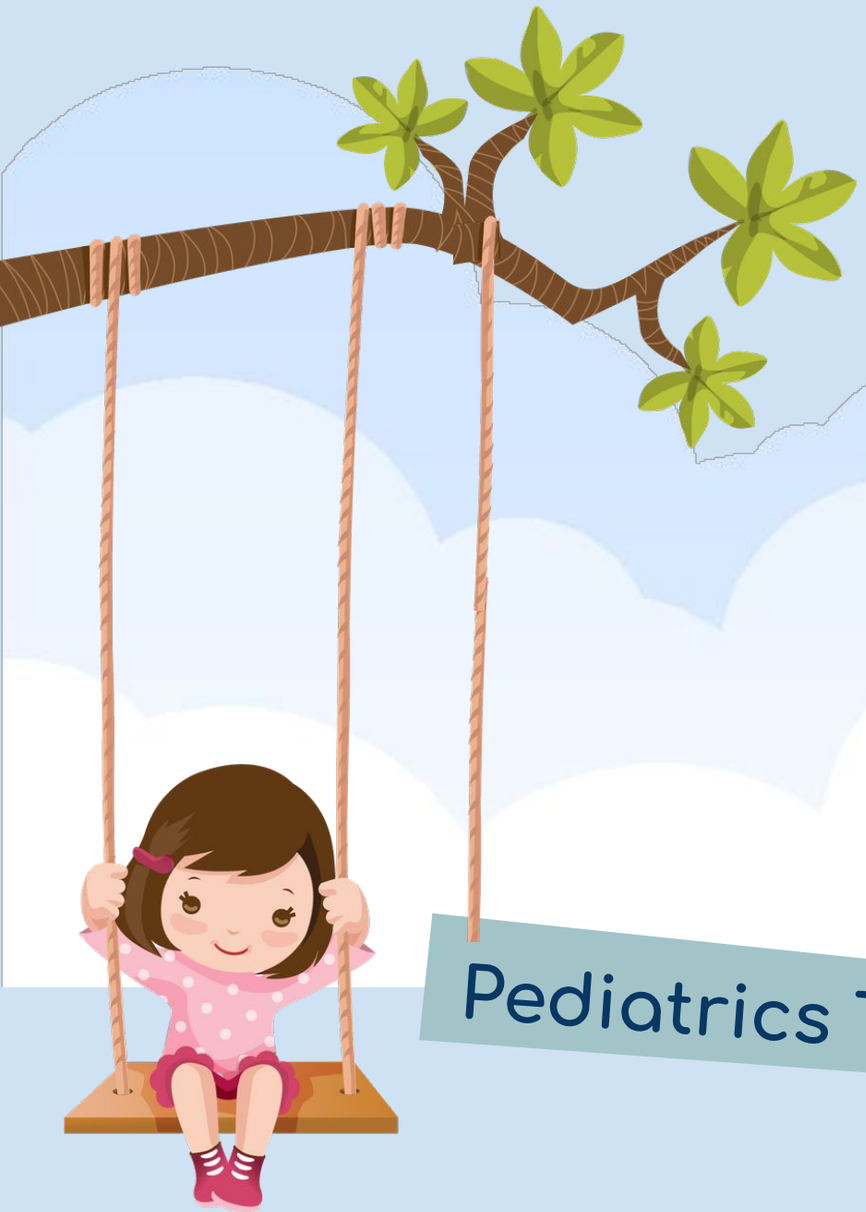

Pediatrics TeamWork

437

Thyroid Diseases

Done by:

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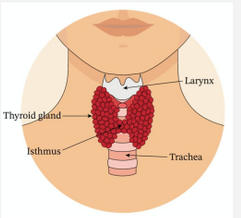
Notes Previous Notes Book Important!

Basics!



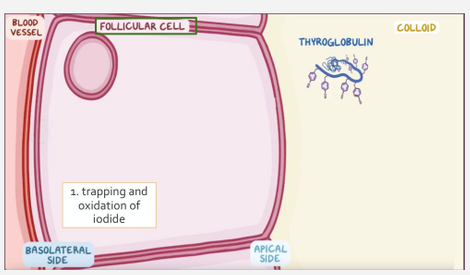
Physiology

Butterfly shaped gland, located in the anterior neck, consists of two lobes (left & right), which are connected by a central isthmus anteriorly.

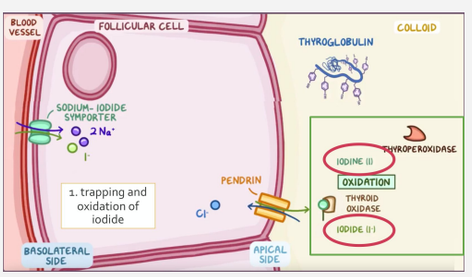
- Thyroid hormones: Thyroid gland synthesize **TWO forms of the thyroid hormone**
  - T4 (thyroxine)
  - T3 (triiodothyronine)

T4 (thyroxine)	T3 (triiodothyronine)
• Secreted in larger quantities compared to T3 (> 90% of hormone secreted by thyroid) • Majority is bound to plasma proteins (only 0.03% is free T4) • Half-life of T4 (6-8 days) longer compared to T3 ; that's why we like to measure it • Metabolism: 85% of T4 is converted to T3 or reverse T3 (RT3) in the periphery by deiodinase enzymes	• More biologically active (approximately 4x as potent as T4) • but T3 is secreted in smaller quantities and has a shorter half-life compared to T4 • Majority is bound to plasma proteins (only 0.3% is free T3) • Half life (1-2 days)

