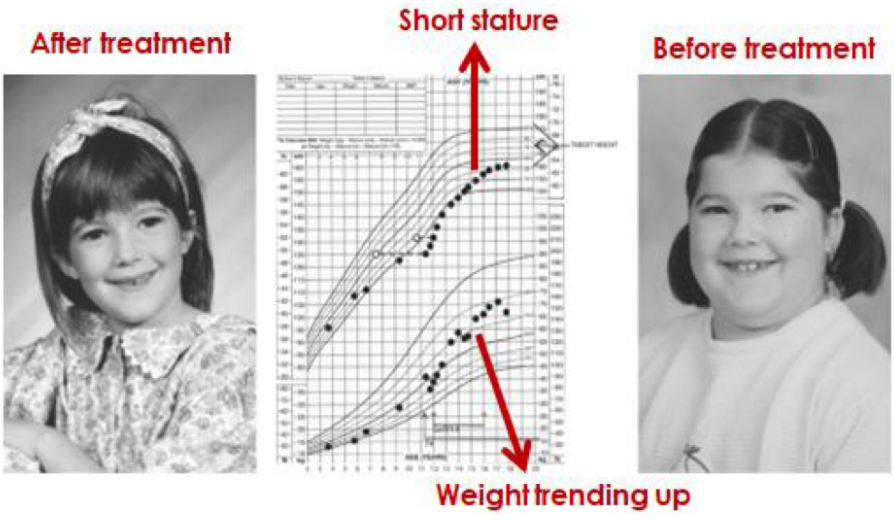
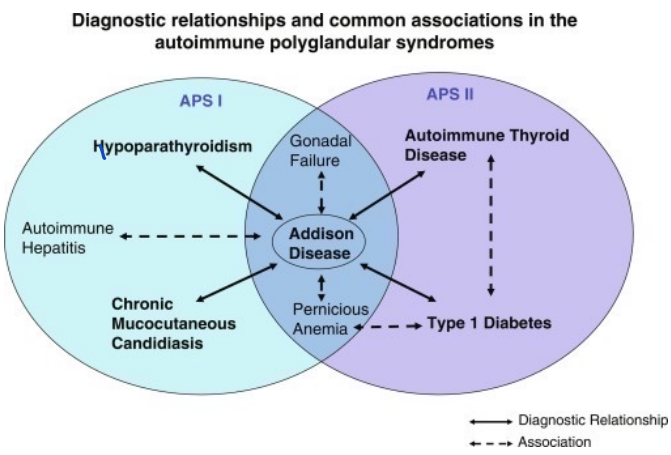
1. Hypothyroidism

- is one of the most common preventable causes of intellectual disability (mental retardation)
- Mostly it is primary
- Incidence 1 in 4000
- F>M (2:1)
- Usually we do screening for :
    1. Galactosemia
    2. Phenylketonuria
    3. G6PD
    4. Congenital hypothyroidism
    5. congenital adrenal hyperplasia (It may be added recently)

Acquired Hypothyroidism	
Etiology	• **Most common:** Lymphocytic thyroiditis • **Other causes:** ◦ Autoimmune polyglandular syndrome (APS) ◦ Genetic syndromes: Down, Turner, Klinefelter ◦ Subtotal thyroidectomy ◦ Histiocytic infiltration ◦ Secondary causes: medications, irradiation
Clinical Features	• **Growth & Development:** ◦ Deceleration of growth ◦ Delayed or precocious puberty ◦ Delayed osseous maturation • **Skin & Metabolism:** ◦ Myxedematous skin changes ◦ Cold intolerance ◦ Constipation • **Neurobehavioral:** ◦ Decreased energy & concentration ◦ Increased need for sleep ◦ Deterioration in school work ◦ Restlessness, short attention span ◦ Behavioral problems • **Treatment Consideration:** ◦ Dose & duration of untreated hypothyroidism → gradual increase of thyroxine
	

