

Thyroid Disorders

Thyroid Physiology

- Iodine is converted to iodide in the stomach - active transport to follicular cells - oxidized by thyroid peroxidase - iodination of tyrosine in the thyroglobulin - formation of monoiodotyrosine and diiodotyrosin - coupling - T3 and T4 and rT3 production - storage in follicles - secretion by stimulation of TSH - Deiodination of monoiodotyrosine and diiodotyrosine by iodotyrosine deiodinase releases iodine - reenters the thyroid iodine pool
- T4 and T3 are tightly bound to serum carrier proteins : thyroxine binding globulin TBG , thyroxine binding prealbumin and albumin .. and they are inactive when bound
- Most of the circulating T3 is derived from deiodination of circulating T4 in the peripheral tissues
- Deiodination of T4 can occur at the outer ring producing T3 or at the inner ring producing reverse T3 rT3
- TRH - transported through the hypothalamic hypophyseal portal system - thyrotrophs of the anterior pituitary gland - synthesis and release of TSH - increase thyroidal iodide uptake and iodination of thyroglobulin - increasing hydrolysis of thyroglobulin and stimulation of thyroid cell growth - releases T3 and T4
- Total T4 and T3 levels are elevated in hyperthyroidism and low in hypothyroidism
- Increased production of TBG increases the total T4 and T3 levels without actual hyperthyroidism and vice versa
- TSH assay can distinguish thyroid disorders
 - clinical hyperthyroidism : elevated free T4 and free T3 and suppressed TSH
 - subclinical hyperthyroidism : normal free T4 and free T3 and suppressed TSH
- The thyroid scan is performed in conjunction with radioactive iodine 123I uptake by the thyroid
- Functioning thyroid nodules are called warm or hot nodules /cold nodules are nonfunctioning (malignant)
- There are Autoantibodies to several different antigenic components in the thyroid gland including
 - thyroglobulin TgAb
 - thyroid peroxidase TPOAb aka antimicrosomal antibodies (positive indicate autoimmune thyroid disease)
 - TSH receptor antibodies (Graves disease)
- hyper and hypothyroidism are related to TSH levels
 - hyperthyroidism : low TSH

- hypothyroidism : high TSH

Hyperthyroidism (Thyrotoxicosis)

- Thyrotoxic crisis or thyroid storm is a life threatening complication of hyperthyroidism that can be caused by surgery, radioactive iodine therapy, or severe stress (uncontrolled diabetes, MI, acute infection)
- Patients develop fever, flushing, sweating, significant tachycardia, atrial fibrillation, cardiac failure, agitation, restlessness, delirium, coma, SOB, weight loss, increased appetite, Oligomenorrhea or amenorrhea, brisk reflexes, bruit, diarrhea and fine tremors
- Causes : (all have low TSH and high T3 T4)
 - Graves disease
 - toxic adenomas (solitary)
 - toxic multinodular goiter
 - Subclinical Hyperthyroidism
 - thyroiditis
 - thyrotoxicosis factitia
 - TSH secreting pituitary tumor
 - Struma ovarii occurs when an ovarian teratoma contains thyroid tissue that secretes thyroid hormone
- Toxic Adenoma
 - benign
 - more in older patients
 - low TSH / high T3 / high normal T4
 - hot nodule
 - treated with radioactive iodine
 - Euthyroidism results if the unaffected lobe has suppressed
- Toxic Multinodular Goiter
 - presentation : tachycardia, heart failure and arrhythmias
 - The treatment of choice is ¹³¹I ablation
- Subclinical Hyperthyroidism / T3 toxicosis
 - low TSH / normal T3 T4
 - The causes of this condition include early presentation of any form of hyperthyroidism and end of first trimester in pregnancy
 - should be treated with thiocarbamide or beta blockers
- Acute Thyroiditis

- may eventually result in clinical hypothyroidism but the initial presentation is often that of hyperthyroidism
- Hyperthyroidism caused by thyroiditis is differentiated from other causes by suppressed uptake of radioactive iodine in the thyroid gland, reflecting decreased hormone production by damaged cells
- Subacute Thyroiditis
 - aka de Quervain thyroiditis or granulomatous thyroiditis
 - caused by viral infections
 - fever and anterior neck pain
 - is triphasic : hyper - euthyroid - hypo (then return to euthyroid)
 - An increase in radioactive iodine uptake on the scan reflects recovery of the gland
 - treatment : aspirin and NSAIDs
- Chronic Thyroiditis
 - aka Hashimoto thyroiditis
 - caused by destruction of the normal thyroidal architecture by lymphocytic infiltration
 - results in hypothyroidism and goiter
 - Hashimoto thyroiditis have transient hyperthyroidism with low radioactive iodine uptake owing to the release of T4 and T3 into the circulation
 - the gland is nontender to palpation and antithyroid antibodies are present in high titer
- Thyrotoxicosis Factitia
 - ingestion of excessive amounts of T4 in an attempt to lose weight
 - Serum T3 and T4 levels are elevated and TSH is low normal, as is the serum thyroglobulin
 - Radioactive iodine uptake is absent
 - Patients may require psychotherapy
 - typical presentation : athlete with cardiac arrest
- Secondary hyperthyroidism : normal TSH with high T3 and T4
- TSHoma or pituitary adenoma : high TSH T3 T4

