Thyroid gland

Physiology and diseases in children

Hormonal products

- Follicular cells
  - thyroid hormones: T4, T3

- Parafollicular cells
  - calcitonine

- The main source of iodide - food, water
- Follicular cells
  - trap and concentrate iodide,
  - synthesize and store thyroid hormones
    - Na/I symporter, thyroidal peroxidase, thyroglobulin, pendrine

- Tetraiodothyronine T4
  - -The only source - thyroid
  - - Prohormon
- Triiodothyronine T3
  - - Source: thyroid, peripheral deiodination of T4
  - - Really acting hormone, regulating the axis

Thyroid hormones function

In children:

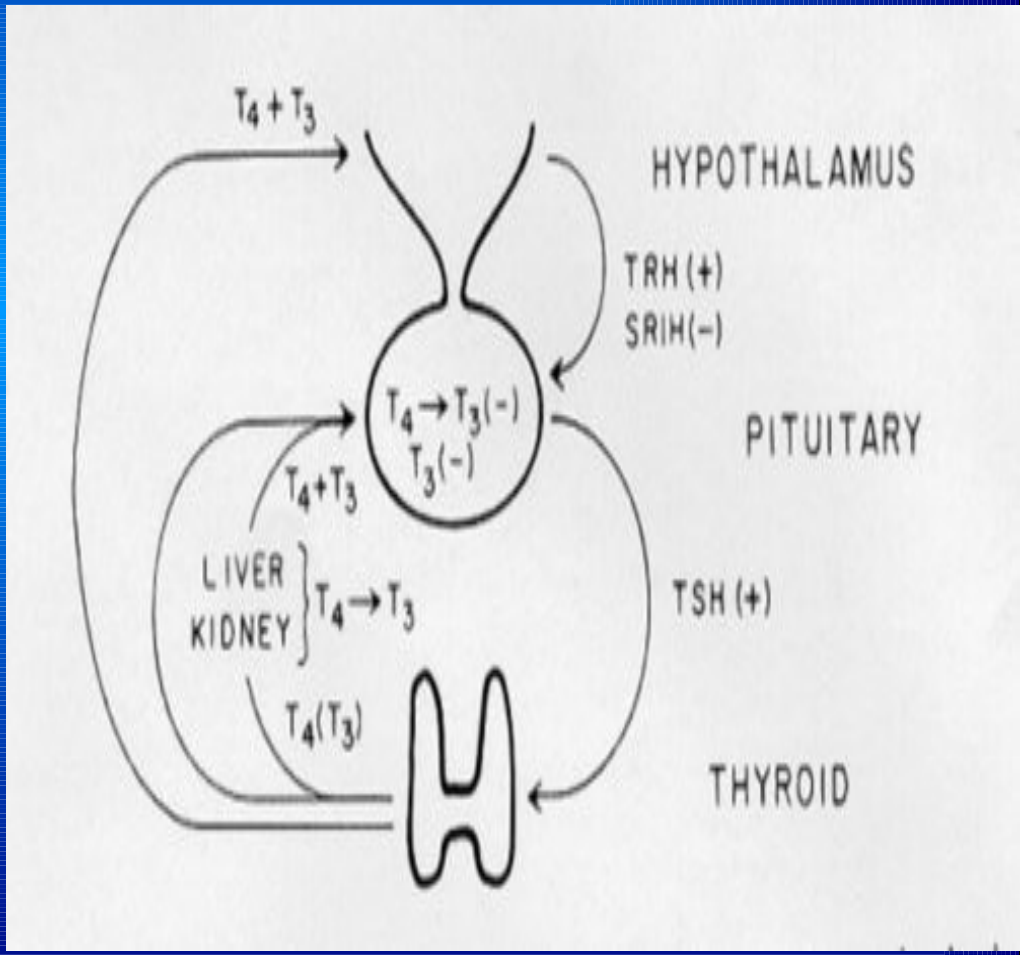
- Growth and development promotion
- Maturation of bone and brain

At every age:

- Regulation of metabolism (energy, heat production)

Classic hypothalamic-pituitary-thyroid axis

- TRH- thyrotropin releasing hormone
- TSH- thyroid stimulating hormone
- TSH-R-TSH receptor



Basic elements in the regulation of thyroid function.