Hashimoto Thyroiditis	
Etiology	• **Immune pathology:** ◦ Lymphocytic infiltration → T cells 60%, B cells 30% ◦ Thyroid antibodies: ◦ **TPOAb (antimicrosomal): 90%)** ▪ Antithyroglobulin → more common in adults • **Familial clustering:** 25–30% • **Sex**: 4–7x more in girls • **Onset**: Insidious, after 6 years, peak in adolescence • **Clinical**: Growth retardation, goiter (may regress later) • **Other autoimmune associations**: DM1, adrenal insufficiency, hypoparathyroidism, pernicious anemia, vitiligo, alopecia, congenital rubella • **Syndromes**: Turner, Trisomy 21 • **APS associations:** ◦ Type 1: hypoparathyroidism, Addison, mucocutaneous candidiasis, hypothyroidism (10%) ◦ Type 2: Addison, DM1, hypothyroidism (more with Hashimoto)
Clinical Features	• May present as: ◦ **Hypothyroid**, **Euthyroid**, rarely **Hyperthyroid** (hashitoxicosis) • Most common cause of **goiter & hypothyroidism** in older children/adolescents • Can be **hypothyroidism without goiter**
Diagnosis	• **Lab:** ◦ T3/T4: often normal ◦ TSH: slightly elevated ◦ Antithyroid antibodies: TPOAb, antithyroglobulin • **Imaging:** ◦ Thyroid U/S: scattered hypoechogenicity ◦ Thyroid scan: ~50% irregular/patchy • **Definitive**: Biopsy (rarely needed) • **Notes**: Neither biopsy nor U/S/scan are usually required if family history + labs + antibodies are consistent
Treatment	• **Hypothyroid**: Levothyroxine → normalize TSH • **Euthyroid**: Follow-up every 6–12 months (check T3/T4) • **Goiter with normal TSH**: Usually no treatment (controversial) • **Subclinical hypothyroidism**: Controversial • **Follow-up**: Periodic re-evaluation for all patients; may be self-limited • **Euthyroid + high TSH**: Subclinical hypothyroidism / hyperthyrotropinemia



Congenital Hypothyroidism (Cretinism)

Definition

- cretinism is defined as arrested physical and mental development with dystrophy of bones and soft tissues, due to congenital lack of thyroid secretion.

Types

- Permanent (hypoplastic thyroid gland) vs. transient(eg.iodine exposure or in mother who take anti thyroid medication)
- Primary vs. secondary (central)
- Goiterous (Dyshormogenesis) vs. nongoiterous (ectopic thyroid)

Risk Factors

- Prematurity
- Multiple gestations
- Babies of old age mothers
- Asians and hispanics
- Down syndrome

Etiology

1. Thyroid Dysgenesis (≈90%)

→ No thyroid tissue / no goiter
→ Often with other congenital anomalies (ECHO + renal US)

Subtypes
• Aplasia: no thyroid
• Hypoplasia / Ectopic: small or misplaced
• Genetic TF defects: TTF-1, TTF-2, PAX-8
• Usually sporadic

2. TSH-Receptor Blocking Antibodies

• Maternal antibodies
• Cross placenta → transient hypothyroidism
• Resolves by 3 months

3. Dyshormogenesis

• Defect in thyroid hormone synthesis
• Goiter almost always present
• Rare (1:30,000)
• Inherited metabolic errors
• Or due to maternal antithyroid drugs

4. Iodide Transport / Iodine Metabolism Defects

• Poor iodide uptake or organification
• ↓ Thyroid hormone production

5. Pendred Syndrome

• Hypothyroidism
• Sensorineural hearing loss
• Defect in iodine organification + inner ear abnormality

Clinical Features

1. At Birth

- Most infants asymptomatic → due to maternal T3/T4
- Breast milk thyroid hormones: inadequate for protection
- Birth weight & length: usually normal
- Head size: slightly increased if prolonged intrauterine exposure

Risk Clues / Early Signs

- Gestation > 42 weeks
- Birth weight > 4 kg
- Hypothermia
- Acrocyanosis
- Associated anomalies (cardiac, CNS)

2. Early Symptoms (Weeks to Months)

- **Respiratory distress**
- **Large posterior fontanelle**
- **Abdominal distention**
- **Lethargy & poor feeding**
- **Prolonged jaundice → may be earliest sign**
- Edema
- Umbilical hernia
- Mottled skin
- Constipation
- Dry skin
- Hoarse cry (cry little, sleep much, poor appetite)

