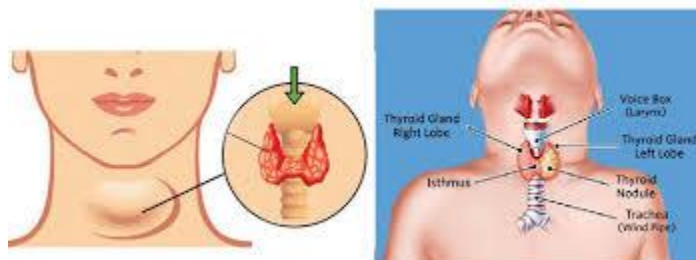


# Hypothyroidism in childhood and adolescence



Fatemeh Tabatabaei

Pediatric Endocrinologist

# Case 1

- Boy 14 yrs old -short stature
- TSH=14 mIU/l
- T4= 4 mg/dl
- Diagnosis?
- Treatment?



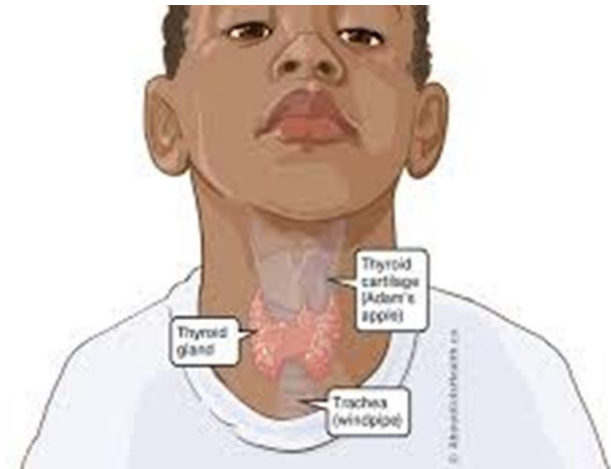
## Case 2

- Girl 8 yrs in routine lab test :
- TSH=8 mIU/l
- T4= 9 mg/dl
- Diagnosis?
- Treatment?



## Case 3

- Boy 5 yrs in routine lab test :
- TSH=4 mIU/l
- T4= 4 mg/dl
- Diagnosis?
- Treatment?



## Case 4

- In PICU boy 5 yrs with sepsis :
- TSH=2 mIU/l
- T4= 4 mg/dl
- Diagnosis?
- Treatment?



# Hypothyroidism

- ↓Free T4

Thyroid (primary)

Pituitary (secondary)

Hypothalamus (tertiary)

} central hypothyroidism

- Hypothyroidism

- ❖ Congenital

- ❖ Acquired

- May be associated with a goiter



Primary hypothyroidism:  
thyroid can't produce  
amount of hormones  
pituitary calls for

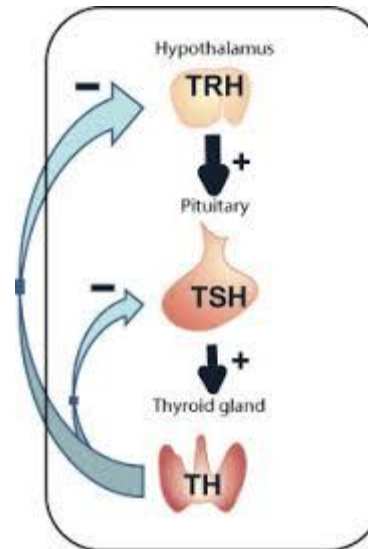


Secondary hypothyroidism:  
thyroid isn't being  
stimulated by pituitary  
to produce hormones

ADAM

# Hypothyroidism in childhood and adolescence

- Hypothyroidism is most common disturbance of thyroid function in children
- Acquired hypothyroidism is most often caused by autoimmune thyroiditis



## CHECK TSH – T4

TSH slightly elevated  
T4 normal

- Subclinical hypothyroidism
- Obesity

TSH high  
T4 low

Primary hypothyroidism

TSH normal or low  
T4 low

- Central hypothyroidism
- TBG deficiency
- Euthyroid Sick Syn

TSH high  
T4 high

- Hypothyroidism +  
levo before test
- Resistance to thyroid  
hormone

TSH high  
T4 normal

macroTSH



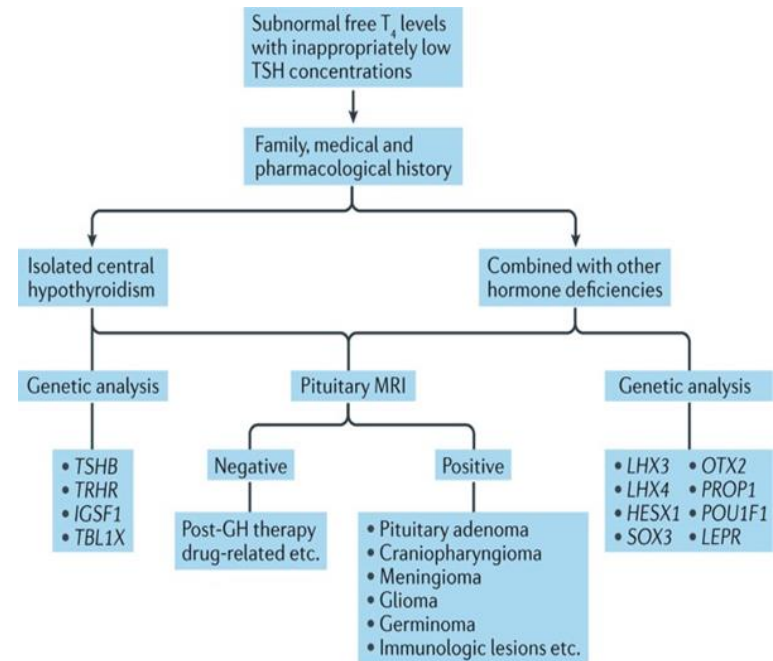
# Primary hypothyroidism may be:

- ❑ **Subclinical** ( $\uparrow$ TSH  $\{<10\}$  and normal free T4)
- ❑ **Overt** ( $\uparrow$ TSH and low free T4)



# Central hypothyroidism

- low Total T4 + low or inappropriately normal TSH
- Differential diagnosis for central hypothyroidism:
  - **Thyroxine-Binding Globulin Deficiency**
  - ❑ X-linked pattern
  - ❑ Acquired forms of TBG deficiency → androgens
  - **Euthyroid sick syndrome**

