HYPOTHYROIDISM IN CHILDREN
OBJECTIVES

• Introduction
• Congenital hypothyroidism
  – Etiology, clinical features, diagnosis, approach, treatment and prognosis
• Acquired hypothyroidism
  – Etiology, clinical features, diagnosis, approach, treatment and prognosis
INTRODUCTION

• Hypothyroidism occurs due to decreased production of thyroid hormone either
  – From the gland (primary hypothyroidism)
    or
  – Due to reduced thyroid-stimulating hormone (TSH) stimulation (central or secondary hypothyroidism)
• It may be manifested from birth (congenital) or acquired.
CONGENITAL HYPOTHYROIDISM
INTRODUCTION

• Congenital hypothyroidism is one of the most common preventable causes of mental retardation
• May not have obvious manifestations at birth
  – Due to transplacental passage of maternal thyroid hormone (T4)
  – Half-life of T4 is 6 days
  – Maternal T4 will be metabolized and excreted by 3 to 4 wks of age.
  – Around 3 – 4 weeks of age clinical features of congenital hypothyroidism are appreciated.
• INCIDENCE: 1:3000 to 1:4000
MATERNAL & FETOPLACENTAL UNIT IN THYROID HORMONE TRANSPORT

MOTHER
TRH

PLACENTA
TRH
HCG
TYPE 3 MONO DEIODINASE
rT3
T2
T3
T4

FETUS
T4
T3
rT3

IODINE
RADIOIODINE
TSH receptor Ab
ANTI THYROID DRUGS
β BLOCKING AGENTS

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THYROID FUNCTION IN THE PRETERM

- Hypothalamo pituitary thyroid axis is immature
  - Reduced hypothalamic TRH production and secretion
  - Immature response of the thyroid gland to TSH
- Inefficient organification of iodine
- Reduced capacity to convert T4 into active T3
- Loss of the maternal T4 contribution
- Immaturity of peripheral tissue deiodination
ETIOLOGY OF CONGENITAL HYPOTHYROIDISM

• PRIMARY / THYROIDAL:
  – Thyroid dysgenesis: (80 – 90%)
    • Athyrosis, Hypoplasia, Ectopic thyroid
  – Dyshormonogenesis: (10–20%)
    • Sodium-iodide symporter (trapping) defect, Thyroid peroxidase defect, Thyroglobulin defect, Deiododinase defect
  – Others:
    • Transient – maternal TSH-receptor blocking antibodies, Maternal anti thyroid drugs, Maternal or neonatal Iodine deficiency/ excess iodine exposure

• SECONDARY/ CENTRAL (hypothalamic & pituitary):
  – Isolated TSH deficiency, hypopituituitarism
CLINICAL FEATURES OF CONGENITAL HYPOTHYROIDISM (NEONATAL PERIOD)

• Most common symptoms:
  – Prolonged jaundice
  – Feeding difficulty
  – Sluggishness / Lethargy
  – Constipation
  – Umbilical hernia
  – Macroglossia
  – Hypothermia
  – Hoarse cry
CLINICAL FEATURES OF CONGENITAL HYPOTHYROIDISM (NEONATAL PERIOD)

- Birth weight & length – normal
- Head/CNS:
  - Increased head circumference (due to myxedema of brain)
  - Wide open anterior and posterior fontanel
  - Lethargy/ sluggishness/ excessive sleepiness
  - Poor cry, hypotonia
- GIT:
  - Constipation
  - Prolongation of physiological jaundice (delayed maturation of glucuronide conjugation)
  - Protruded abdomen, umbilical hernia, protruded tongue
CLINICAL FEATURES OF CONGENITAL HYPOTHYROIDISM (NEONATAL PERIOD)

• Goiter / Thyromegaly – most commonly seen in dyshormonogenesis
• Skin:
  – Hypothermia (<35°C), cold & mottled skin
• CVS:
  – Bradycardia, slow pulse, cardiomegaly, pericardial effusion
• Respiratory difficulties (due to large tongue)
  – Apnea, nasal obstruction, choking
CLINICAL FEATURES OF CONGENITAL HYPOTHYROIDISM (LATER AGE)