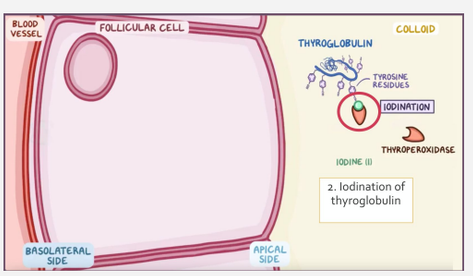
- Thyroid hormone synthesis and secretion : If you understand physiology you will understand pathology



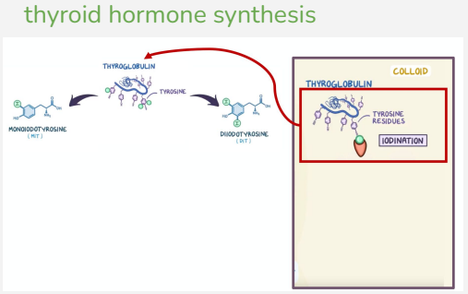
Thyroglobulin plays major role in thyroid hormone synthesis



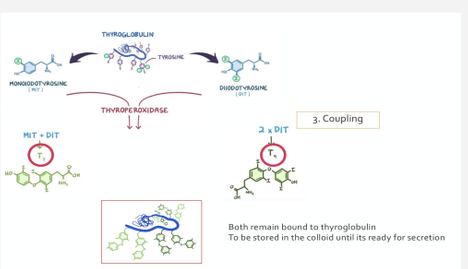
Pathology : iodine deficiency



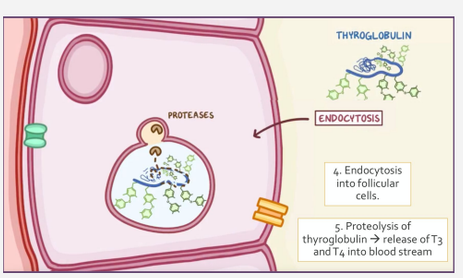
Iodine get attached to thyroglobulin



In the blood

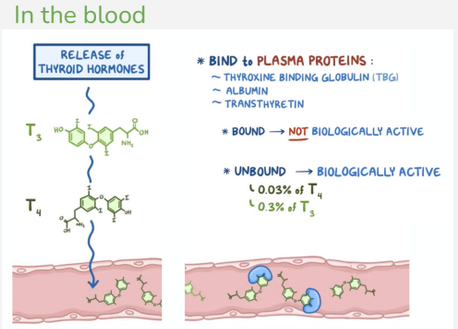


Coupling of :
MIT+DIT= T3 , 2 DIT = T4



Stay inactive attached to thyroglobulin and sits in the colloid until we need it

When needed and ready for secretion it gets engulfed by the follicular cells (Endocytosis) and then thyroglobulin is cleaved to T4 and T3



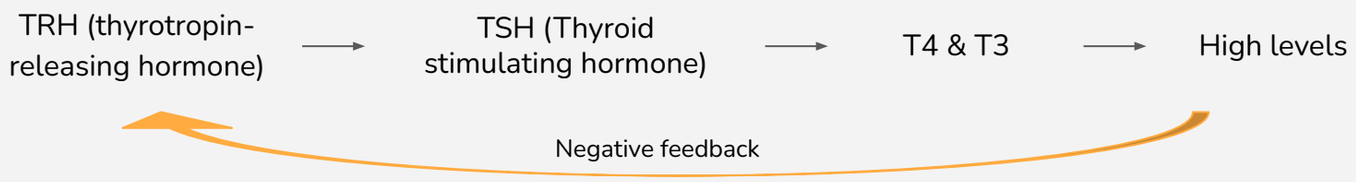
Why is it important to know this? Bc when we measure it we measure the total T4 and T3 any effect on the proteins that they are bound to may affect the measurement
-Free form is the most accurate

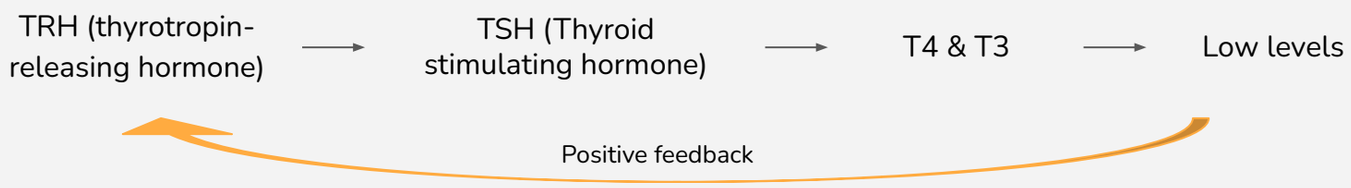
Thyroid hormone action:

- Diffuse actions, affecting nearly every organ system
    1. Increase the basal metabolic rate including: increased Na+/K+ ATPase activity, increased O2 consumption, increased respiration, heat generation, and **increased sympathetic and cardiovascular activity**
    2. Required for normal growth of the fetus and child
    3. Required for normal brain development
- When present at higher than normal levels:
    1. Potentiates the actions of GH, catecholamines (epinephrine, norepinephrine), glucagon and cortisol
    2. resulting in increased gluconeogenesis, ketogenesis and proteolysis, mimicking what happens in starvation

Regulation of thyroid hormones:

- Hypothalamic - pituitary - thyroid axis:





How to assess thyroid axis?

