HYPOTHYROIDISM

Dr. Sajili Mehta
Fellowship in Pediatrics Endocrinology
MIMER Medical College

THYROID PHYSIOLOGY

- Physiologic role of iodine – synthesis of T3 and T4
  RDA of iodine 50microgm/d – **infant**
- 70 – 120 microgm/d- **children**
- 150 microgm/d – **adolescent or adults**

- Thyroid gland has affinity for iodine where iodine is trapped transported &concentrated for synthesis of thyroid hormones.
- Iodide ----oxidised/ peroxidase--→oxidised iodine +tyrosine
- ↓
- MIT {monoiodotyrosine} DIT
- 2 mol of DIT →t4 DIT+MIT -→t3 stored in the

- Lumen of follicle as thyroglobulin--→T3 T4 liberated
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- T3 is intracellular -→enters nucleus-→acts on TH receptors→ action is 3-4 times metabolically potent than T4 ..Physiologically active..
- In circulation derived by →20% by thyroid secretion
- T4→T3 by deiodination{80%}
- ↓
- peripheral tissue pituitary, brain 80%T3 is
- liver , kidney produced by type 2
- type 1 5'deiodinase 5' deiodinase

- About 70% circulating T4 is firmly bound to TBG and rest to thyroid binding prealbumin and albumin.
- Free T4 –0.03% of T4 in serum.
- As against only 50% circulating T3 is bound to TBG and 50% to albumin.

- Free T3 –0.3%
- Regulation – **1)**central→TRH {hypothalamus}→ TSH{anterior pituitary} →TH{ thyroid gland }

- **2)**peripheral→Many nonthyroid illnesses production of T3reduces..Factors that inhibit 5'deiodinase –fasting, chronic malnutrition, acute illness, drugs..

- Hypothyroidism→ deficient production of TH
- Defect in receptor
- May manifest at birth
- **Delayed**→ acquired
- late presentation of congenital defect
- **Congenital** →sporadic/familial
- goitrous/non goitrous
- **Aetiology**→
- 1] Thyroid dysgenesis—1:4000 worldwide
- F:M—2:1 90%of cases of low thyroid function – commonest

- 1/3rd cases—aplasia
- 2/3rd cases –ectopia—lingual ,sublingual,subhyoid thyroglossal cyst
- Adequate TH for many years<fail in childhood—delayed c/f

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- Most infants with congenital hypothyroidism {C.H} are asymptomatic at birth . Since transplacental passage of moderate amount of maternal T4 , WHICH PROVIDE FOETAL LEVEL 25-50% NORMAL AT BIRTH.

- Neonatal screening→ ↓T4 ,↑TSH AND CYTOTOXIC ab in some pt with thyroid dysgenesis and their mothers suggest probable mech.

- 2] Thyrotropin receptor blocking antibody {TRBab}
- 50000—100000 infants
- H/O Maternal autoimmune disease →Hashimoto, Graves hypothyroidism on replacement treatment or recurrent CH of a transient nature in subsequent sibling .

- Transient CH – transplacental passage of maternal ab that inhibit binding of TSH to its receptor in the neonate

- Mother and baby often have TRBAb and antiperoxidase antibodies .
- Technitium pertechnate and I125 seen→ may fail to detect thyroid gland , but after the condition remits N thyroid gland after discontinuation of replacement.

- Half life Ab-7.5 D Remission of CH – 3 months

- 3] Defective synthesis of thyroxine →
- 1 in 30000-50000
- Goitre almost always present
- A] Defect of iodide transport→ scan- low uptake

- Treatment with large dose potassium iodide but treatment with thyroxine preffered

- B] thyroid peroxidase defect of organification and coupling

- Pendred syndrome – sensorineural deafness and goitre
- C] Defect of thyroglobulin synthesis
- D] Defect in deiodination → increased urinary losses nondeiodinate thyroxine

- 4] Radioiodine→inadvertant treatment in preg , lactation for conver , for increase Throtoxicosis

- 5] Thyrotropin defficiency→ developmental defect pituitary and hypothalamus . More often def TSH is secondary to def of TRH 1 in 30000-90000

- Multiple pituitary def –hypoglycemia , persistent jaundice , micropenis in asso with GH , prolactin def
- Mutation in TSH receptor gene
- Isolated def of TSH –rare

- 6] Thyroid hormone unresponsiveness→ autosomal dominant
- Most have goitre , clinically euthyroid subtle reduced TH {mild MR growth red delayed skeletal maturation}

- Increased T3 free T3
- Normal/increased {inappropriate} , resp TRH +increased asso with ADHD

- Treatment suggested when T4 increased on neonatal screening
- No treatment unless growth and skeletal retardation present