• If undetected/ untreated: (by 3-6 months of age)
  – Physical & mental retardation
    • Stunted growth, short extremities
    • Delayed milestones, Delayed dentition
  – Facies:
    • Narrow palpebral fissures with swollen eyelids (myxedema)
    • Mouth kept open, and the thick, broad tongue protrudes
    • Short and thick neck
    • Dry skin with pale/ sallow complexion and coarse hair
  – Muscles:
    • Hypotonia
    • Pseudo hypertrophy - **Kocher-Debré-Sémélaigne syndrome**
CONGENITAL HYPOTHYROIDISM

3 month old child with undetected congenital hypothyroidism

(note: apathic facies, dry and coarse skin, puffy eyelids and depressed nasal bridge)
INVESTIGATIONS

• Low serum T4 and elevated TSH level
• Best and most sensitive identification strategy is newborn TSH screening program by heel prick
  – The best window for testing is 48-72 hours of age
• Other helpful investigations:
  – Serum thyroglobulin, Technetium 99m Scintigraphy of neck for thyroid morphology, ultrasonography of thyroid
  – X-ray: Absent distal femoral epiphysis and stippled epiphysis, intra sutural wormian bones
NEWBORN THYROID SCREENING

• Heel prick capillary TSH level > 40 mU/L
  – Send venous sample for TSH & FT₄ for confirmation
  – Start on thyroxine
• Capillary TSH level < 40 mU/L
  – Send venous sample for TSH & FT₄ for confirmation
    • Venous TSH > 20 mU/L : start on thyroxine
    • Venous TSH 6 -20 mU/L and FT₄ –low: (Probable secondary hypothyroidism) – start on thyroxine, work up for hypopituitarism
    • Venous TSH between 6 -20 mU/L and FT₄ – normal: Diagnostic imaging and repeat testing
• Capillary TSH level < 6 mU/L
  – Normal and reassure
SKELETAL X-RAY IN CONGENITAL HYPOTHYROIDISM

Absence of distal femoral epiphysis in untreated congenital hypothyroidism

Epiphyseal dysgenesis in the head of the humerus in untreated hypothyroidism
MANAGEMENT OF CONGENITAL HYPOTHYROIDISM

• Treatment:
  – Replacement with levothyroxine (LT$_4$)
  – Dosage: 10-15 µg/kg
  – Administration: fasting state, early morning and avoid food for 30-60 min or pre-feed in neonates
MONITORING TREATMENT

- Clinical: growth monitoring, hearing and developmental assessment
  - Laboratory – TSH & FT4 levels
    - 2 weeks after starting treatment
    - Every 2 weekly till normalization of TSH (0.5 – 2 mU/L)
    - Every 1-3 months till 1 year of age
    - Every 2-4 months from 1-3 years of age
    - Every 3-12 monthly till growth is completed
    - 4-6 weeks after change in dose
PROGNOSIS

• Delay in diagnosis, inadequate treatment & poor compliance results in variable degrees of brain damage
• Early diagnosis and adequate treatment from the 1st weeks of life
  – Result in normal linear growth and development, normal scoring in psychometric testing
• Most severely affected infants (having lowest T4 levels and retarded skeletal maturation)
  – Can have reduced IQs (by 5-20 points) and other neuropsychological sequelae
• 20% can have a neurosensory hearing deficit
ACQUIRED HYPOTHYROIDISM
INTRODUCTION

• Incidence – 0.3%
• Female : male – 2:1
• Acquired hypothyroidism can be
  – Overt hypothyroidism (high serum TSH level and low serum free T4 level)
  – Subclinical hypothyroidism (high serum TSH level and normal serum free T4 level)
ETIOLOGY OF ACQUIRED HYPOTHYROIDISM