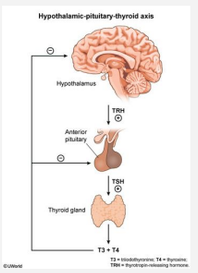
By thyroid function test

1. TSH
2. Thyroid hormones
    - Free T4(biologically active form)
    - +/-Total T4(bound to proteins)
    - Total T3 (bound to proteins) = helpful for T3 thyrotoxicosis
    - Free T3 (biologically active) - not used because unreliable assay results
3. Others:
    - TBG (thyroid binding globulin)
    - Free T4 index, calculated using the T3 uptake (or THBI) – old method to estimate free T4 levels

When total T4 is low while T4 is normal may be the protein is low

Thyroid Disorders

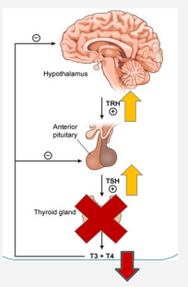
Hypothyroidism



- It is a state of thyroid hormone deficiency
- **Classified into**
  1. Primary hypothyroidism: thyroid gland defect
  2. Secondary hypothyroidism: pituitary defect
  3. Tertiary hypothyroidism: hypothalamic defect

1. Primary hypothyroidism (90%)

- Inadequate thyroid hormone production secondary to **intrinsic thyroid defect**, differential diagnosis:
  - Congenital (1/4000 births)
  - Acquired:
    - Autoimmune: Hashimoto's thyroiditis
    - Iodine deficiency
    - Hypothyroid phase of subacute thyroiditis
    - Drugs: goitrogens (iodine), PTU, MMI, lithium
    - Infiltrative disease (progressive systemic sclerosis, amyloid)
    - Iatrogenic: post-ablative (I-131 or surgical thyroidectomy)
    - Neoplasia



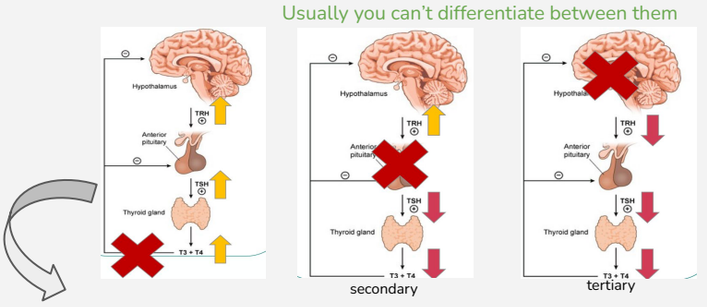
2. Secondary hypothyroidism

- Insufficiency of pituitary TSH

3. Tertiary hypothyroidism

- Decrease TRH from the hypothalamus (rare)

Usually you can't differentiate between them



- **Note:** Peripheral tissue resistance to thyroid hormone can lead to hypothyroidism clinical features
  Thyroid resistance syndrome: Tissue don't see the thyroid hormone (everything HIGH)
- **Signs & symptoms:**

Any age	In infancy (congenital hypothyroidism)

• **Growth deceleration WITH delayed skeletal maturation**
• Weight gain
• Fatigue, lethargy
• **Constipation**
• Cold intolerance
• Bradycardia
• **Myxedema or "puffy skin,"** dry skin
• Delayed deep tendon reflexes
• Amenorrhea or oligomenorrhea in adolescent girls
• Delayed puberty
• +/- Goiter
	Usually asymptomatic in neonatal period (because maternal T4 crosses the placenta)
	• Postmaturity, macrosomia
	• **Wide fontanelle**
	• Prolonged jaundice
	• Macroglossia and feeding problems
	• Hoarse cry
	• Abdominal distention, constipation
	• **Umbilical hernia**
	• **Hypotonia or lethargy**
	• **+/- Goiter**
	• If left untreated:
	  ◦ Slowed development, late teeth, late milestones, short stature.
	  • Eventual mental retardation.

Clinical Features

Table 21. Clinical Features of Hypothyroidism

General	Fatigue, cold intolerance, slowing of mental and physical performance, hoarseness, macroglossia
CVS	Pericardial effusion, bradycardia, hypotension, worsening CHF + angina, hypercholesterolemia, hyperhomocysteinemia, myxedema heart
Respiratory	Decreased exercise capacity, hypoventilation secondary to weak muscles, decreased pulmonary responses to hypoxia, sleep apnea due to macroglossia
GI	Weight gain despite poor appetite, constipation
Neurology	Paresthesia, slow speech, muscle cramps, delay in relaxation phase of deep tendon reflexes ("hung reflexes"), carpal tunnel syndrome, asymptomatic increase in CK, seizures
GU	Menorrhagia, amenorrhea, impotence
Dermatology	Puffiness of face, periorbital edema, cool and pale, dry and rough skin, hair dry and coarse, eyebrows thinned (lateral 1/3), discolouration (carotenemia)
Hematology	Anemia: 10% pernicious due to presence of anti-parietal cell antibodies with Hashimoto's thyroiditis

- **Diagnostic workup:**
  - Thyroid function test

	TSH	*T4*	*FT4*	*T3U (free T4 index)*
Primary hypothyroidism	High	Low	Low	Low
Secondary and Tertiary hypothyroidism	Low or (inappropriately normal)	Low	Low	Low
Subclinical hypothyroidism	Normal or slightly high	Normal	Normal	Normal

- **Treatment:** Levothyroxine (T4) replacement

Acquired Hypothyroidism:

- Prevalence in children is **0.15% with a female-to-male ratio of 3:1**.
- Etiology:

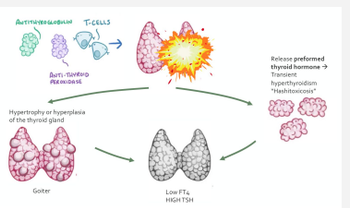
1. **Hashimoto disease** (Autoimmune hypothyroidism):
   * Most common cause of childhood hypothyroidism in **developed** countries
2. **Iodine deficiency:**
   * The most common causes of acquired hypothyroidism **worldwide**
   * Universal Salt Iodization (USI) is a strategy to ensure sufficient intake of iodine
   * In the Middle East, 64% of households consume adequately iodized salt with wide variation between countries.
3. Other causes:
   * Thyroid surgery and irradiation
   * Medications (iodine, lithium, amiodarone, etc.)
   * Pituitary or hypothalamic dysfunction (secondary or tertiary acquired hypothyroidism)

