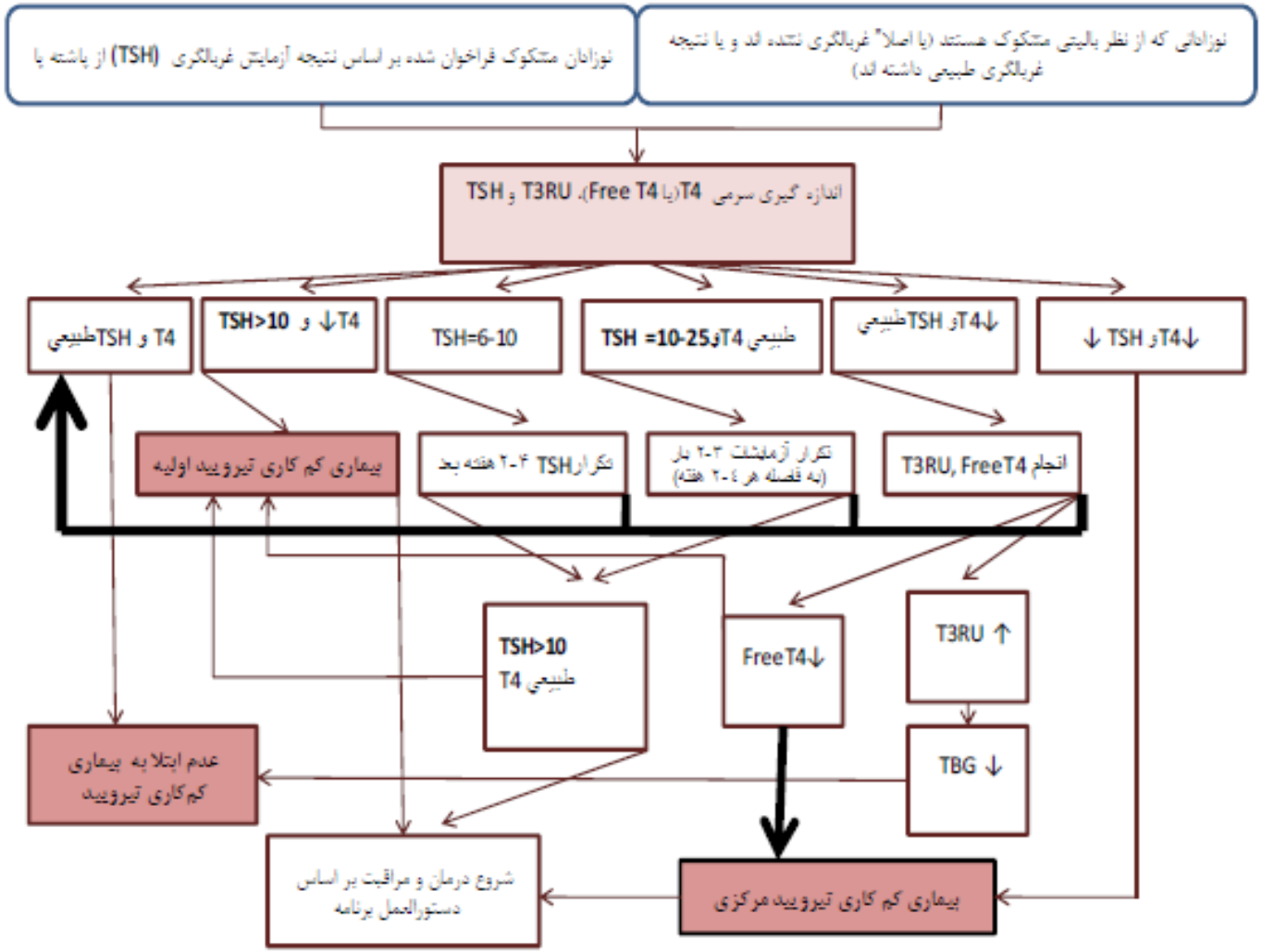
Normal Values Of A Number Of Hormonal Parameters Of Thyroid Function

آزمایش	سن	مقدار	
TSH mU/L	نوزاد ترم در هفته اول تولد	۱ -۳۸/۹	
	هفته ۲۰-۲ تولد	۱/۷-۹/۱	
	۵ ماهگی تا ۳ سالگی	۰/۷-۶/۴	
T4 (µg/dl)	۳-۱ روزگی	۸/۲-۱۹/۹	
	هفته اول تا پایان ۱ ماهگی	۱۵-۶/۹	
	از ۲ تا ۱۲ ماهگی	۶/۱-۱۴/۹	
	۳-۱ سالگی	۶/۸ -۱۲/۸	
Free T4	۳-۱ روزگی	۲۰۰-۶۱۰ (pmol/L)	۴-۲/۹ (ng/dl)
	۴ روزگی تا ۲ ماهگی	۲۴۰-۵۶۰ (pmol/L)	۰/۲-۸/۲ (ng/dl)
	۲ ماهگی تا قبل از بلوغ	۲۳۰-۶۶۰ (pmol/L)	۰/۲-۸/۳ (ng/dl)
T3 (ng/dl)	ماه اول تولد	۷۵-۲۶۰	
	۱ ماهگی تا ۵ سالگی	۱۰۰-۲۶۰	
	۱۰-۵ سالگی	۹۰-۲۴۰	
T3RU (%)	ماه اول تولد	۲۶-۳۶	
	۱ ماهگی به بعد	۲۶-۳۵	
TBG (mg/dl)	ماه اول تولد	۹-۱	
	۱۲-۱ ماهگی	۷-۲/۶	
	۵-۱ سالگی	۲/۵-۹/۴	

Neonatal Screening And Diagnosis Algorithm For Hypothyroidism



Algorithm For Diagnosing And Treating Neonatal Hypothyroidism



اندیکاسیون های درمان بیماری کم کاری تیروئید در نوزادان نارس

TSH غیرطبیعی نمونه پاشنه پا بر کاغذ گاتری

در هر سنی TSH بیش از ۲۰ = درمان

اندازه گیری TSH و T4 و یا free T4 سرم در هفته دوم تولد

TSH≥ 20 سرم

درمان با لووتیروکسین با هر میزان T4

10<TSH<20 سرم

اگر Free T4 یا T4 پایین باشد

درمان

Free T4 یا T4طبیعی

چک مجدد TSH ۲ هفته بعد

اگر به همین میزان باشد یا افزایش یابد درمان می کنیم. ولی اگر طبیعی باشد طبق پروتکل کشوری در هفته های ۶ و ۱۰ تولد غربالگری انجام شده و در صورت نیاز تصمیم به درمان گرفته شود.

TSH<10سرم

T4 و یا FREE T4 پایین

چک مجدد ۲ هفته بعد

اگر TSH بیشتر ویا مساوی ۱۰ و FREE T4 کم باشد

درمان

اگر TSH کم تر از ۱۰ و FREE T4 کم باشد

با شک به Central Hypothyroidism **ارجاع** به متخصص غدد کودکان

T4 طبیعی

چک مجدد در هفته های۴ و ۶ و ۱۰

T4 طبیعی و TSH<6

پیگیری

اگر در هر مرحله 6<TSH<10

ارجاع به متخصص غدد کودکان

Any Question?

Thanks For Your Attention