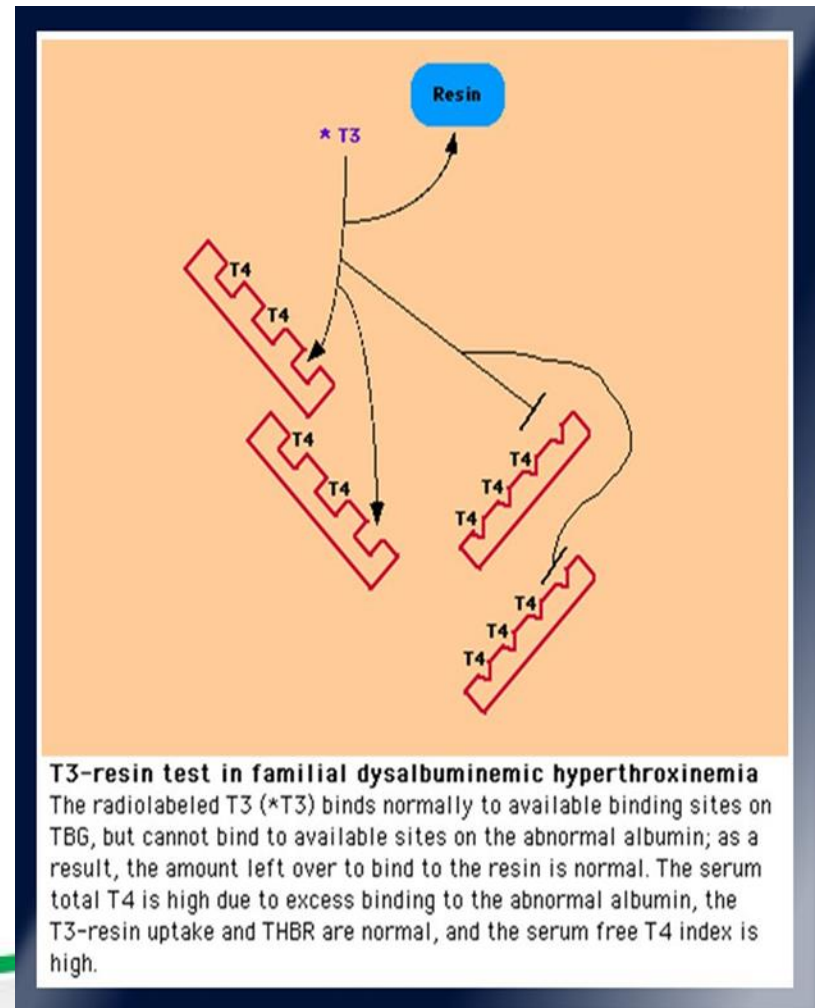


## ❑ Central hypothyroidism

- T4↓
- TSH normal or ↓
- ↓T3RU
- ↓FT4

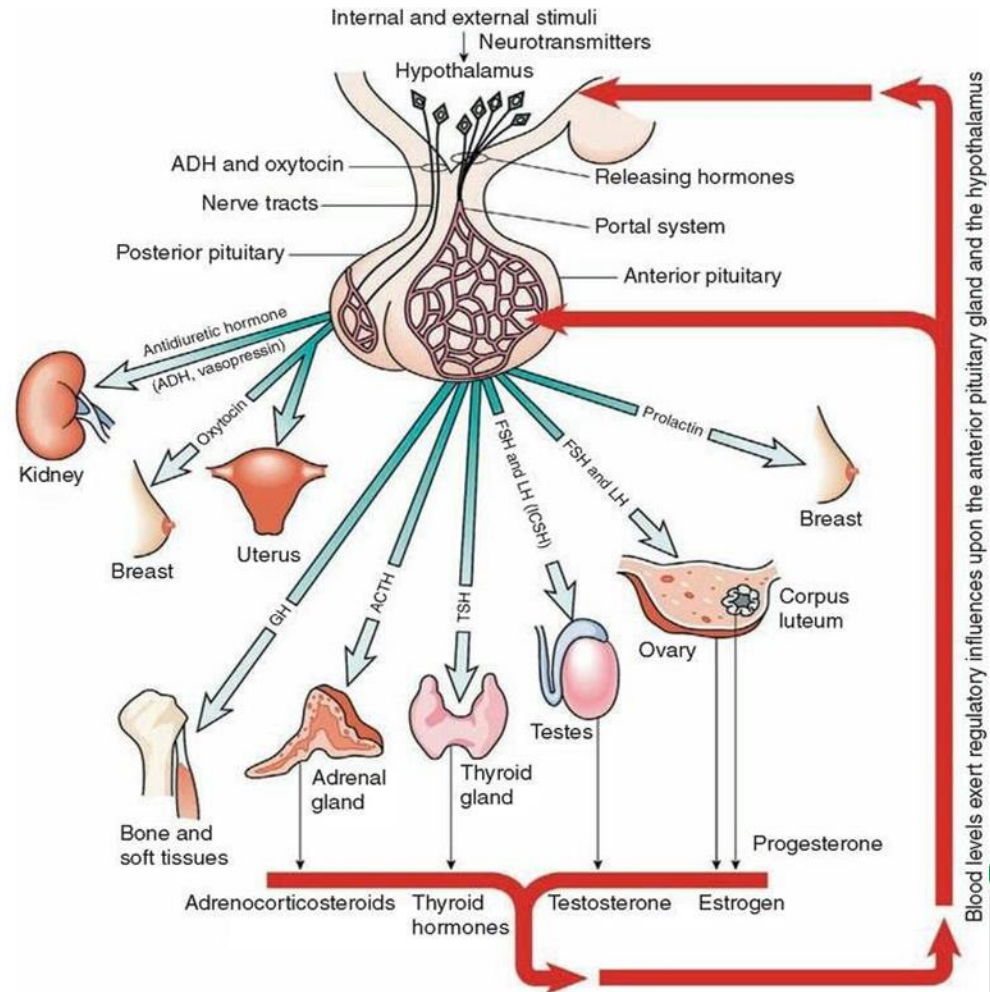
## ❑ TBG deficiency

- T4 ↓
- TSH normal
- T3RU ↑
- FT4 normal



# Central hypothyroidism

1. Check other pituitary axis hormones:  
**Cortisol**
  2. Brain MRI with contrast
- Levotyroxine increases urinary excretion of cortisol  
→ Adrenal crisis
  - **Hydrocortisone before Levotyroxine**



# Euthyroid sick syndrome

## Changes in Thyroid Hormone Levels During Illness

Severity of illness	Free T3	Free T4	Reverse T3	TSH	Probable Cause
Mild	↓	N	↑	N	↓ D2,D1
Moderate	↓↓	N, ↓, ↑	↑↑	N, ↓	↓↓ D2,D1, ↑ D3
Severe	↓↓↓	↓	↑↑	↓↓	↓↓ D2,D1, ↑ D3
Recovery	↓	↓	↑	↑	?

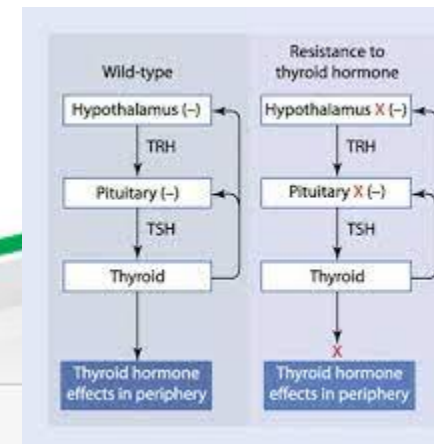
# TSH high T4 high

- In patients with primary hypothyroidism who do **not take drug properly**, levothyroxine may be taken in **large amounts 2-3 days before test**
- Resistance to thyroid hormone (RTH)



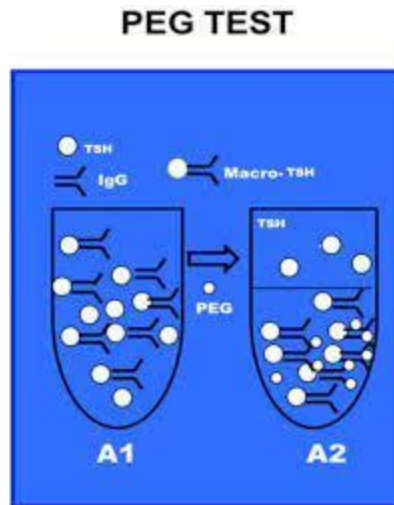
# Resistance to thyroid hormone (RTH)

- Impaired sensitivity to thyroid hormone (TH)
- Mutations in thyroid hormone receptor beta (THRB) gene
- Rare syndrome thyroid hormone  $\uparrow\uparrow$  but TSH is not suppressed
- Generalized RTH are **usually euthyroid** because  $\uparrow\uparrow$  thyroid hormone overcome nuclear receptor defect
- However, they may have some tissue-specific clinical manifestations of hypothyroidism  $\pm$  hyperthyroidism



# Elevations of TSH with normal free T4

- Occasionally, are caused by confounders that affect assay measurement of TSH, such as heterophile antibodies or **macro-TSH**





## CHECK TSH – T4

TSH slightly elevated  
T4 normal

- Subclinical hypothyroidism
- Obesity

TSH high  
T4 low

Primary hypothyroidism

TSH normal or low  
T4 low

- Central hypothyroidism
- TBG deficiency
- Euthyroid Sick Syn


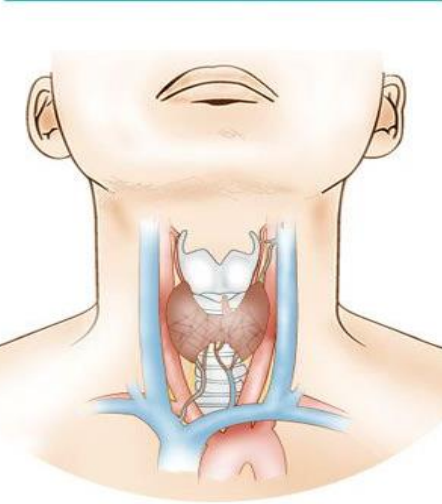








TSH high  
T4 high

- Hypothyroidism +  
levo before test
- Resistance to thyroid  
hormone

TSH high  
T4 normal

macroTSH

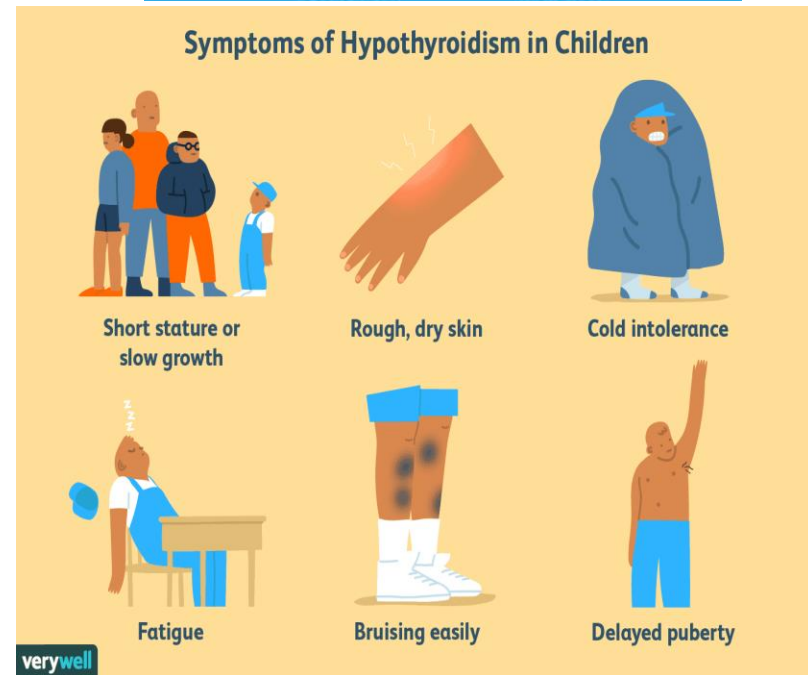
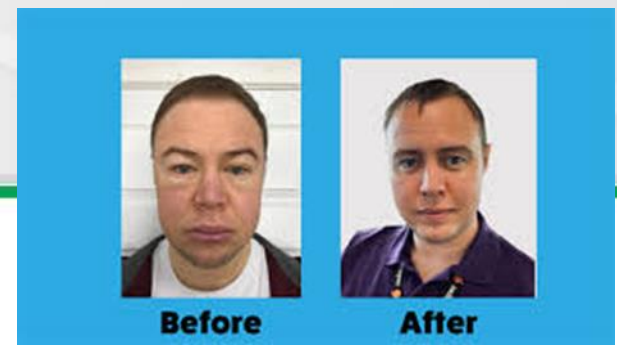
# CLINICAL MANIFESTATIONS

SYMPTOMS OF UNDERACTIVE THYROID	<b>THYROID?</b>	SYMPTOMS OF OVERACTIVE THYROID
 <p>Unexplained Weight Gain</p>		<p>Unexplained Weight Loss</p> 
<p>Constant Fatigue and Tiredness</p> 		<p>Feeling Fatigued</p> 
<p>Muscle Soreness &amp; Pain</p> 		<p>Bulging Eyes</p> 
<p>Hair Loss</p> 		<p>Panic Attacks</p> 
<p>Dry and Flaky Skin</p> 		

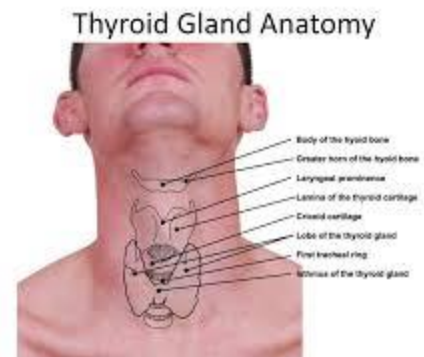
**Top10**  
Home Remedies  
To explore more, visit  
[www.Top10HomeRemedies.com](http://www.Top10HomeRemedies.com)