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- 7]Others →foetal exposure to active iodides or antithyroid drugs , to iodine containing antiseptics . LBW older children –drugs for asthma , amiodarone– antiarrythmics--%iodine content
- -- inhibition of 5'deiodinase
- Usually goitre +

CLINICAL MANIFESTATIONS

- F:m 2:1 ▲-neonatal screening
- -early weeks of life..
- Birth wt.and. ht Normal. increased head circumference, open AF PF
- Prolonged physiological jaundice—delayed maturation of glucuronide conjugation –earliest sign after birth.
- Feeding difficulties –sluggishness, reduced interest, somnolence , chocking spells during nursing..
- Resp difficulties-large tongue , apnoeic episodes. Noisy respiration.
- Cry little, sleep much, poor appetite , constipation
- Abdomen large , umbilical hernia , oedema -genitalia extremities
- Temp. less than 35ºc, hypertelorism, swollen eyelids, narrow palpebra, reduced HR, murmur , cardiomegaly, pericardial effusion, anemia refractory to treatment..

- 3-6 months life retardation of physical and mental development, fully developed clinical picture
- Depressed nasal bridge, mouth open broad tongue, growth stunted, extremities short, head size N to increased, dentition delayed, hands broad , fingers short..
- Neck short and thick, deposits fat above clavicle and between neck and shoulders, skin dry scaly no sweat
- Myxoedema over skin of eyelid , back of hands, ext genitalia, scalp- thick hair coarse , brittle, scanty, hairline reaches for down forehead, wrinkled.
- Development retarded-lethargy, late in learning to sit/ stand, voice hoarse, delay talking, sexual maturation delayed, may not occur
- Hypotonia, with longstanding hypothyroidism and severe in consanguinous marriage,

LABORATORY DIAGNOSIS

- 1] Biochemical→
- Reduced T3 T4 increased TSH→100microu/ml and increased prolactin correlate with increased TSH. undetectable- aplasia, reduced Tg thyroid dysgenesis or with defect in Tg synthesis or secretion.

- 2] Radiological→
- Absent distal femoral epiphyses at birth in 60%cases of CH
- Untreated patients increased discrepancy chronological age and bone age..
- Multiple foci of ossification – epiphyseal dysgenesis

- Deformity, breaking T12,L1,L2
- Skull-large fontanelle, wide sutures, wormian bones ,'sella turcica 'often increased , delayed formatn/ eruption of teeth
- CXR- cardiomegaly, pericardial effusion
- Scintigraphy-99mTc sodium pertechnate ,125I sodium iodide superior

- 3] Goitrous hypothyroidism→ extensive evaluation radioiodine studies, perchlorate discharge tests, kinetic studies , chromatography, biopsy etc

- 4] ECG- low voltage P, T, reduced amplitude QRS
- 5] Increased serum cholesterol > 2 yrs of age

- PROGNOSIS→
- Early diagnosis and adequate treatment from first weeks of life result in N linear growth and intelligence

- Severely affected→ lowest T4, marked bone retardation
- Without treatment –mentally depressed dwarf..

- Thyroid hormone critical for N cerebral dev. In early postnatal months. Therefore when onset hypothyroidism>2 yrs outlook N dev. Much better even if diagnosis and treatment have been delayed..

TREATMENT

- Sodium and thyroxine orally..
- **Neonates** 10-15 microgm/kg/d {37.5-50 microgm/d}
- **Children** 4 microgm/kg/d
- **Adults** 2 microgm/kg/d

- Level of T4 TSH should be monitored and maintained in N range.

- Discontinuation treatment for 3-4 weeks result in marked increased TSH in children with permanent hypoth.

- Older children after catch-up growth is complete ,growth rate provides an excellent index of adequacy of treatment..

ACQUIRED HYPOTHYROIDISM

- AETIOLOGY→ common cause lymphocytic thyroiditis , typically seen in adolescence , it occur early in first 2 yrs life.
- Some with cong thyroid dysgenesis or incomplete gentic defect- dev c/f later, subtotal thyroidectomy for treatment or cancer, removal of ectopic , nephropathic cystinosis histiocytic infiltration , irradiation- HL, NHL, before BMt drugs- containing iodides – amiodarone..

- c/f→ Deceleration of growth usually first clinical manifest. Myxoedema., constipation , cold intolerance, reduced bone age

- Treatment → eltroxin
- During 1st yr treatment deterioration school work , reduced sleep, reduced attention span, behavioural problems may ensue are transient
- During first 18 mo skeletal maturation often exceeds expected linear growth , resulting in loss of ht 7 cm

Thank You