Hashimoto disease:

- Lymphocytic thyroiditis "chronic lymphocytic thyroiditis [CLT]"
- The most common cause of acquired hypothyroidism in developed countries.
- It is an **autoimmune disorder**: screen for it periodically in diseases mentioned below
  - **Higher prevalence** in children with **Trisomy 21 (Down syndrome), turner syndrome, type 1 diabetes mellitus, celiac disease, and Klinefelter syndrome**
  - FHx or personal hx of autoimmune disease

Hashimoto disease cont.:

- Characterized by:
  - Lymphocytic infiltration of the thyroid gland→ resulting in varying degrees of **follicular fibrosis** and **atrophy and follicular hyperplasia**
  - Presence of thyroid antibodies: Antithyroglobulin antibodies, Anti–thyroid peroxidase (anti-TPO) antibodies.
- Clinical features – variable:
  - Initial signs and symptoms **may be subtle.**
  - Growth retardation is usually not severe. However, if it remains unrecognized and untreated (chronic), **linear growth is severely retarded and sexual maturation** is also delayed.
  - **+/- Goiter** (hyperplasia) > hallmark of classic Hashimoto disease (small rubbery goiter)
  - **Some patients have Transient hyperthyroidism ("Hashitoxicosis")**



- Work up:
  - The results of the thyroid function test depend on stage of disease:
    * TSH is elevated.
    * FT4 low
    * Not necessary to measure T3 as it will be low as well
  - **Presence of Antithyroglobulin and anti- TPO antibody in the serum**
- Treatment: is replace with L-thyroxine (analog of T4)

Case Presentation

- A **13-year-old girl** comes to the office for checkup. **She has not experienced** any recent change in appetite or weight, diarrhea, constipation, heat or cold intolerance, dyspnea, or hoarseness. The patient's **mother has hypothyroidism** treated with levothyroxine and hypertension treated with hydrochlorothiazide. Examination shows **a symmetrically enlarged, nontender, firm thyroid gland**. There is no cervical lymphadenopathy, and the rest of the physical examination is normal. Her **TSH level is 7.2μU/ml (mildly elevated)**and free **T4 is normal**.

- **Which of the following auto-antibodies is most likely associated with this patient's medical condition?**
  A. Anticardiolipin antibody
  B. Antimitochondrial antibody
  C. Antithyroid peroxidase antibody
  D. Thyroid-stimulating immunoglobulin
  E. TSH-receptor-blocking antibody

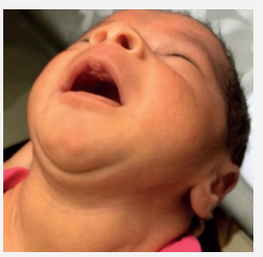
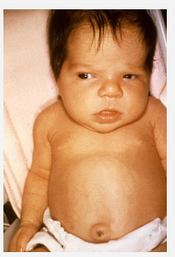
  Answer:C

- **Of the following conditions, which are associated with an increased prevalence of autoimmune thyroid disease and require periodic screening for hypothyroidism?**
  A. Type 1 diabetes, Turner syndrome, and Down syndrome
  B. Turner syndrome, Prader–Willi syndrome, and McCune–Albright syndrome
  C. Down syndrome, type 1 diabetes, and congenital adrenal hyperplasia (CAH)
  D. Prader Willi syndrome, Down syndrome, and CAH
  E. McCune–Albright syndrome, type 1 diabetes, and CAH

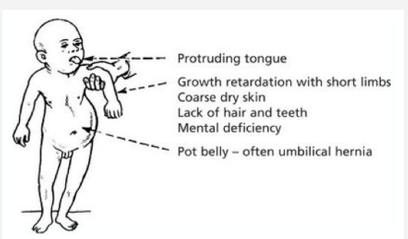
  Answer:A

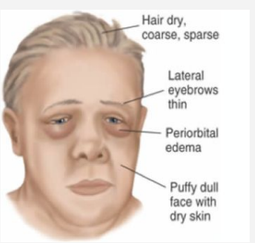
Congenital Hypothyroidism:

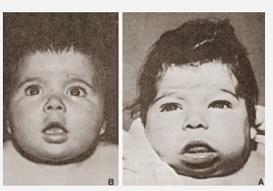
- Incidence is same worldwide (1 in 4000).
- **Most common preventable cause of intellectual disability**.
- Etiology:
  - **Sporadic:**
    * Majority of cases and most due to **thyroid dysgenesis** (absent thyroid, hypoplastic thyroid, ectopic thyroid).
  - **Hereditary (rare):**
    * Thyroid dyshormonogenesis (defect in synthesis of thyroid hormone), or
    * Generalized thyroid hormone resistance.
  - **Transient** congenital hypothyroidism:
    * maternal-antibody-mediated
    * Prenatal exposure to radioiodine or antithyroid medications Ex.mom has Grave's
    * Iodine deficiency (rare in developed countries)
  - **Secondary** (central hypothyroidism)
- Clinical features:
  - Usually **asymptomatic** in neonatal period (because maternal T4 crosses the placenta)
  - Postmaturity, macrosomia
  - **Wide fontanelle**
  - Prolonged jaundice
  - **Macroglossia** and **feeding problems**
  - Hoarse cry
  - Abdominal distention, **constipation**
  - **Umbilical hernia**
  - **Hypotonia** or lethargy
  - **+/- Goiter**

- If left untreated > **"cretinism"**
  - Slowed development, late teeth, late milestones, short stature.
  - Eventual **mental retardation**.








cretinism

- Abnormal NBS > Confirm with venous sample
- Treatment:

1. Oral levothyroxine is the only treatment of choice
2. should be initiated as early as possible at 10–15 µg/kg/day.

Treatment should be started before 2 weeks of age to reduce risk of impaired neurodevelopment.