# symptoms

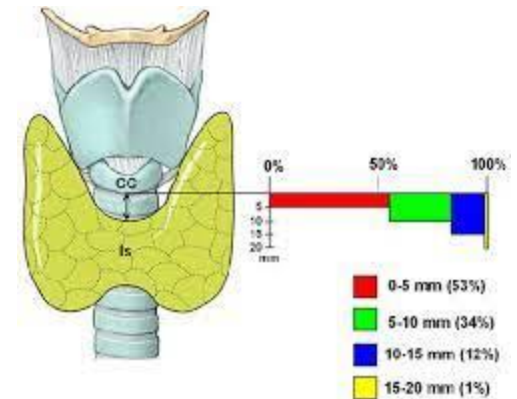
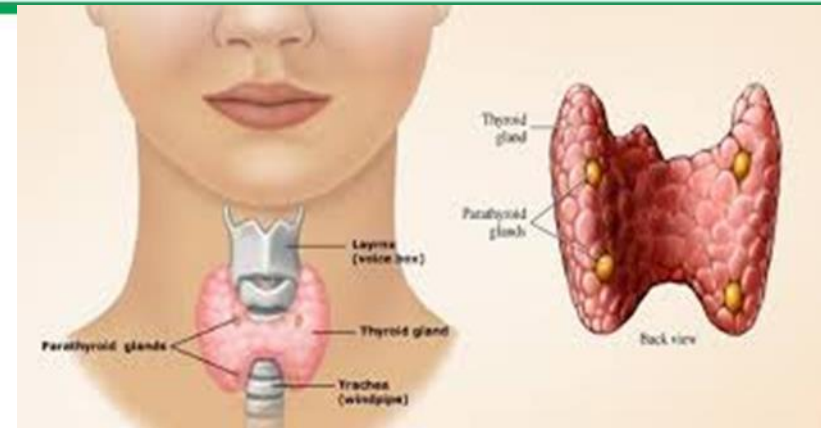
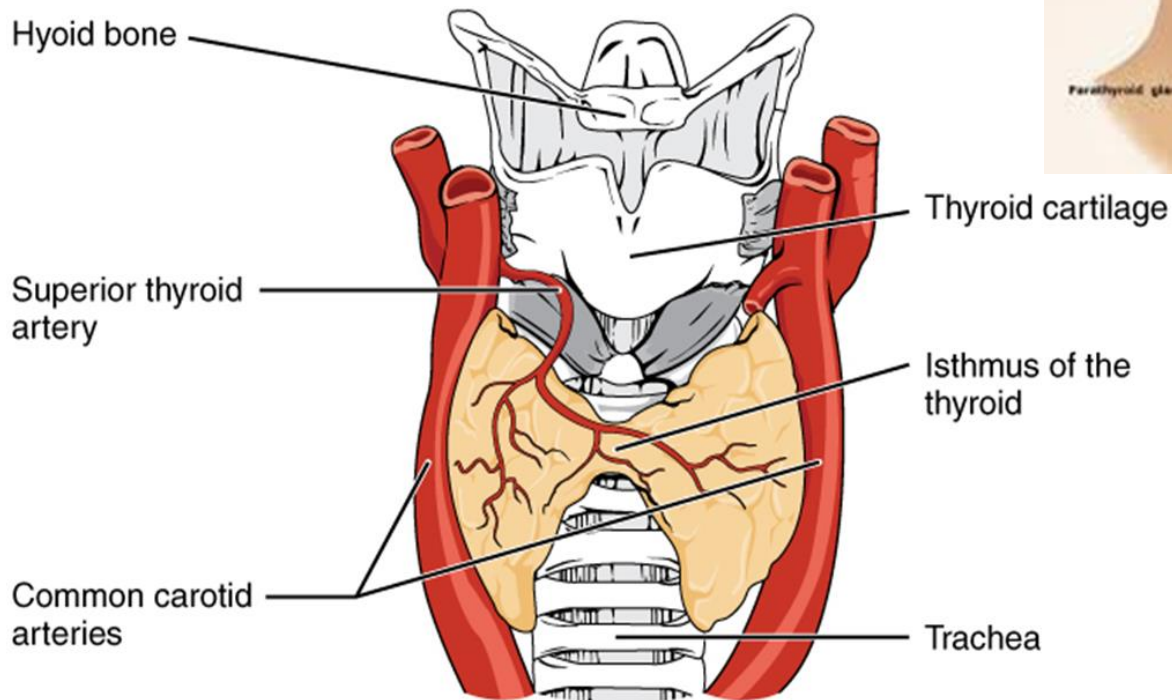
- Sluggishness
- Lethargy
- Cold intolerance
- Constipation
- Dry skin
- Brittle hair
- Facial puffiness
- Muscle aches and pains
- Weight gain, typically minimal and due to fluid retention
- If hypothalamic or pituitary disease, may have headaches, visual symptoms, or manifestations of other  $\downarrow$  pituitary hormone



# Physical Examination



# Physical Exam



- Special tests:
1. Crile's method



- **Palpation** →feel and examine size, consistency, nodularity and motion of gland.
- **Watch** during swallow to note enlargement or asymmetry of thyroid lobes
- **Auscultation** →bruit over gland should be differentiated from carotid bruit.

# Examination findings

- Most common physical finding at presentation is diffusely enlarged thyroid gland (goiter).
- Noticeable goiter in **39.5 %** of children autoimmune thyroiditis
- Thyroid **may be normal in size** or not palpable at all





## Assessing the severity of iodine deficiency in the community

The prevalence of goiter: WHO CLASSIFICATION OF GOITER SIZE:

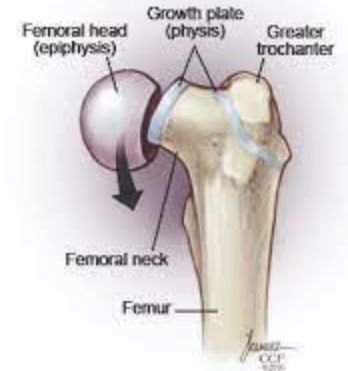
Grade	Description
0	no goiter
1 A	thyroid lobes more than end of the thumb
1 B	thyroid enlarged, visible when the head tilted back
2	thyroid enlarged, visible when neck in normal position
3	thyroid greatly enlarged, visible from about 10m

# Physical Examination

- Short stature
- Apparent overweight (more fluid retention than obesity)
- Pseudohypertrophy of muscles
- Delayed deep tendon reflexes
- Bradycardia
- Auscultation chest and cardiac → pleural or pericardial effusion
- Higher risk of slipped capital femoral epiphysis



**Slipped Capital Femoral Epiphysis**  
(unstable)

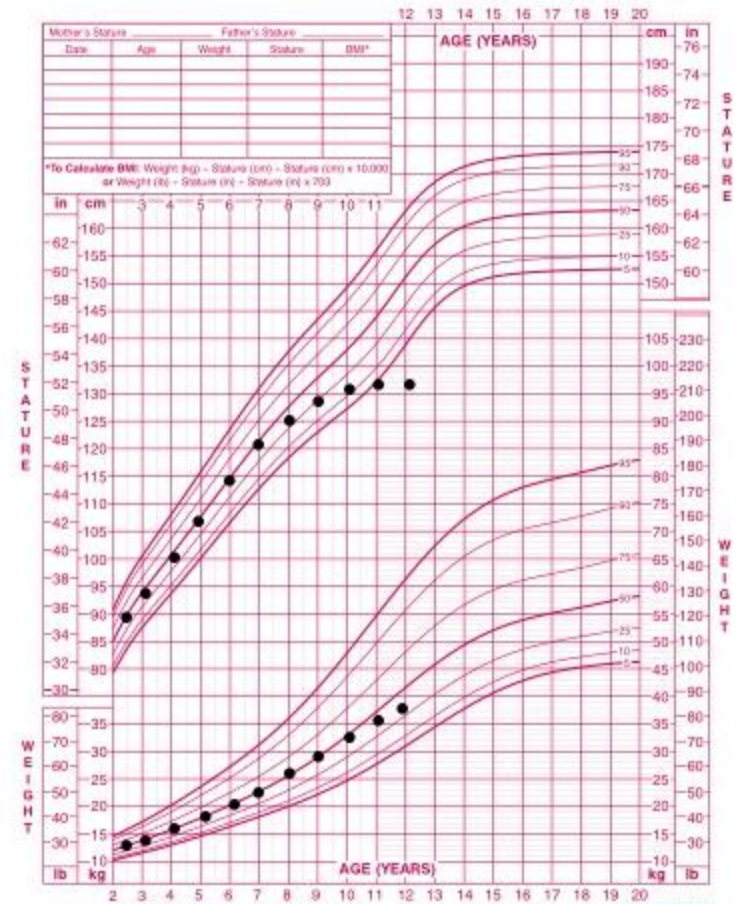


# Declining growth velocity/ short stature

- ↓Height velocity
- Short stature
- Skeletal maturation is delayed
- Bone age and height age < chronologic age



2 to 20 years: Girls  
Stature-for-age and Weight-for-age percentiles



Published May 20, 2006 (revised 11/21/06)  
SOURCE: Downloaded for the National Center for Health Statistics in collaboration with  
the National Center for Chronic Diseases Prevention and Health Promotion (2006).  
<http://www.cdc.gov/growthcharts>

( a ) A 14-year-old boy with primary congenital hypothyroidism having short stature, distended abdomen, and umbilical hernia. Myxedematous features in same child



# Abnormal pubertal development

- Delayed puberty is common



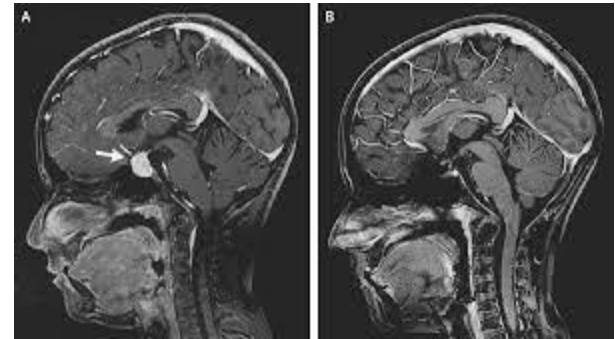
**Fig. 3.1** (a) A 14-year-old child with myxoedematous features, (b) short stature with poor secondary sexual characteristics (c). Note the breast budding (B<sub>2</sub>) in the same child

# Abnormal pubertal development

- Some **long primary hypothyroidism** have **sexual precocity**→
  - Breast development and vaginal bleeding in girls
  - Enlarged testes in boys
- Slightly ↑ (for age) FSH
- Bone age may not be delayed, due to sex steroid
- Rarely galactorrhea secondary to hyperprolactinemia



# Pituitary Hyperplasia from Primary Hypothyroidism



- A 10-year-old girl presented with headache and poor growth. Laboratory studies showed primary hypothyroidism, and MRI revealed an enlarged pituitary

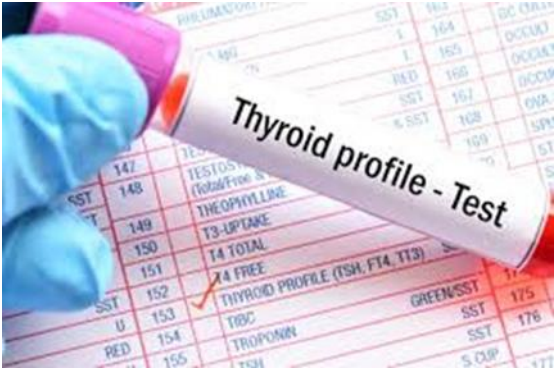
# Functioning in school

- Performance **often declines, but it improves in some children**, perhaps because they are less active and, therefore, less easily distracted حواس پرتی and better able to concentrate
- One reason for delay in diagnosis is that parents see latter changes as positive.