• Primary Hypothyroidism - Most common
  – Autoimmune Hypothyroidism
    • Hashimoto thyroiditis – most common
    • Autoimmune polyglandular syndrome (APS -1 & 2)
    • Down syndrome (30% prevalence)
    • Turner syndrome (40% prevalence)
    • Klinefelter syndrome (20% prevalence)
  – Thyroid surgery / Irradiation/ Post thyroiditis/ infiltrative disorders
  – Drugs - lithium, iodine, amiodarone, methimazole, propylthiouracil, anticonvulsants
ETIOLOGY OF ACQUIRED HYPOTHYROIDISM

• Secondary / Central Hypothyroidism
  – CNS tumors / CNS irradiation/
    meningoencephalitis/ infiltrative disorders
  – Hypopituitarism (multiple pituitary hormone
deficiency)

• Peripheral Hypothyroidism:
  – Resistance to thyroid hormones
  – Consumptive hypothyroidism (large hemangiomas)
CLINICAL FEATURES OF ACQUIRED HYPOTHYROIDISM

• Goiter
• Growth retardation
• Delayed bone age
• Pubertal disorders
  – Pubertal delay
  – Pseudo precocity (breast development, vaginal bleed in girls/ macrorchidism in boys)
  – Menometorrhagia
  – Galactorrhoea
• Lethargy, fatigue
CLINICAL FEATURES OF ACQUIRED HYPOTHYROIDISM

• Weight gain (fluid retention due to impaired renal free water clearance)
• Bradycardia, pericardial effusion, heart failure
• Constipation
• Cold intolerance, hypothermia, dry and myxedematous skin
• CNS:
  – Muscle hypotonia, Delayed deep tendon reflexes
  – Muscle pseudo hypertrophy
  – Scholastic performance – unaffected
• Headaches & vision problem (due to thyrotroph hyperplasia)
Smooth, uniform enlargement of thyroid – Hashimoto’s thyroiditis

Asymmetric enlargement of thyroid – benign adenoma Rt. Lobe of thyroid
Multinodular goiter – papillary ca. thyroid
DIAGNOSIS OF ACQUIRED HYPOTHYROIDISM

• Serum Free T4, Serum TSH (to use age specific ranges)
• Serum thyroid peroxidase and thyroglobulin antibodies
• X-ray Bone age – for assessment of retarded skeletal maturation (delayed bone age)
• Ultrasonography for thyroid morphology
• Technetium 99m scan of thyroid – rarely required (if nodular goiter)
APPROACH TO ACQUIRED HYPOTHYROIDISM

• Elevated TSH and low FT$_4$
  – **Overt Primary hypothyroidism**
    • Do thyroid antibodies
      – Positive - Autoimmune thyroid disease
      – Negative - Autoimmune thyroid disease, Drug induced, Dyshormonogenesis
    • **Start thyroxine**

• Elevated TSH and normal FT$_4$
  – Subclinical hypothyroidism – start thyroxine if thyroid antibodies are positive
APPROACH TO ACQUIRED HYPOTHYROIDISM

• Low FT$_4$ and normal TSH
  – Secondary hypothyroidism – screen for hypopituitarism

• Goiter with normal Thyroid function test and negative for thyroid antibodies
  – Reassure, Needs only follow up
TREATMENT OF ACQUIRED HYPOTHYROIDISM

- Levothyroxine (L-T<sub>4</sub>) is the treatment of choice
- Dosage:
  - For children age 1-3 yr: 4-6 μg/kg/day
  - For age 3-10 yr: 3-5 μg/kg/day
  - For age 10-16 yr: 2-4 μg/kg/day
- Administration: fasting state, early morning and avoid food for 30-60 min
- Monitoring:
  - Clinical – growth monitoring
  - Laboratory – TSH and FT4 – 6 weeks after starting treatment and dosage change; otherwise 4-6 monthly
PROGNOSIS

• 1\textsuperscript{st} year of therapy - Transient deterioration of schoolwork, poor sleeping habits, restlessness, short attention span, and behavioral problems can occur.
  – Needs only reassurance
• Catch up growth – adequate growth can be achieved if diagnosed early and adequately treated.
• Poor catch up growth is observed in long standing or untreated hypothyroidism
THANK YOU