Screening:

- Newborn screening program to detect congenital hypothyroidism early > Prevent mental retardation consequence!
- Types of thyroid newborn screening:

- Primary T4 - sequential TSH: some just test for T4 if abnormal they move on to TSH
  - Used by most North American programs.
  - Initial filter paper blood spot: **T4 > TSH measurement in specimens with low T4 values.**
  - Uses a **percentile** as the **cutoff**, with **10th percentile** being the usual standard.
- Primary TSH - sequential T4: In SA we start w/ TSH if abnormal → check T4
  - Used in all European countries (except the Netherlands), Japan, Australia, and parts of North America.
  - I**nitial TSH measurement**, supplemented by **T4 in cases of high TSH.**
  - **Cutoff** point for recall is **TSH 20–50 µU/mL with low T4 (<5 µg/dL) or TSH >50 µIU/mL.**
  - **picks up most cases but it can miss central hypothyroidism and potentially mild primary hypothyroidism.**
- Screen both T4 and TSH

Saudi National Newborn Screening Program:

- By Saudi Ministry of Health, aims to screen **all newborns within 24 - 72h of delivery.** To avoid the mix of maternal hormones w/ the baby's
- currently performed in 183 hospitals all over the kingdom.
- **TSH** > Cut-off levels were established using population data and data obtained from retrospective samples with proven disorders.
- TSH≥21µU/m

Case Presentation

- 2-month-old boy is brought to the emergency department due to **progressively worsening "floppiness" and poor feeding**. The infant was **born in rural village via an uncomplicated vaginal delivery** to a 38-year- old woman and then moved to Riyadh with his family. The parents describe the infantas a "good baby" who **rarely cries and sleeps through the night** but has lately been **difficult to rouse** for breastfeeding. Stools have also **decreased to every other day and are small and pellet-like**. Physical examination shows a **hypotonic** infant with a **large anterior fontanelle**, **large tongue, and a reducible umbilical hernia**. He has **low tone** and is unable to hold his head erect on his own. No other abnormalities are seen.

- **Which of the following is the most likely cause of this patient's condition?**
  A. Botulism
  B. Down syndrome
  C. Galactosemia
  D. Hirschsprung disease
  E. Hypothyroidism
  F. Phenylketonuria

Answer:E

- The laboratory calls your office telling you that a newborn infant, now **8 days old**, has an **elevated** thyroid stimulating hormone **(TSH)** and **low** thyroxine **(T4)** on his newborn screen. If this condition is left untreated, **the infant is likely to demonstrate which of the following in the first few months of life?**
  A. Hyperreflexia
  B. Hyperirritability
  C. Diarrhea
  D. Prolonged jaundice
  E. Hyperphagia

Answer:D Primary hypothyroidism

Hyperthyroidism

- It is a state of thyroid hormone excess.
- “Thyrotoxicosis” > clinical, physiological, and biochemical findings in response to elevated thyroid hormone.
- Differential diagnosis:
  1. Grave’s Disease
  2. Thyroiditis (subacute)
  3. Exogenous
- Signs and Symptoms:

Table 18. Clinical Features of Thyrotoxicosis

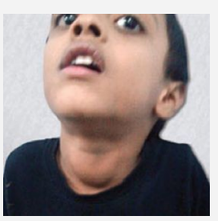
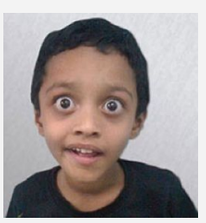
General	**Fatigue, heat intolerance, irritability, fine tremor**
CVS	Tachycardia, atrial fibrillation, palpitations Elderly patients may have only cardiovascular symptoms, commonly new onset atrial fibrillation
GI	Weight loss with increased appetite, thirst, increased frequency of bowel movements (hyperdefecation)
Neurology	Proximal muscle weakness, hypokalemic periodic paralysis (more common in Asians)
GU	Oligomenorrhea, amenorrhea, decreased fertility
Dermatology	Fine hair, skin moist and warm, vitiligo, soft nails with onycholysis (Plummer’s nails), palmar erythema, pruritis Graves’ disease: clubbing (acropachy), pretibial myxedema (rare)
MSK	Decreased bone mass, proximal muscle weakness
Hematology	Graves’ disease: leukopenia, lymphocytosis, splenomegaly, lymphadenopathy (occasionally)
Eye	Graves’ disease: lid lag, retraction, proptosis, diplopia, decreased acuity, puffiness, conjuctival injection NOTE: Lid lag is a reflection of a hyperadrenergic state and can be present in any form of thyrotoxicosis

Grave’s Disease

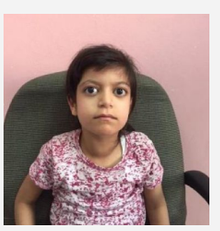
- **Most common cause** of hyperthyroidism in **children and adolescents** (95% of thyrotoxicosis in children).
- Occurs more frequently in females (male-to-female ratio 1:5).
- An autoimmune disorder: **Autoantibodies** that **stimulate the TSH receptor** leading to hyperthyroidism
- **Triad of:**

1. Hyperthyroidism with diffuse goiter.
2. Ophthalmopathy (present in over one- half of the patients) with proptosis.
3. Dermopathy: Pretibial myxedema (rough skin+puffiness around the tibia w/ orange tinge to it)is present in 1–2% of adults; it rarely occurs in children.