3. Later / Fully Developed Manifestations (3–6 Months)

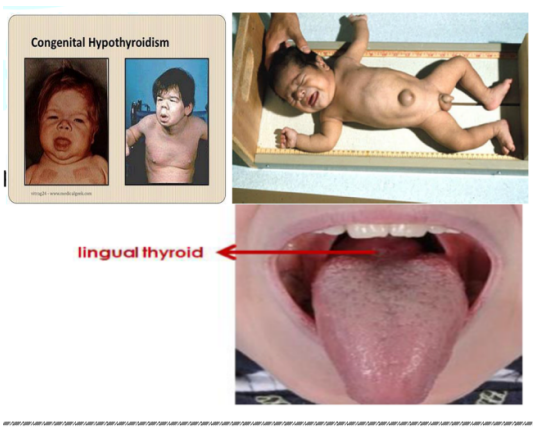
- **Growth retardation**: stunted, short extremities
- **Head**: normal or slightly increased
- **Fontanelle**: remains open
- **Mouth**: open, large protruding tongue
- **Delayed dentition** (starts ~4 months)
- **Neck**: short, thick
- **Myxedema**: eyelids, dorsum of hands, external genitalia
- **Carotenemia**: yellow skin, white sclera, dry & scaly skin, little perspiration
- **Hair & scalp**: thickened scalp, coarse, brittle, scanty hair, low hairline
- **Hands & fingers**: broad hands, short fingers

5. Neuromuscular & Developmental Findings

- Bone age delay
- Brain maturation delayed → thyroid hormone essential for bone & CNS maturation
- Overall developmental delay
- Muscles hypotonia with pseudohypertrophy (proximal myopathy)
- Deep tendon reflexes: slow relaxation phase

6. Risk of Intellectual Disability

- If diagnosed after 1 month → risk of intellectual disability
- Reversible with early treatment, but progression unpredictable if delayed



4. Investigative Clue

- **Knee X-ray** → absence of distal femoral epiphyseal growth plate indicates **long intrauterine hypothyroidism**

Diagnosis

Laboratory Tests

- TFTs:
  - T3/T4: **low**
  - TSH: **high** (>100 mU/L)
- Thyroglobulin:
  - If present → thyroid tissue present
  - Levels ↑ with TSH stimulation, ↓ with suppression
  - Increased in neonates, Graves, autoimmune thyroid disease, endemic goiter

Imaging

- **Thyroid Ultrasound (U/S):**
  - No thyroid → agenesis, ectopic, or very small tissue
  - Thyroid present → **Dyshormogenesis** (usually associated with goiter)
  - May miss ectopic glands detectable by **scintigraphy**
- Scintigraphy:
  - Defines underlying cause
  - Treatment should **not be delayed** for imaging
- Skeletal:
  - Delay in osseous development → absent distal femoral & proximal tibial epiphyses
  - Multiple foci of ossification → epiphyseal dysgenesis
- Skull X-ray:
  - Large fontanelle, wide sutures, wormian bones, large & round sella turcica
- ECG:
  - Low voltage P, T wave, QRS complex

Newborn Screening Strategies

- Three approaches:
  1. Initial **T4** → follow-up TSH if T4 <10th percentile
  2. Initial **TSH** assay
  3. Simultaneous **T4 + TSH** assay
- Notes:
  1. Approach 1 → detects delayed TSH rise & central hypothyroidism
  2. Approach 2 → detects subclinical hypothyroidism (high TSH, normal T4)
  3. Most programs may **miss central hypothyroidism** if relying on T4 alone
  4. **Preferred**: T4 + TSH combination or TSH alone initially

Treatment

Sodium Thyroxine (T4)

- **Newborns**: 10–15 µg/kg
  - Highest dose → thyroid agenesis or TSH >40
  - Lowest dose → subclinical hypothyroidism or TSH 20–40
  - Admin: **Empty stomach, morning, avoid soy/iron 30 min after**
- **Childhood**: 3–5 µg/kg
- **Adults**: 2 µg/kg

Prognosis

- **Inverse relation**: Age at diagnosis & treatment initiation ↔ IQ later
- **Best outcomes**: RX started **within first 2 weeks**
- **After 6 months**: Poor intellectual development, but growth may still improve
- **Onset after 2 years**: Outlook for normal development **better**

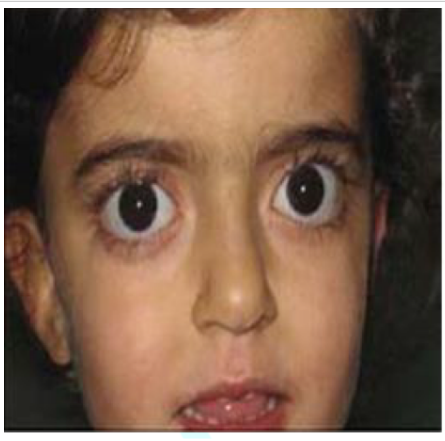
2. Hyperthyroidism

1. Definitions

- Thyrotoxicosis with hyperthyroidism: Graves disease, diffuse thyroid hyperplasia, multinodular goiter
- Thyrotoxicosis without hyperthyroidism: High dose exogenous T4 intake