TRH - a necessary tonic stimulus to TSH synthesis and release.

TRH synthesis is regulated directly by thyroid hormones.

Both circulating T3 and T4 directly inhibit TSH synthesis and release independently; T4 via its rapid conversion to T3.

Control of thyroid function

- Classic axis
- Additional regulation:
  - Deiodinases
  - Autoregulation depending on iodide supply
  - Antibodies against TSH receptor

hypothyroidism

- Congenital
- Acquired

- Pimary
- Secondary
- Tertiary

Congenital hypothyroidism

- **1: 4 000 live births**

- In most cases caused by dysgenesis (agenesis, aplasia, ectopia) 80-85%
- Dyshormonogenesis 10-15%
- Secondary or tertiary hypothyroidism <5%.

Symptoms of hypothyroidism in newborn

- Gestation greater than 42 weeks
- Birth weight geater than 4kg
- Hypothermia
- Acrocyanosis
- Respiratory distress
- Large posterior fontanel
- Lethargy
- Poor feeding
- Prolonged jaundice
- Umbilical hernia
- Mottled skin
- Large tongue
- Hoarse cry
- Delayed bone age

Congenital hypothyroidism

- In newborn – subtle clinical manifestations
- Irreversible mental retardation- when not treated early

Neonatal screening for hypothyroidism

- Heel-stick TSH values evaluation after 3rd day of life

Tests

- Decreased fT4 and proportionally increased TSH
  - in primary hypothyroidism
- Inadequatly increased TSH in comparison to low fT4
  - in secondary and tertiary hypothyroidism

Symptoms of hypothyroidism after neonatal period

- Ectodermal:
  - Growth retardation
  - Oedemas: dull face, thick lips, large tongue, periorbital oedema, puffy hands and feet
  - Dry scally skin
  - Sparse, brittle hair
  - Diminishet sweating

Symptoms of hypothyroidism after neonatal period

- Circulatory:
  - Sinus bradycardia
  - Cold extremities
  - Cold intolerance
  - Pallor
  - Low voltage of QRS complexes in ECG

Symptoms of hypothyroidism after neonatal period

- Neuromuscular
  - Hypotonia,
  - Constipation, protruberant abdomen
  - Umbilical hernia
  - Pseudohypertrophy of muscles
  - Muscle weakness
  - Physical and mental lethargy
  - Developmental delay
  - Delayed relaxation of reflexes

Symptoms of hypothyroidism after neonatal period

- Skeletal:
  - Delayed bone age
  - Large anterior and posterior fontanels (delayed ossification)
  - Epiphyseal dysgenesis
  - Increased upper-to-lower segment ratio (Long trunk, short limbs)

Symptoms of hypothyroidism after neonatal period

- Metabolic:
  - Myxoedema
  - Serous effusions (pleural, pericardial, ascites)
  - Hoarse voice
  - Weight gain
  - Anaemia
  - Hypercholesterolemia
  - Menstrual irregularity
  - In severe cases- precocious puberty

Symptoms of hypothyroidism after neonatal period

Progressive
irreversible
mental retardation !

Therapy- synthetic left-thyroxine

- Immediatly after diagnosis
- Not later than after 2 weeks of life (for normal mental development)
- doses: fast increment of serum free thyroxine into the upper half of the range of normal

  Neonates:10-15 micrograms thyroxine per kilogram daily

  After 2 and 4 weeks control of hormonal tests

  doses modification according to results

Monitoring of therapy

- Clinical and hormonal controls

  Recommended intervals:

  - 6 weeks in the first 6 months of life
  - 3 months until end of second year of life
  - 6 months in older children

Diagnostics

- Serum TSH, fT4 values
- Ultrasonography of the neck
- Thyroglobulin level
- Scintiscan
- Antithyroid antibodies
- Bone age

Causes of hypothyroidism in infancy

- Without goiter:
  - dysgenesis, ectopic location
  - TSH or TRH deficiency
  - TSH receptor failure
- With goiter:
  - Defects in hormone synthesis
  - Maternal goitrogens ingestion, thyreostatics, iodide
  - Severe iodide deficiency (endemic)