- **Clinical features**:
  * Gradual onset (6–12 months)
  * Emotional disturbance, Insomnia
  * Change in academic performance
  * **Palpitations**, ↑ sweating
  * Fatigue, muscle weakness
  * ↑appetite with↓**or no weight gain**
  * **Heat intolerance** (always hot)
  * Fine tremors
  * Exophthalmos
  * Menstrual irregularities
  * **Goiter** > almost always present in hyperthyroidism (usually symmetrical, smooth, soft, and nontender)

Exophthalmos , lid lag/retraction
Thin due to high metabolism



Non-tender big
(thyromegaly)

- **Thyroid storm:** Life-threatening condition that is characterized by: triggers: stress / surgery -> over activation of sympathetic system

- Hyperpyrexia(fever)up to 104°F (40°C)
- Severe tachycardia out of proportion to fever → leading to high-output cardiac failure
- Central nervous system (CNS) manifestations (agitation, delirium, psychosis, confusion, obtundation, coma, and convulsions)
- Other symptoms include severe vomiting, diarrhea, abdominal pain

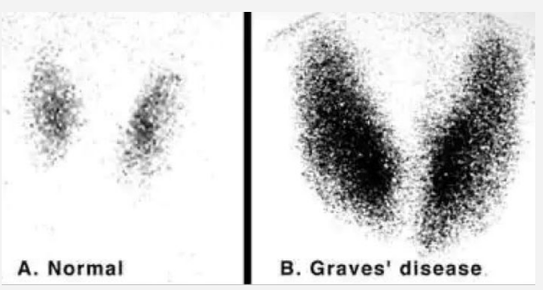
Grave's Disease cont.

- **Diagnostic workup:**

- Labs:
    * Elevated T4 & FT4 and T3 levels
    * LOW TSH
    * Elevated TSHR-Ab
- Thyroid Imaging/Scans > Radioactive iodine uptake (RAIU)
    * Test of function: order if patient is thyrotoxic
    * RAIU **measures the turnover of iodine by thyroid gland** in vivo:
        1. If **increased** uptake (e.g. incorporated) > gland is **overactive** (hyperthyroid)
        2. If **decreased** uptake (e.g. not incorporated)a > gland is **leaking** thyroid hormone (e.g. thyroiditis), **exogenous** thyroid hormone use, or **excess iodine intake** (e.g. amiodarone or contrast dye, which has high iodine content)
    * In Grave's >increased radioactive iodine (I-131) uptake > homogeneous uptake

- **Management: Treatment depends on the age and severity of the disease and may include**

1. Anti-thyroid medications - typically first-line treatment:
    - Methimazole > Side effects occur in 20–30% and include agranulocytosis (risk of fever) , hepatotoxicity, urticaria, arthralgia, and very rarely vasculitis
    - Propylthiouracil (NOT USED) > risk of severe hepatotoxicity
2. Radioiodine ablation permanent
    - used for those who do not achieve remission or experience side effects with anti-thyroid medication, or in those >10 years.
    - Often requires lifelong thyroid hormone replacement.
    - may worsen ophthalmopathy
3. Surgical thyroidectomy permanent
    - very safe (ONLY if surgeons are experienced with high-volume thyroid surgeries ' 50 thyroid surgery /year') and effective immediately.
    - Also requires lifelong thyroid hormone replacement.
    - Risks: hypoparathyroidism and vocal cord palsy
4. For thyroid storm:
    - Antithyroid hormones
    - Beta-blocker to decreased adrenergic effects
    - Can also give **iodides** (saturated solution of potassium iodide [SSKI] or Lugol's solution) every 6–8 hours and **glucocorticoids**. > glucocorticoids inhibit the peripheral conversion of T4 to T3.



Medical treatment is given for about 2 years, which should control the thyroid hormones excess, but eye signs may not resolve. If first course of medications failed after withdrawal, we may give second course or do surgery or radioiodine

Thyroiditis (painful thyroid) - rare

	Subacute thyroiditis (De Quervain's)	Acute suppurative thyroiditis
Cause	• Presumed to **viral infection** or post-viral inflammatory process	• **Bacterial infections** (gram-positive cocci) most common route is **through** a left **pyriform sinus fistula**
Clinical features	• Hyper > hypo > euthyroid • Painful goiter • Transient vocal cord paresis, malaise, fatigue, myalgia, fever • Painful condition lasts for a week to few months	• **Quite ill** with **extreme thyroid pain and tenderness, fever**, and possibly localized **compressive symptoms.** • May have **signs of sepsis** • **Mortality rate of almost 15%** • **Usually euthyroid**
diagnosis	• Initial elevated T4 and T3 • Near absent RAIU • ESR and CRP often elevated	• **TFT** → often **normal** (Unlike subacute thyroiditis) → although hypothyroidism or hyperthyroidism can present as the disease progresses.
Treatment	• **NSAID/prednisone** for pain	• **IV antibiotics** directed at the most common offending organisms. • **+/- incision and drainage of the abscess**

Case Presentation

- An infant is born to a woman who has received **very little prenatal care**. The mother is **anxious**, complains of heat intolerance and **fatigue**, and reports that she has **not gained much weight despite having an increased appetite**. On examination, the mother is **tachycardic**, **has a tremor, and has fullness in her neck and in her eyes**.
  The infant is most likely at risk for development of which of the following?
  A. Constipation
  B. Heart failure
  C. Macrocephaly
  D. Third-degree heart block
  E. Thrombocytosis

Answer:B
D: is w/ SLE

- A**16-year-old girl** develops **tachycardia** the **postoperative recovery room**. She was admitted for a **right femur fracture following a motor vehicle accident** and had an open reduction and internal fixation of the fracture. While in the recovery area, she began experiencing **nausea and vomiting**, and became **anxious** and **agitated**. The patient has no known medical problems. Her Temperature Is 39.4C(103F),blood pressure is **160/90 mmHg**, pulse is **148/min,** and respirations are **24/min**. Pulse oximetry shows 98% on room air. On examination, the patient is **delirious and has fine tremor.** Mild lid lag and **exophthalmos** is present. She has no muscle rigidity and deep-tendon reflexes are 2+ in the bilateral extremities. Laboratory Results Are As Follows:
- **Which of the following is the best next step in management of this patient?**
    A. Echocardiogram
    B. Fluid bolus and intravenous dexamethasone
    C. Intravenous dantrolene
    D. Intravenous lorazepam
    E. Plasma free metanephrines
    F. Thyroid function tests and propranolol