# Laboratory abnormalities

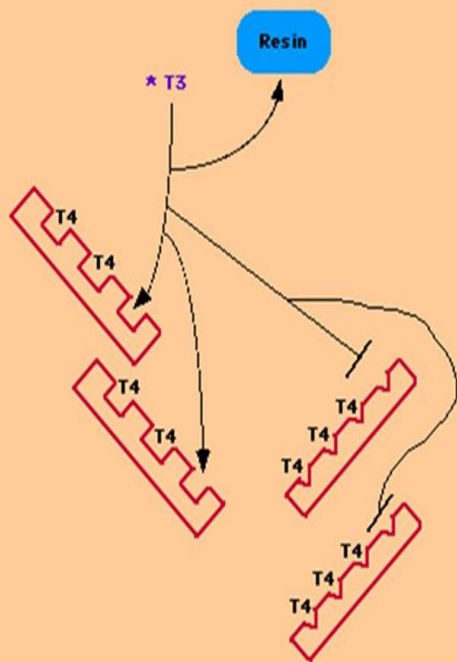


# Laboratory abnormalities

- In addition thyroid function testing:
    - T3RU
    - Hyperlipidemia (hyperTG and low HDL)
    - Normocytic or macrocytic anemia
    - Hyponatremia (infrequently)
    - Rarely, myopathy and  $\uparrow$  CPK
- (Kocher-Debre-Semelaigne syndrome)



# T3RU



## T3-resin test in familial dysalbuminemic hyperthyroxinemia

The radiolabeled T3 (\*T3) binds normally to available binding sites on TBG, but cannot bind to available sites on the abnormal albumin; as a result, the amount left over to bind to the resin is normal. The serum total T4 is high due to excess binding to the abnormal albumin, the T3-resin uptake and THBR are normal, and the serum free T4 index is high.

- کمبود مادرزادی TBG وابسته به جنس غالب است

- T4 ↓

- TSH نرمال

- T3RU ↑

- FT4 نرمال

- تشخیص افتراقی با کم کاری مرکزی تیروئید

- T4 ↓

- TSH نرمال یا ↓

- T3RU ↓

- FT4 ↓

# Antithyroid peroxidase antibodies (TPOAb) and Antithyroglobulin antibodies (TgAb)

- Primary hypothyroidism ( $\uparrow$ TSH,  $\downarrow$ FT4) be tested for autoimmune thyroiditis by measuring Anti TPOAb and Anti TgAb
- ~ 85 to 90 % autoimmune thyroiditis have positive TPOAb, 30 to 50 % have positive TgAb
- TSH receptor-blocking antibodies may in 9.2 % of autoimmune thyroiditis
- **Measurement of TSH receptor-blocking antibodies is not recommended as part of routine care.**



# Paraclinic Imaging

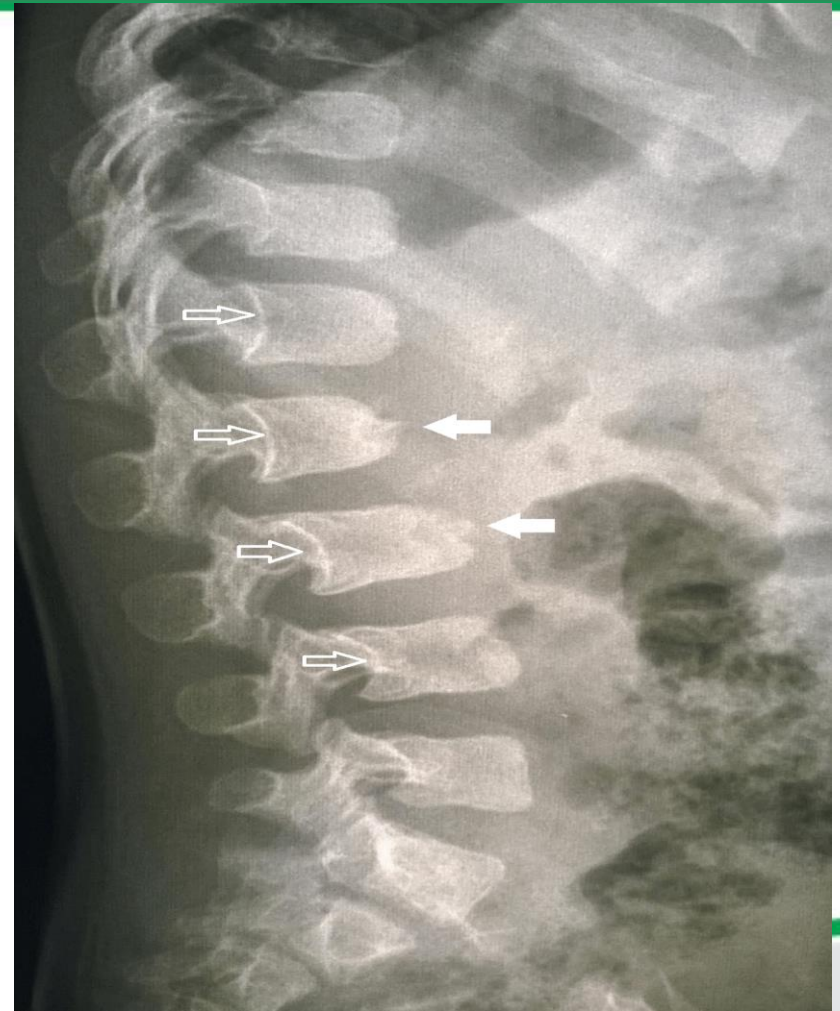


# Imaging abnormalities

- **Brain MRI**→
  - Central hypothyroidism
  - Primary hypothyroidism must be excluded in any child with an enlarged sella turcica due to secondary hyperplasia of thyrotroph cells
- Reversible with levothyroxine therapy.
  
- **CXR**→pericardial and pleural effusions may present in severe hypothyroidism
- **BA**→skeletal maturation (bone age) is delayed

# Congenital hypothyroidism

- Dysplastic bullet-shaped vertebrae with anterior beaking (solid arrows)



- left normal neonate with both knee epiphyses present
- Right a neonate with congenital hypothyroidism in whom both epiphyses are small





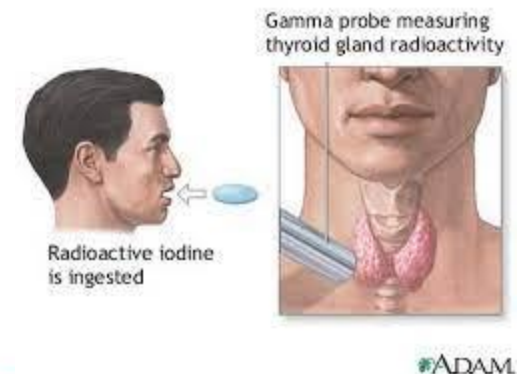
# Ultrasound Examination and FNA

- In child with **hypothyroidism and positive thyroid antibodies who has a palpable goiter**→ we suggest an ultrasound examination
- If **markedly asymmetric goiter or a palpable nodule**, ultrasound examination for determine size and echo characteristics of goiter and nodule and determine if fine-needle aspiration biopsy of nodule is indicated.



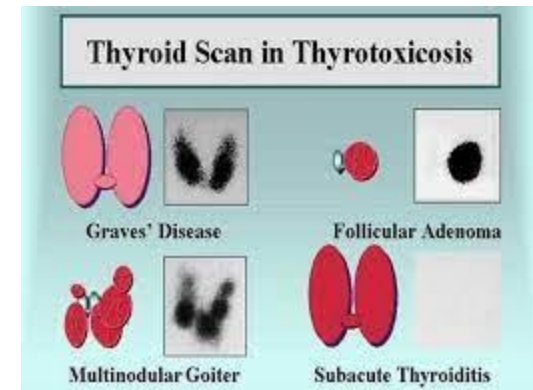
# Radioactive iodine uptake

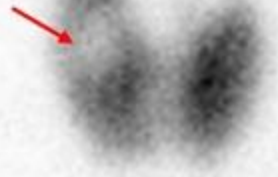
- **RAIU** → how much radioactive iodine is taken up by thyroid gland in a given time period.
- Asked to ingest (swallow) a small dosage radioactive iodine (I-123 or I-131) in liquid or capsule form
- After a time (usually 6 and 24 hours later), measures amount of radioactive iodine (taken by mouth) that accumulates in thyroid gland
- **Normal Values:**
  - 6 hours: 3 to 16%
  - 24 hours: 8 to 25%



# Radioactive iodine uptake

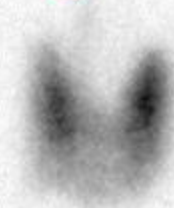
- RAIU, is a test of thyroid function.
- **Increased** (>35% at 24 hours):
  - Hyperthyroidism due to Graves, multinodular goiter or thyroid adenoma
  - Hashimoto's thyroiditis (early)
  - Iodine deficiency
- **Decreased** (<8% at 24 hours):
  - hypothyroidism
  - subacute thyroiditis
  - iodine overload (excessive iodine ingestion)