Acquired hypothyroidism

- In patients who had previously normal thyroid function
- In majority of cases- primary hypothyroidism
- subclinical (minimal) hypotyroidism is often previously present

Causes of acquired hypothyroidism in children

- Hashimoto's thyroiditis
- Iodide deficiency
- Goitrogens and goitrogenic drugs
- After thyroid surgery
- Thyroid gland infiltration (sarcoid, lymphoma)
- Inborn defects of hormone synthesis

Hashimoto's thyroiditis

- Autoimmune (lymphocytic thyroiditis)
- Genetic predisposition, environmental factors

- ➔ Lymphocytic infiltration of thyroid,
- ➔ Destruction of normal thyroid tissue,
- ➔ Fibrosis
- ➔ Atrophy

Clinical manifestation

- Firm, nontender diffuse goiter / or normal size
- Insidious onset (the incidence peaks in adolescence, female preponderance)
- Symptoms of hypothyroidism (often euthyroidism or subclinical hypothyroidism)
- increased predisposition to disease in some patients (Turner syndrome, Down syndrome)

Diagnosis

- Presence of antithyroid antibodies:
  - Anti- thyroid peroxidase antibodies
  - Anti- thyroglobuline antibodies
- Hypoechogeneity in ultrasonography of thyroid gland
- TSH, fT4(ev.fT3) examination

Treatment

- Thyroid hormone - when elevated TSH
- Regular monitoring of thyroid function

Hyperthyroidism in children

- ~ 95%- 98% of cases – Graves' disease
- Other:
  - Transient thyrotoxicosis in Hashimoto's thyroiditis (hashitoxicosis)
  - Mc Cune Albright syndrome,
  - thyroid cancer,
  - TSH secreting pituitary tumours,
  - ingestion of iodine or thyroid hormone

Graves' disease (Graves'- Basedov)

- Peak incidence in adolescence
- Girls to boys ratio 5:1
- Autoimmune thyroid disease
  - antibodies stimulating the TSH receptor
- Graves' ophtalmopathy: exophtalmos in 50% of children

Diagnosis

- Suppressed TSH, elevated serum fT4 and fT3 levels
- Antibodies against TSH-receptor
- Antibodies against TPO and Tg
- USG

Clinical manifestations in children

- Psychological disorders:
  - personality changes, mood instability, poor school performance, anxiety, inability to concentrate
- Weight loss with increased appetite
- Growth velocity increment
- Goiter, often with a bruit over the gland
- Advanced bone age

Clinical manifestation of hyperthyroidism

- Catecholamine effects:
  - nervousness
  - palpitations
  - tachycardia
  - systolic hypertension
  - tremor
  - brisk reflexes

Clinical manifestation of hyperthyroidism

- Hypermetabolism:
  - Increased sweating
  - Shiny, smooth skin
  - Hot extremities
  - Heat intolerance,
  - Fatigue
  - Weight loss with increased appetite
  - Increased bowel movement (hyperdefecation)
  - Hyperkinesis

Myopathy

- Weakness
- Symptoms of myasthenia gravis

Treatment

- First choice in children- thyrostatics:
  - Methimazole
  - Propylthiouracil

Additionally in severe cardiac manifestation:

- propranolol

- Treatment for 1- 2 years
- Side effects of thyrostatics treatment:
  - Rash, granulocytopenia, jaundice, lupus like syndrome

Surgical treatment

- Complete thyroidectomy (more rarely-partial)

Expected consequence: hypothyroidism

- Complications:
  - recurrent laryngeal nerve palsy,
  - hypoparathyroidism,
  - keloid formation.

Radioiodine (^{131}I).

- In children : ablative doses
- Desired outcome – permanent hypothyroidism
- Easy and safe in patient over 5year of life

Graves disease in newborn

- Transplacental passage of maternal TSH-R antibodies
- Transient, but dangerous (cardiac failure, craniosynostosis, bone age advancement)
- Treatment: propranolol, propylthiouracil
- Outcome: spontaneous improvement after 2-3 months

Goiter

The thyroid gland enlargement

or

an ectopic location of the thyroid tissue