Hematocrit 30%
Sodium 132 mEq/L
Potassium 4.5 mEq/L
Bicarbonate 24 mEq/L
BUN 32 mg/dL
Creatinine 1.2 mg/dL
Glucose 120 mg/dL
Creatine kinase 176 U/L

Answer: F B: they want to trick you w/ adrenal insufficiency (hypotension)

- An **18-year-old girl** comes to the office due to **fatigue, anxiety, and difficulty sleeping** over the last several months. The patient has used **melatonin** as a sleep aid but with no benefit. Medical history is remarkable only for menorrhagia, for which she takes a combination estrogen/progesterone **contraceptive pill**. Her **mother has hypothyroidism** and hypertension. Blood pressure is 120/78 mm Hg and pulse is 82/min. BMI is 18.8 kg/m2. Examination of the neck shows a normal-size thyroid gland without nodules. **Serum TSH is 1.5 µU/ml (normal) and total T4 is 15 µg/dl (high)**.
- **Which of the following is the most likely explanation of this patient's laboratory findings?**
    A. Displacement of thyroid hormones from binding proteins
    B. immunoglobulin-induced hyperthyroidism
    C. Increased thyroid hormone-binding protein level
    D. Pituitary tumor
    E. Pregnancy
    F. Thyroid hormone resistance

Answer: C **High total T4** (bound to protein and effected by it) one of which is TBG (excess estrogen → ↑TBG) like in cases of pregnancy or in this case OCP . False high T4 but when you measure free T4 → normal

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- A 16-year-old girl comes to the office with an **uncomfortable sensation of rapid heartbeat** for the last few weeks. She has had no associated chest pain or shortness of breath. The patient reports that her **anxiety level** has been high recently due to stress at school, and she has lost close to 2 kg (4.4 lb) during this time. Her last menstrual period was 5 days ago. Medical history is unremarkable, and she takes no medications. On examination, the thyroid gland is **diffusely enlarged and nontender**. ECG shows sinus tachycardia at 120/min. **Radioactive iodine uptake is <5%, and anti-thyroid peroxidase antibodies are present in high titers**. Laboratory results are as Follows:
- **Which of the following is the most appropriate next step in management of this patient?**
    A. Alprazolam
    B. Levothyroxine
    C. Methimazole
    D. Prednisone
    E. Propranolol
    F. Radioactive iodine

Hemoglobin 12.9 g/dL
Hematocrit 39%
Platelets 200,000/mm3
Leukocytes 8500/mm3
Sodium 139 mEq/L
Potassium 4.2 mEq/L
Chloride 100 mEq/L
Bicarbonate 25 mEq/L
BUN 10 mg/dl
Creatinine 1.0 mg/dl
Calcium 9.1 mg/dl
Glucose 102 mg/dl
TSH <0.001 µU/ml
Free T4 - 4.6 ng/dl (0.9-2.4 ng/dl)

Answer: E → to treat symptoms
This is a case of Transient hyperthyroidism (“Hashitoxicosis”)
A: for anxiety
B: in cases of hypothyroidism
D:thyroid storm

Goiter in children

- Thyroid enlargement, sign of wide range of pathologies.

Congenital goiter > at birth	Acquired goiter > present at any age
• Can be caused by a **wide range of disorders**, including: - inborn errors of thyroid hormone production - anomalies of thyroid embryology (Thyroglossal duct cysts) - in utero exposure to maternal antithyroid antibodies - maternal ingestion of antithyroid drugs - iodine excess or deficiency • Thyroid function depends on etiology	• Wide causes - In the **United States and other iodine-sufficient** areas of the world > most common causes is chronic **autoimmune (Hashimoto) thyroiditis** and **colloid goiter** - **Worldwide** > **iodine-deficiency goiter** is far more common. • Thyroid function depends on the cause and stage of the disorder

- **Classification:**

Toxic Goiter	Non Toxic Goiter
• Goiter with hyperthyroidism • **E.g:** - **Graves disease→ (diffuse toxic goiter)** - Singular (toxic adenoma), Or - Multiple (toxic multinodular goiter [Plummer's disease])	• Thyroid gland enlargement **withOUT disturbance** in **thyroid function** • E.g. > Colloid goiter - characterized by **negative** antithyroid antibodies (TPO and Tg), normal TSH, and colloid cysts on ultrasonography. - Usually diffusely enlarged (can be asymmetric or nodular) - usually occur in adolescent females - The disorder may be familial, with an autosomal dominant pattern of inheritance. - Colloid cyst usually we do anything about it

Clinical evaluation

- ***History:*** iodine intake, medication history, FHx of thyroid disease.
- ***Physical Exam:*** cues from thyroid exam
  - Diffuse Thyroid Enlargement:
    * Hashimoto thyroiditis > bumpy firm small, nontender gland
    * Grave's > symmetrical, smooth, soft, and nontender
  - Tenderness > subacute granulomatous thyroiditis or acute suppurative thyroiditis.
  - Thyroid nodules or masses >
    * Most commonly associated with autoimmune thyroiditis or toxic multinodular goiter
    * Thyroid cancer most commonly presents as a solitary nodule without goiter
- ***Compressive symptoms****:* Some children with very large goiters may develop compressive symptoms, including:
  - Difficulty swallowing (dysphagia)
  - Shortness of breath (dyspnea)
  - Cough
  - Change in characteristics of the voice (dysphonia)

Clinical evaluation cont.

