॥ स्वास्थ्य-सेवा-सुशिक्षणम् ॥
MIMER MEDICAL COLLEGE

HYPOTHYROIDISM

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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} AND DIT**
- **2 mol of DIT →t4 DIT+MIT -→t3 stored in the**
- **follicle as thyroglobulin--→T3 T4 liberated**

- **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**
- **liver , kidney produced**
- **type 1 5'deiodinase 5' deiodinase**

- **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→ defficient production of TH**
- **Defect in receptor**
- **May manifest at birth**
- **1)Acquired**
- **late presentation of congenital defect**
- **2)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 in childhood— hence 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 PROVIDE FOETAL LEVEL.**

- **2] Thyrotropin receptor blocking antibody {TRBab}**
- **50000—100000 infants**
- **H/O Maternal autoimmune disease →Hashimoto, Graves.D.**

- **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 OR treatment with thyroxine prefered**

- **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 treatment →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}**

- **.Thyrotropin hormone unresposiveness due to generalised impairment of CAMP activation caused by genetic defect. alpha subunit of guaninenucleotide regulatory protein.**

- **7]Others →foetal exposure to active iodides or antithyroid drugs , to iodine containing antiseptics in LBW babies.In older children –drugs for asthma , amiodarone– antiarrythmics-**
- **Usually goitre +**

CLINICAL MANIFESTATIONS

- **F:m 2:1 ▲-neonatal screening**
- **-early weeks of life..**
- **Birth wt.and. ht Normal. increased head circumference, open AF and PF**
- **Prolonged physiological jaundice—delayed maturation of glucuronide conjugation –earliest sign after birth.**
- **Feeding difficulties –sluggishness, reduced interest, somnolence , choking 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 35°c, 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 betwn 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.**

LABORATORY DIAGNOSIS

- **1] Biochemical→**
- **Reduced T3 T4**
- **increased TSH→100microu/ml and increased prolactin. 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 CongHypo**
- **Untreated patients show increased discrepancy in 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**

TREATMENT

- Sodium L-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. growth rate provides an excellent index of adequacy of treatment..

- 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.**

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 IS THE 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 cmELPOP**