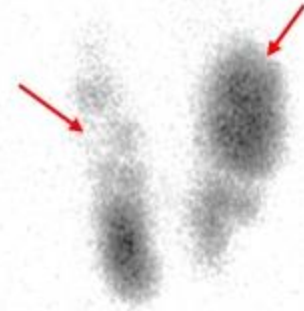
COLD NODULE

pyramidal  
lobe

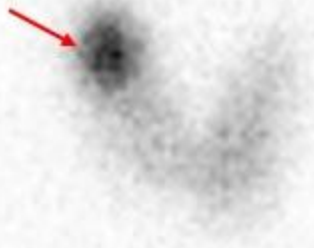


GRAVE DISEASE

hot and cold nodules



TOXIC MULTINODULAR



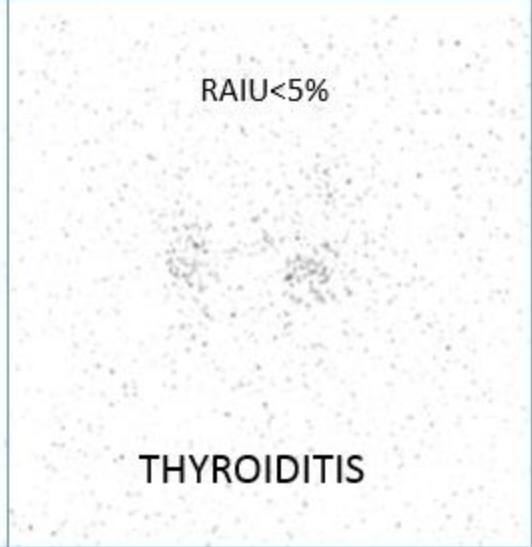
HOT NODULE

suppression of  
remainder of gland



AUTONOMOUS NODULE

RAIU < 5%



THYROIDITIS

# ETIOLOGY



## Causes of hypothyroidism in children and adolescents

Autoimmune thyroiditis
Disorders with a short course of hyperthyroidism, followed by transient hypothyroidism
Hashitoxicosis
Subacute granulomatous thyroiditis
Iodine
Deficiency
Excess exposure (eg, nutritional supplements, drugs [amiodarone, expectorants])
Drugs
Antithyroid drugs (eg, methimazole, propylthiouracil)
Anticonvulsant drugs (eg, phenytoin, phenobarbital, valproate)
Lithium
Tyrosine kinase inhibitors
Interferon alfa
Thyroid injury
External radiation therapy
Radioactive iodine treatment
Thyroidectomy
Infiltrative diseases
Langerhans cell histiocytosis
Cystinosis
Late-onset congenital hypothyroidism
DiGeorge syndrome
Williams syndrome
Prader-Willi syndrome
Hemangiomas
Thyroid hormone resistance*
Central hypothyroidism (hypothalamic-pituitary disease)

\* Patients with generalized thyroid hormone resistance are usually euthyroid because the elevated thyroid hormone concentrations are able to overcome the nuclear receptor defect. However, they may have some tissue-specific clinical manifestations of hypothyroidism and/or hyperthyroidism.

# TERMINOLOGY

● **Autoimmune thyroiditis** – is most common cause of acquired hypothyroidism.

Synonymous terms → chronic lymphocytic thyroiditis and Hashimoto thyroiditis

● **Autoimmune thyroid disease** – This is a broader term, encompassing disorders with autoimmune mechanisms that have a risk of both hypothyroidism (Hashimoto disease) and hyperthyroidism (Graves disease).

# Disorders associated with autoimmune thyroid disease

- some chromosomal disorders or other autoimmune disorders are at ↑ risk for autoimmune thyroiditis :
  - Down syndrome (trisomy 21)
  - Klinefelter syndrome
  - Turner syndrome
  - Type 1 (autoimmune) diabetes mellitus
  - Celiac disease
- periodic screening TSH and free T4 or TSH followed by test free T4 if TSH is abnormal



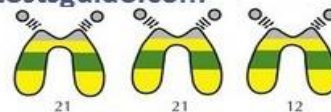
# Down syndrome

- The American Academy of Pediatrics recommends screening at birth (newborn screen), at 6 and 12 months, and then annually thereafter

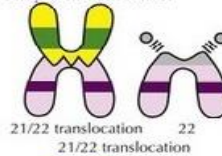
web: [www.labtestsguide.com](http://www.labtestsguide.com) | Email: [info@labtestsguide.com](mailto:info@labtestsguide.com)



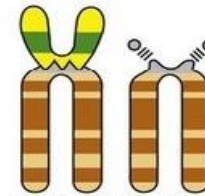
Typical facies, with epicanthal folds and slanted palpebral fissures



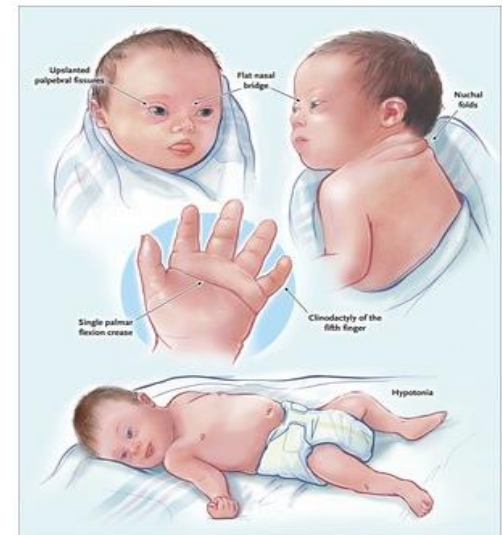
Trisomy of chromosome 21



21/22 translocation  
21/22 translocation



12/21 translocation  
12/21 translocation



Brushfield spots on iris

Short, broad hands, with simian crease and clinodactyly of 5th digit



Clinodactyly  
Single palmar crease



Small, hypoplastic ears



Wide gap between first and second toes



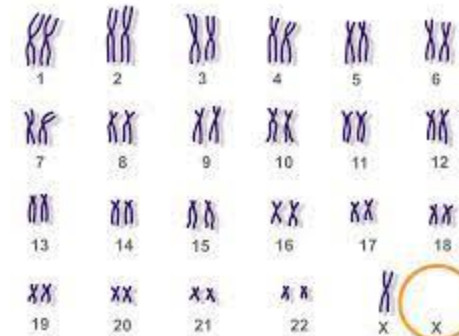
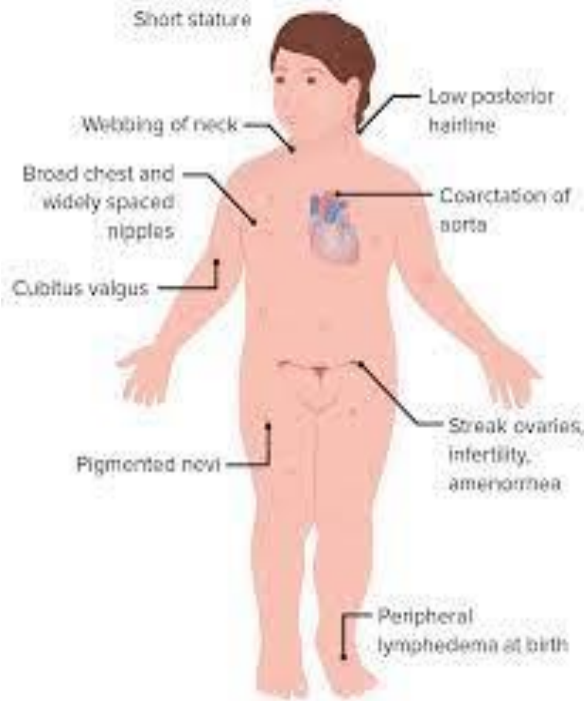
Fissured tongue in adults



Hypotonia

# Turner syndrome

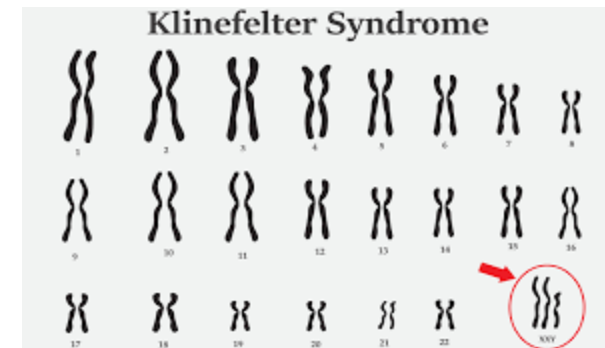
- **Annual** screening for thyroid disease is recommended in all patients with Turner syndrome.



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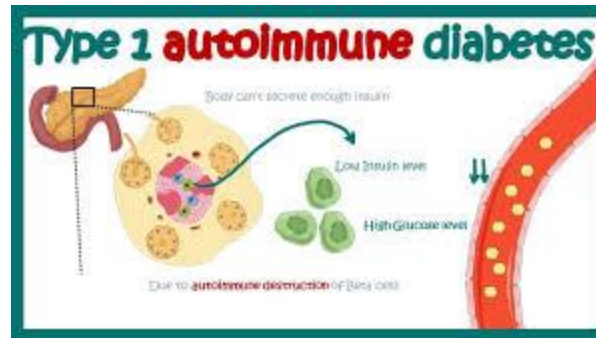
# Klinefelter syndrome

- one study reported hypothyroidism in **one of eight boys** with Klinefelter syndrome



# Type 1 diabetes mellitus

- Children with type 1 diabetes should be screened for thyroid disease at diagnosis (**after metabolic control** is established) and then **every one to two** years thereafter.