- ***Testing:***
  - Thyroid function test (TSH and FT4, T3 if hyperthyroid) Thyroid antibodies
  - Thyroid US
  - +/- RADIOACTIVE UPTAKE SCAN

Case Presentation

- A 9-year-old healthy girl presents for her yearly well child visit. On physical exam, her thyroid is **full, smooth, symmetric, and easily palpable**. Blood tests reveal that her **TSH is mildly elevated at 9.634 mcU/mL and total T4 is normal at 6.5 mcg/dL**. **Which of the following is the best additional test to perform to confirm the diagnosis?**
  - A. MRI of the brain
  - B. Thyroid ultrasound
  - C. TSH receptor antibody
  - D. Thyroid peroxidase antibody
  - E. Total T3 level

  Answer: D (not sure)

- A **neonate** is found to have **increased TSH** and **low thyroxine (T4)** on routine screening.He was born by vaginal delivery to a 32-year-old woman at 39 weeks gestation. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. Physical examination reveals an **enlarged thyroid gland in the normal position**. Neck **Ultrasound Confirms** Thyroid Enlargement. **Which of the following is the most likely cause of this patient's findings?**
  - A. Maternal intake of levothyroxine
  - B. Maternal intake of propranolol
  - C. Maternal intake of propylthiouracil (PTU)
  - D. Transplacental passage of thyroglobulin
  - E. Transplacental passage of TSH receptor- stimulating antibodies

  Answer: C

  This pt has goiter bc the mom was taking anti-thyroid medications → reach the fetus through the placenta → hypothyroidism + goiter. (after 1-2 wks the body excretes all PTU and normalizes the thyroid hormones level)
  If the mom is taking it for grave's disease the antibodies will pass too that baby shouldn't be dismissed ' the medication is cleared from the body the baby is going to be fine" no ! → testing for anti-bodies in the baby is important
  A: wouldn't cause goiter and it will last for 1-2 days and will go (shouldn't affect the baby)
  B: affect the the conversion of T4 to T3 but it shouldn't cause a goiter and hypothyroidism
  D: thyroglobulin doesn't cross the placenta , in the colloid serves as a storage for the thyroid hormone.
  E: it's a trick , it can happen but the baby would have hyperthyroidism.

- A **13-year-old asymptomatic girl** is shown below. She states that the findings demonstrated began **more than a year ago.**
- **Which of the following is the most likely diagnosis?"**
  - A. Iodine deficiency
  - B. Congenital hypothyroidism
  - C. Graves disease
  - D. Exogenous ingestion of Synthroid
  - E. Lymphocytic (Hashimoto) thyroiditis

  Answer:E
  A: hypothyroidism + present earlier
  B: will present 1 year ago
  C: symptomatic
  D: don't have a goiter

Practice Questions

- A17-year-old girl comes to the office with **5 months of fatigue,excessive sweating, and palpitations.** The patient is **slightly overweight** and had previously been **unsuccessful in losing weight** with caloric restriction and exercise.However,she has lost weight during the past 6 months with an **over the counter weight loss remedy**. The patient has had **no menstrual periods for the last 3 months,** Her blood pressure is **136/70 mmHg and pulse is 100/min.** Her **BMI is 26 kg/m^2**. The patient has **lid lag but no Proptosis**. Examination Of The Thyroid Show Small Gland Without nodules or tenderness. Laboratory Findings Are As follows:TSH-low,Free T4-high,b-hCG negative. Radio iodine uptake by the **thyroid gland is diffusely decreased**. **Which of the following would most likely be found in this patient?**
    A. Elevated antithyroid peroxidase antibody titer
    B. Elevated erythrocyte sedimentation rate
    C. Elevated serum alpha-subunit level
    D. Elevated TSH receptor antibody titer
    E. Low serum thyroglobulin level

A: Hashimoto thyroiditis
B:subacute thyroiditis (tender goiter + preceded by viral infection)
D: Grave's (diffuse increased uptake)

Answer :E
(a good way to differentiate between endogenous vs. exogenous)
it reflects how much the thyroid is producing → shouldn't be low should be normal but in this case the pt is taking exogenous synthroid

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- A 2-day-old boy is evaluated in the newborn nursery for jaundice. He was born to a 24-year-old primigravid woman who is in good health. The mother consumed a well-balanced diet and took prenatal vitamins throughout the pregnancy. The infant is breastfeeding poorly, with a weak latch and suck. On examination, the patient has jaundice, scleral icterus, a large tongue, and a hoarse cry. His tone is normal but his activity is decreased. Laboratory results are as follows:
- **Which of the following is the most likely cause of this infant's condition?**
    A. Defective synthesis of thyroxine
    B. Iodine deficiency (endemic goiter)
    C. Panhypopituitarism
    D. Thyroid dysgenesis
    E. Transplacental TSH-receptor antibody

Total bilirubin 15.3 mg/dL
Direct bilirubin 0.7 mg/dL
TSH 110 µU/mL
Thyroxine (T4) -0.6 µg/dL

Answer: D

- A13-year-old girl comes to the office due to recent - onset tremor, palpitations, weight loss, and fatigue. She has no other medical conditions and takes no medications or over-the-counter supplements. The patient's mother had hypothyroidism and osteoporosis. Blood pressure is 144/80 mmHg,pulse is 110/min,and respirations are 18/min. On examination, there is diffuse, non tender enlargement of the thyroid gland. Ocular examination shows bilateral proptosis, lid lag, and periorbital puffiness. The patient has diplopia and ocular discomfort on extremes of lateral gaze. Laboratory tests show a suppressed TSH and elevated thyroid hormone levels. Which of the following treatment options is most likely to worsen this patient's eye disease?
    A. Prednisone
    B. Propranolol
    C. Propylthiouracil
    D. Radioactive iodine
    E. Thyroidectomy

Answer: D