2. Etiology

- Most common: Graves disease
- Others:
  - McCune-Albright syndrome (mutation on LH/FSH → precocious puberty; TSH receptor → hyperthyroidism)
  - Toxic uninodular goiter (Plummer disease)
  - TSH-secreting pituitary tumors
  - HCG-secreting tumors (choriocarcinoma)

Graves Disease	
Definition	• Lymphocytic & plasma cell infiltration in thyroid & retro-orbital tissue • Peripheral lymphocytosis • Antibodies: ◦ TRSAb (stimulating) → hyperthyroidism ◦ TRBAb (blocking) • • Genetic associations: HLA-B8, HLA-DR3 (whites) • Other associations: Addison, DM1, myasthenia gravis, celiac, SLE, RH arthritis, vitiligo, ITP, pernicious anemia
Clinical Features	• Epidemiology: ◦ 5% of patients < 15 years ◦ 5x more common in girls ◦ Onset gradual; 6–12 months from onset to symptoms • Neurologic / Behavioral: ◦ Emotional disturbances, irritability, hyperactivity, crying ◦ Poor school performance, short attention span • Systemic signs: ◦ Tremor ◦ Voracious appetite with weight loss ◦ Goiter ◦ Exophthalmos (50–75%, mild in children) ◦ Smooth, flushed skin, excessive sweating ◦ Muscle weakness ◦ Tachycardia, palpitations, dyspnea, cardiomegaly ◦ Mitral regurgitation, systolic BP ↑ ◦ Advanced skeletal maturation, craniosynostosis (neonatal Graves)
	 ❖ From above of head >> look for proptosis ❖ From side of head >> look for lid retraction ❖ From front of pt >> look for ophthalmopathy (H-type movement) And lid lag
Thyroid storm	• Acute onset: hyperthermia, severe tachycardia, restlessness, delirium, coma, death • Can mimic heart failure with hyperdynamic circulation
Lab	• T3, T4, Free T3/T4 ↑ • TSH ↓ • Thyroid peroxidase antibodies present • TRSAb positive in newly diagnosed cases → disappearance indicates remission
Diagnosis	**Differential Diagnosis** • McCune-Albright: precocious puberty, café au lait, polyostotic fibrous dysplasia • Thyroxine resistance: T3 ↑, TSH normal/elevated • Exogenous T4: T4 ↑, TSH ↓, thyroglobulin ↓
Treatment	**A. Medical Therapy (First Line)** • Methimazole: first-line for children (blocks organification of iodide; less hepatotoxic; suppress TRSAb) • PTU: inhibits T4 → T3 conversion; used in pregnancy/lactation; avoid in pediatrics • Beta-blocker (Propranolol 0.5–2 mg/kg): for catecholamine symptoms (tachycardia, tremor, sweating, lid lag) Side Effects of ATD: • Transient leukopenia, rash • Severe: agranulocytosis, hepatitis, hepatic failure (PTU), SLE-like syndrome **B. Surgery / Radioiodine** • Indications: failed or contraindicated medical therapy • Subtotal thyroidectomy: complications → hypoparathyroidism, vocal cord paralysis, recurrence • Radioactive iodine ablation: effective (~88% cured in one dose), complications → hypothyroidism, oncogenesis (prefer ≥15 years)

Congenital Hyperthyroidism	
Etiology	• Transplacental passage of maternal TRSAb (active or in remission Graves) • Usually transient (remission ~3 months), rare permanent if genetic mutation
Causes	- Onset - Prenatal: Fetal tachycardia may be observed. - At birth or within first few days: Clinical signs appear.
Clinical Features	• Premature / IUGR • Goiter • Restless, irritable, hyperactive, anxious • Microcephaly • Exophthalmic eyes • Tachycardia, tachypnea, high temperature • Failure to gain weight • Jaundice, hepatosplenomegaly • Cardiac decompensation, hypertension • Risk of death if untreated
Lab	• **T3/T4 ↑** • **TSH ↓** • Advanced bone age • Frontal bossing, craniosynostosis • **IQ prognosis guarded**
Treatment	• Medications: - Carbimazole, - Propranolol (2 mg/kg/day PO TID), - Lugol solution (1 drop/8 h) KI and iodine in water : reduces the thyroid hormones, T4 and T3 by 1. increasing iodine uptake 2. inhibiting the enzyme thyroid peroxidase • Supportive: IVF, steroids for severe cases • Cardiac: Digoxin if heart failure