# Celiac disease

- ~10 to 20 % celiac disease have autoimmune thyroiditis
- Conversely, ~ 2 to 7 % autoimmune thyroiditis develop celiac disease



# Autoimmune polyglandular syndrome

- Autoimmune thyroiditis occurs in **10 % type I APS**:

- ❖ Mucocutaneous candidiasis
- ❖ Hypoparathyroidism
- ❖ Adrenal insufficiency

APS type 1	Chronic candidiasis, hypoparathyroidism, autoimmune adrenal insufficiency (at least two of them should be present)
APS type 2	Autoimmune adrenal insufficiency (must always be present) + autoimmune thyroid disease and/or type 1 <i>diabetes mellitus</i>
APS type 3	Autoimmune thyroid disease + other autoimmune diseases (excluding autoimmune adrenal insufficiency, hypoparathyroidism, chronic candidiasis)
APS type 4	Two or more organ-specific autoimmune diseases (which do not fall into type 1, 2, or 3)

- Chronic autoimmune thyroiditis occurs in **70 % type II APS**:
- Adrenal insufficiency + autoimmune thyroiditis  $\pm$  Autoimmune diabetes

# Disorders with transient hypothyroidism, developing after a short course of hyperthyroidism

- These disorders are characterized by hyperthyroidism in acute phase, often followed by hypothyroidism, then recovery to euthyroidism.
- **Hyperthyroidism → Hypothyroidism → Euthyroidism**

# "Hashitoxicosis"

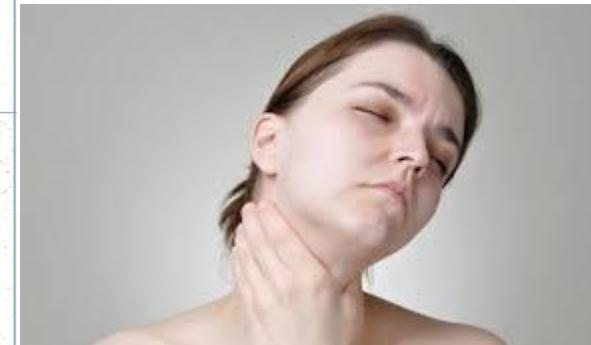
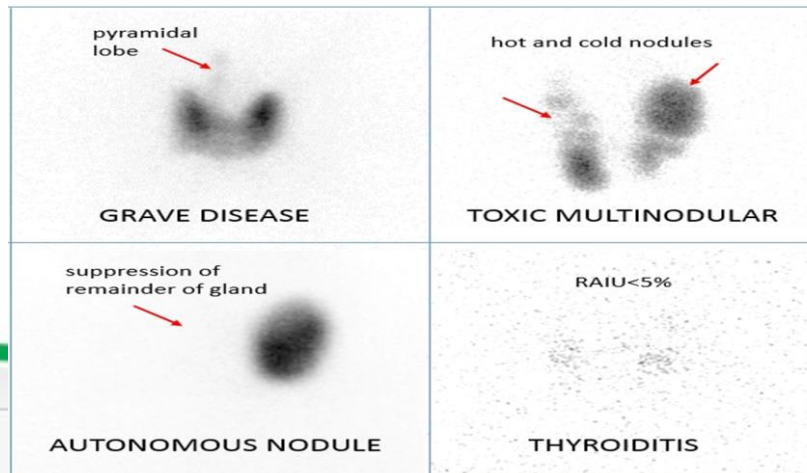
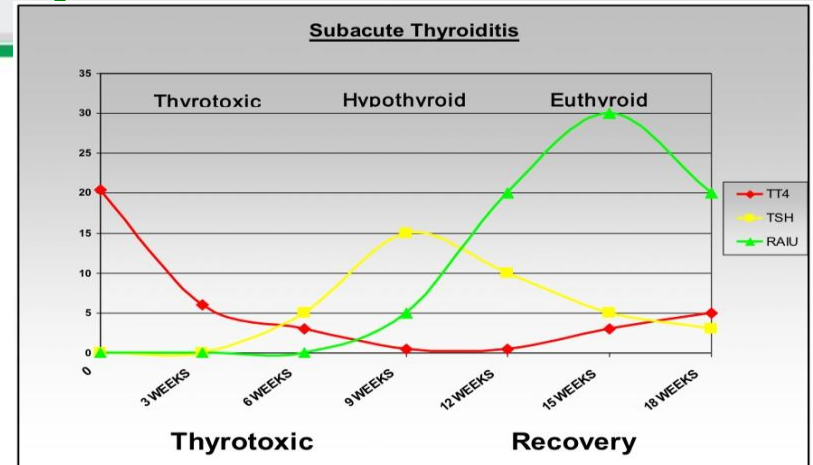
- Transient hyperthyroidism caused by inflammation associated with hashimoto thyroiditis

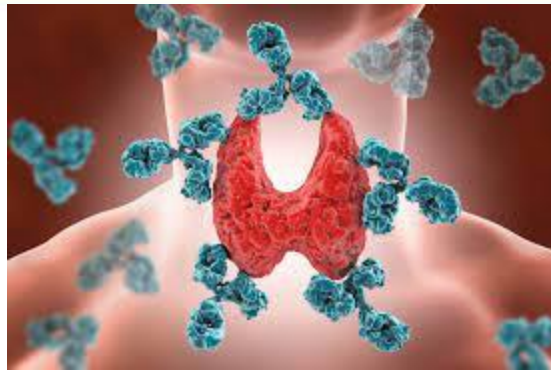




# Subacute granulomatous thyroiditis

- de Quervain disease
- Viral or postviral syndrome
- Tender, diffuse goiter
- 25- 50% fever or leukocytosis
- High ESR
- Brief course of hyperthyroidism (two to six weeks), followed by hypothyroidism and then recovery.
- Radioactive iodine uptake will be low, distinguishing this entity from Graves disease in which uptake is high.





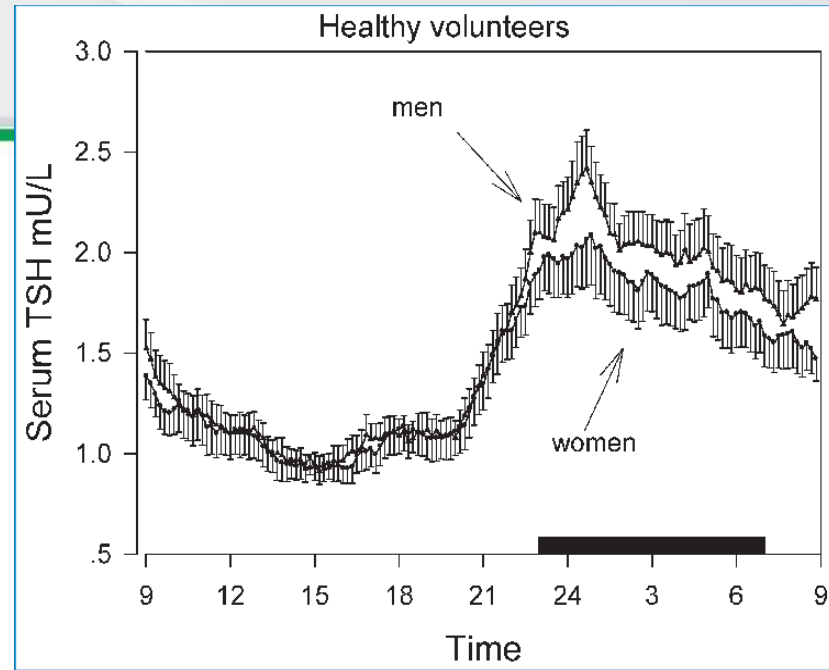
- A recent prospective observational study → SARS-CoV-2 might **directly induce viral thyroiditis**.
- Low fT3 associated with an ↑ clinical deterioration
- May be a **direct effect of SARS-CoV-2 on thyroid function**



# DIAGNOSIS

- Children suspected to hypothyroidism check of **TSH and**
  - Free thyroxine (free T4)  
or
  - Total T4 plus T3RU

- TSH have **diurnal variation** (higher at night, lower during day)
- TSH **at 8 AM** are more sensitive for diagnosis of mild primary hypothyroidism as compared with 4 PM



### Normal ranges for thyroid function tests in infants and children

Age	Free T4* (ng/dL)	T4 (mcg/dL)	Free T3 (pg/mL)	T3 (ng/dL)	TSH (mU/L)	TBG (mg/dL)
Cord blood	0.9 to 2.2	7.8 to 13.1	0.2 to 2.4	15 to 75	2.2 to 10.7	1.4 to 9.4
1 to 4 days	2.2 to 5.3	9.3 to 20.9	1.8 to 7.6	100 to 740	2.7 to 26.5	
4 to 30 days	0.9 to 3.4	8.0 to 21.8	2.93 to 5.08	105 to 387	1.2 to 13.1	1.9 to 4.5
1 to 12 months	0.9 to 2.3	7.2 to 15.7	2.67 to 5.21	105 to 245	0.6 to 7.3	1.9 to 4.4
1 to 5 years	0.8 to 1.8	6.4 to 13.5	2.73 to 4.95	105 to 269	0.7 to 6.6	1.6 to 4.2
6 to 10 years	1.0 to 2.1	6.0 to 12.8	2.73 to 4.69	94 to 241	0.8 to 6.0	1.4 to 3.7
11 to 18 years	0.8 to 1.9	4.7 to 12.4	2.67 to 4.62	80 to 210	0.6 to 5.8	1.2 to 2.9
>18 years	0.9 to 2.5	5.3 to 10.5	2.10 to 4.40	70 to 204	0.4 to 4.2	1.5 to 3.4

T4: thyroxine; T3: triiodothyronine; TSH: thyroid-stimulating hormone; TBG: thyroxine-binding globulin.

\* Because the normal free T4 reference range varies according to the assay method, clinicians need to determine the range for their specific laboratory, which may differ from the data presented in the table.

Data adapted from the following sources:

1. Nelson JC, Clark SJ, Bonut DL, et al. Age-related changes in serum free thyroxine during childhood and adolescence. *J Pediatr* 1993; 123:899.
2. Elmlinger MW, Kühnel W, Lambrecht HG, et al. Reference intervals from birth to adulthood for serum thyroxine (T4), triiodothyronine (T3), free T3, free T4, thyroxine binding globulin (TBG) and thyrotropin (TSH). *Clin Chem Lab Med* 2001; 39:973.
3. Mutlu M, Karagüzel G, Aliyazicioğlu Y, et al. Reference intervals for thyrotropin and thyroid hormones and ultrasonographic thyroid volume during the neonatal period. *J Matern Fetal Neonatal Med* 2012; 25:120.
4. Strich D, Edri S, Gillis D. Current normal values for TSH and FT3 in children are too low: evidence from over 11,000 samples. *J Pediatr Endocrinol Metab* 2012; 25:245.
5. Lem AJ, de Rijke YB, van Toor H, et al. Serum thyroid hormone levels in healthy children from birth to adulthood and in short children born small for gestational age. *J Clin Endocrinol Metab* 2012; 97:3170.
6. Esoterix (Endocrine Sciences).

# Case 1

- Boy 14 yrs old
- TSH=14 mIU/l
- T4= 4 mg/dl
- Diagnosis?
- Treatment?

**Normal ranges for thyroid function tests in infants and children**

Age	Free T4* (ng/dL)	T4 (mcg/dL)	Free T3 (pg/mL)	T3 (ng/dL)	TSH (mU/L)	TBG (mg/dL)
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>18 years	0.9 to 2.5	5.3 to 10.5	2.10 to 4.40	70 to 204	0.4 to 4.2	1.5 to 3.4

# Elevated TSH with low free T4

- overt primary hypothyroidism
- Replacement of thyroid hormone medication: Levothyroxine



Anti TPOAb and Anti TgAb



If goiter → Sonography

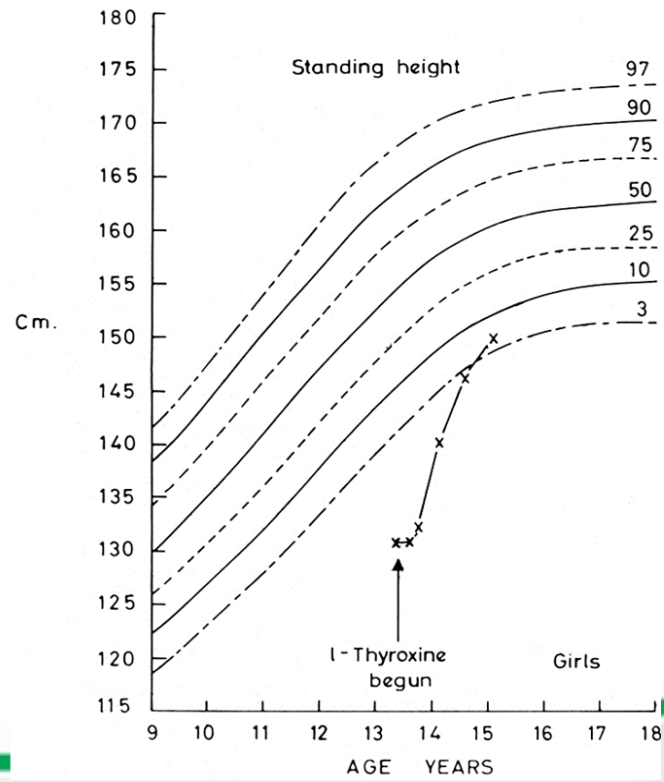


If suspicious sonography → FNA





Miss B.C. 320434



## Case 2

- Girl 8 yrs
- TSH=8 mIU/l
- T4= 9 mg/dl
- Diagnosis?
- Treatment?

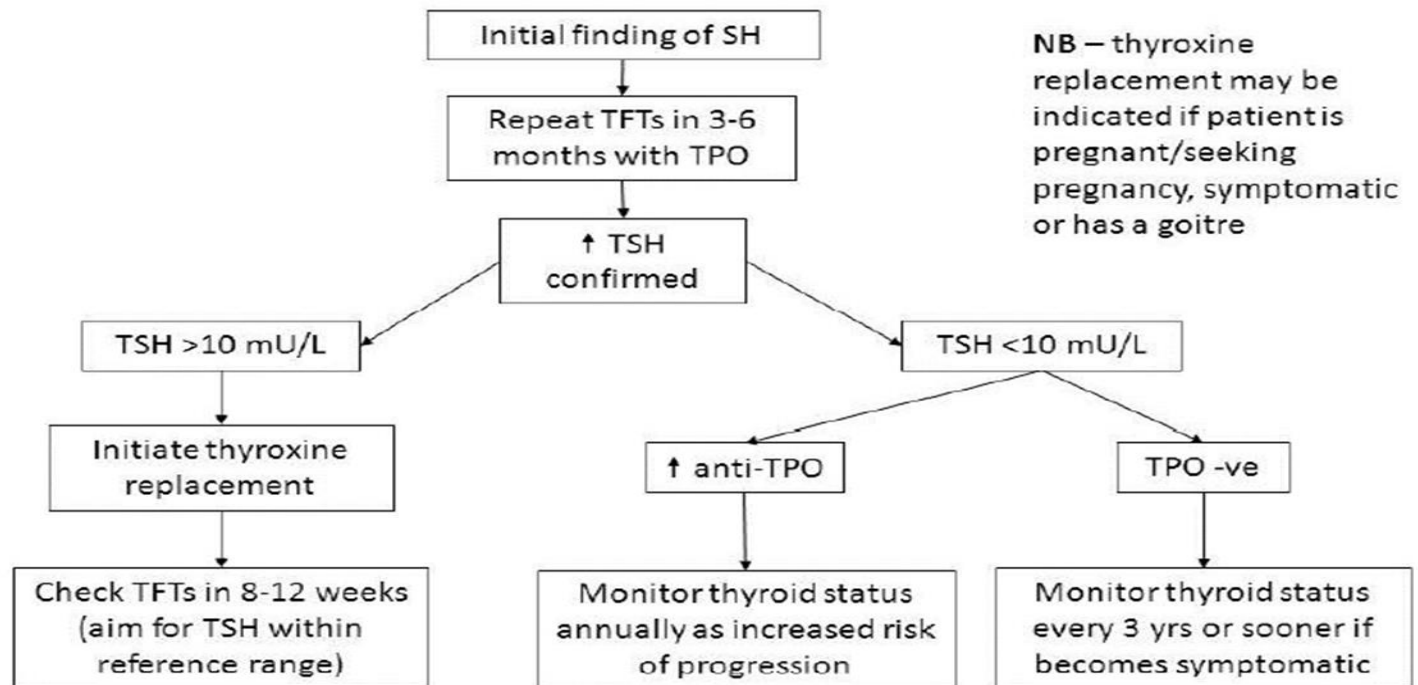
Normal ranges for thyroid function tests in infants and children

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# Elevated TSH with normal free T4

- subclinical hypothyroidism

## Management of subclinical hypothyroidism



# subclinical hypothyroidism, treatment

1. TSH levels  $>10$  mU/L
2. Clinical features such as a decreasing height velocity
3. Goiter
4. Positive antithyroid antibodies
5. Metabolic complications such as dyslipidemia



- most clinicians would treat until growth and puberty are complete, and then reevaluate thyroid function.

## Elevated TSH with normal free T4

- Elevated TSH probably is consequence rather than a cause of obesity that return to normal after weight loss
- Elevated serum leptin, stimulates transcription of TRH gene



# Case 3

- Boy 5 yrs in routine lab test :
- TSH=4 mIU/l
- T4= 4 mg/dl
- Diagnosis?
- Treatment?

Normal ranges for thyroid function tests in infants and children

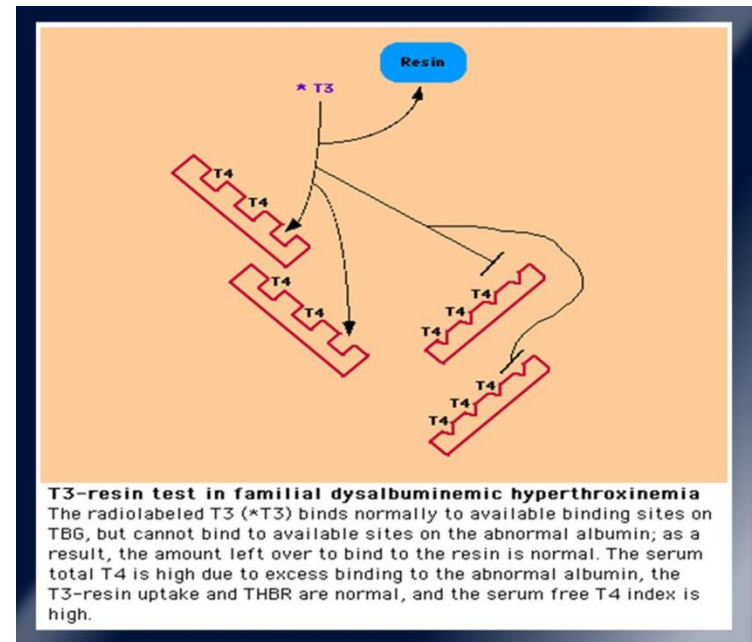
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## ❑ Central hypothyroidism

- ↓T4
- TSH normal or ↓
- ↓T3RU
- ↓FT4

## ❑ TBG deficiency

- T4 ↓
- TSH normal
- T3RU ↑
- FT4 normal



# Normal or low serum TSH with low free T4

- Central hypothyroidism
- Clinical setting suspicious for central hypothyroidism.

- وجود هیپوگلیسمی (ناشی از کمبود هورمون رشد و آدرنوکورتیکوتروپین)
- پرادراری (ناشی از کمبود هورمون آنتی دیورتیک)،
- ناهنجاریهای خط میانی صورت
- Microphallus ناشی از کمبود گونادوتروپینها،
- نیستاگموس مادرزادی و اختلالات بینایی،



## Case 3

- RT3u= 23% ( nl 26- 35%)
- Free T4= 0.5 ng/dl (NI 0.8 – 2.2 )



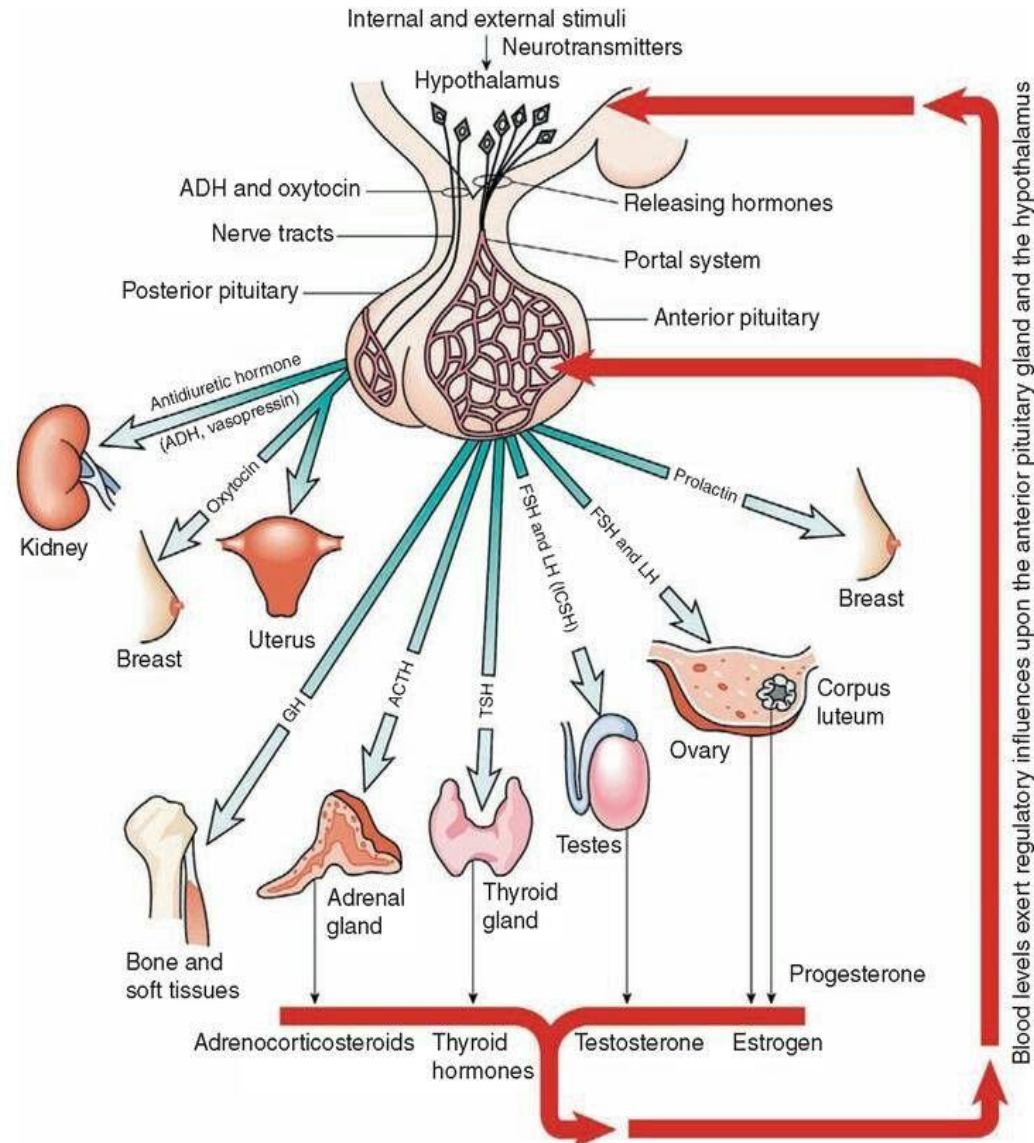
## Case 3

- Central Hypothyroidism
- Treatment?



# Case 3

1. Check other pituitary axis hormones:  
**Cortisol**
  2. Brain MRI with contrast
- Levotyroxine increases urinary excretion of cortisol → Adrenal crisis
  - Hydrocortisone before Levotyroxine



- Similar results may be found with **nonthyroidal illness syndrome**.
- If patient with acute or chronic illness, should be repeated after recovery from illness before making a definitive diagnosis.



# Case 4

- In PICU boy 5 yrs with sepsis :
- TSH=2 mIU/l
- T4= 4 mg/dl
- Diagnosis?
- Treatment?

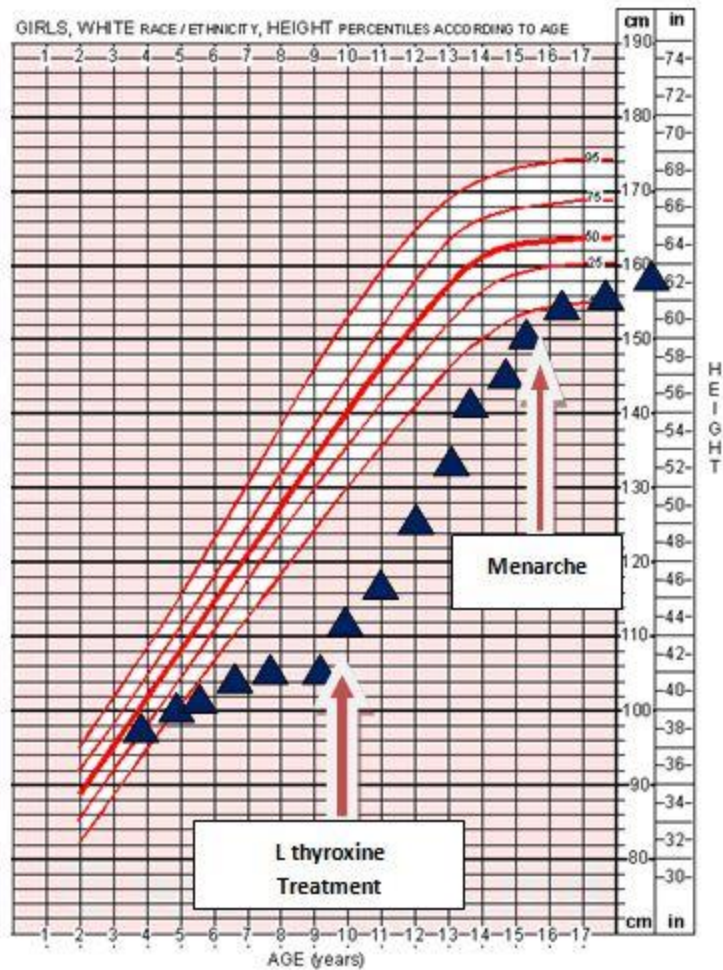
Normal ranges for thyroid function tests in infants and children

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## Changes in Thyroid Hormone Levels During Illness

Severity of Illness	Free T3	Free T4	Reverse T3	TSH	Probable Cause
Mild	↓	N	↑	N	↓ D2,D1
Moderate	↓↓	N, ↓, ↑	↑↑	N, ↓	↓↓ D2,D1, ↑ D3
Severe	↓↓↓	↓	↑↑	↓↓	↓↓ D2,D1, ↑ D3
Recovery	↓	↓	↑	↑	?

# TREATMENT AND PROGNOSIS



# Indications for levothyroxine

- Levothyroxine is recommended treatment for children with primary or central hypothyroidism.
- The goals of treatment are to restore normal growth and development, pubertal development







## اسامی تجاری موجود در ایران

یوتیروکس محصول شرکت مرک

وارد کننده	تولید کننده	نام تجاری
	داروسازی ابوریحان [ایران]	قرص لووتین 0.1 میلی گرم
	داروسازی ایران هورمون [ایران]	قرص لوکسین 0.1 میلی گرم
	داروسازی ایران هورمون [ایران]	قرص لوکسین 50 میکرو گرم
بهستان دارو	HEXAL [آلمان]	قرص ال-تیروکس 50 میکروگرم
بهستان دارو	HEXAL [آلمان]	قرص ال-تیروکس 100 میکروگرم
داروسازی اکتورکو	MERCK KGaA [آلمان]	قرص یوتیروکس 50 میکروگرم
داروسازی اکتورکو	MERCK KGaA [آلمان]	قرص یوتیروکس 100 میکروگرم
	داروسازی ایران هورمون [ایران]	قرص لووکسین 0.075 میلی گرم
داروسازی اکتورکو	MERCK KGaA [آلمان]	قرص یوتیروکس 25 میکرو گرم
داروسازی اکتورکو	MERCK SERONO [آلمان]	قرص یوتیروکس 150 میکرو گرم
داروسازی اکتورکو	MERCK KGaA [آلمان]	قرص یوتیروکس 75 میکرو گرم



# Levothyroxine dose

- Initial treatment at following doses, oral , once daily:
- ● Age 1 to 3 years – 4 to 6 mcg/kg body weight
- ● Age 3 to 10 years – 3 to 5 mcg/kg
- ● Age 10 to 16 years – 2 to 4 mcg/kg
- Dose at any age is approximately 100 mcg/m<sup>2</sup>/day
- Children **clear levothyroxine more rapidly** than adults → weight-adjusted daily replacement dose is higher.



# Levothyroxine dose

- Therapy should be initiated with levothyroxine **dose in middle of appropriate range for age**
- **Lower end of range in subclinical hypothyroidism and central hypothyroidism.**
- Then adjusted based on thyroid hormone



# Levothyroxine dose

- In **longstanding hypothyroidism**, **rapid correction** of hypothyroidism may be associated **with untoward effects**, in particular on **behavior** and **↑ risk of pseudotumor cerebri**.
- we recommend a **slower up-titration** to full dosing →
  - I. one-quarter of full dose for 4-6 weeks
  - II. then ↑ by a one-quarter dose every 4-6 weeks
  - III. full dosing is achieved by 12 to 16 weeks.



# Monitoring and dose adjustment

Check TSH and FT4 :

- 6-8 weeks after initiation of treatment and then every 6 to 12 months
- 6-8 weeks after any dose change or
- If patient develops any clinical manifestations of hypo- or hyperthyroidism



# Monitoring and dose adjustment

- Maintain TSH and free T4 (or T4) in normal reference range for age
- FT4 varies according to assay method, to determine range for their specific lab
- In children grow:
  - Target TSH in lower one-half
  - Free T4 in upper one-half of reference range



# Monitoring and dose adjustment in central hypothyroidism

- Only measurement of FT4 or T4
- **TSH** usually low or undetectable **so is not useful**
- Maintaining FT4 in **upper one-half of reference range**
- As an example, if normal free T4 reference range is 0.8 to 1.8 ng/dL, optimal free T4 range would be 1.3 to 1.8 ng/dL.





## Adverse effects

- Levothyroxine is generally well tolerated and has minimal adverse effects. Considerations are:
  - Longstanding hypothyroidism are at risk pseudotumor cerebri shortly after initiation of levothyroxine
  - Children with more chronic (or severe) hypothyroidism also are at higher risk of temporary poorer school achievement and hyperactivity at initiation of treatment





- Prolonged excessive doses of levothyroxine should be avoided:
- Infants with open cranial sutures may develop craniosynostosis, and older children may develop adverse behavior changes and lower school performance.
- Both hypothyroidism and overtreatment can affect bone mineral density



# Course



- Once levothyroxine therapy is started, it probably is best to **continue treatment until growth and pubertal development are complete.**
- At that time that **question of permanency** of hypothyroidism (eg. subclinical hypothyroidism), it can discontinue levothyroxine and measuring TSH one month later
- Hypothyroidism due to **autoimmune thyroiditis is not invariably permanent** → some treated for several years have persistently normal thyroid function after levothyroxine treatment is discontinued.