Graves disease

- most common cause
- more in women aged 20-50
- associated with goiter, exophthalmos, pretibial myxedema
- cause : TSH stimulating antibodies
- Eye signs associated with Graves : periorbital edema, conjunctival congestion and

swelling, proptosis, extraocular muscle weakness, or optic nerve damage with visual impairment

- Skin signs : Pretibial myxedema (thyroid dermopathy) which is thickening of the skin over the lower tibia without pitting, Onycholysis characterized by separation of the fingernails from their beds and Thyroid acropachy or clubbing
- Diagnosis :
 - Elevated total or free T4 or T3 (or both) and a suppressed TSH confirm the clinical diagnosis of thyrotoxicosis (T3 > T4)
 - TSH antibodies
 - Increased uptake of ¹²³I
- Treatment
 - antithyroid drugs (thiocarbamide) :
 - ◆ TPO inhibitors
 - ◆ propylthiouracil, methimazole, and carbimazole
 - ◆ methimazole is the drug of choice
 - ◆ Side effects : pruritus / rash / jaundice / arthralgia
 - radioactive iodine : ¹³¹I / patients become hypothyroid after radiotherapy and require lifelong thyroid hormone replacement / increase cancer mortality / not given for pregnant women
 - surgery
 - ◆ 6 weeks prior : antithyroid drugs to ensure euthyroidism at the time of surgery
 - ◆ 2 weeks prior : oral saturated solution of potassium iodide is administered daily to decrease the vascularity of the gland
 - ◆ complications : Permanent hypoparathyroidism / recurrent laryngeal nerve paralysis / hypocalcemia
 - beta blockers for palpitations, tremors & heat intolerance

Hypothyroidism

- In infants and children, hypothyroidism causes retardation of growth and development and may result in permanent motor and mental retardation
- Hypothyroidism is usually primary (thyroid failure) but it may be secondary (hypothalamic or pituitary deficiency)
- Causes of Primary Hypothyroidism
 - Autoimmune : Hashimoto (most common)
 - Iatrogenic : ¹³¹I therapy / thyroidectomy

- Drug induced : iodine excess and deficiency / lithium / Amiodarone / opioids / glucocorticoids
- congenital : agenesis / dysgenesis / lingual thyroid
- Cretinism : feeding problems, hypotonia, inactivity, an open posterior fontanelle, edematous face and hands, Mental retardation, short stature and delayed puberty occur if treatment is delayed
- Clinical Symptoms : Fatigue, Cold intolerance, Weight gain, Constipation, Dry coarse cold skin, Periorbital and peripheral edema, Delayed hung up reflexes, Bradycardi, Arthralgias, myalgias, menorrhagia and Myxedema (puffy edema)
- severe manifestation : myxedema coma
- Diagnosis : elevated serum TSH and low total and free T4
- Hypothyroidism is often associated with hypercholesterolemia and elevated creatine phosphokinase skeletal muscle fraction
- TPO Ab is usually positive in Hashimoto thyroiditis
- Hypothyroidism should be treated initially with synthetic levothyroxine T4
- Subclinical Hypothyroidism
 - Normal T3 and T4 with elevated TSH
 - Treated when associated with positive anti TPO Ab test or a goiter
- Non toxic goiters : inadequate thyroid hormone synthesis leads to TSH stimulation with resultant enlargement of the thyroid gland
- Central Hypothyroidism : low TSH T3 T4

Goiter

- Enlargement of the thyroid gland
- may be euthyroid (simple goiter), hyperthyroid (toxic nodular goiter or Graves disease), or hypothyroid (nontoxic goiter or Hashimoto thyroiditis)
- Goitrogens : iodine and lithium / soybeans / cabbage / peanuts / strawberries / peaches
- A smooth, symmetrical gland, often with a bruit, and hyperthyroidism : Graves disease
- A nodular thyroid gland with hypothyroidism and positive antithyroid antibodies : Hashimoto thyroiditis
- A diffuse, smooth goiter with hypothyroidism and negative antithyroid antibodies : iodine deficiency / non toxic

Thyroid Carcinomas

- Poor prognosis include : thyroid capsule invasion / size greater than 2.5 cm / age at onset older than 45 / tall cell or Hürthle cell variant / lymph node involvement
- Papillary : associated with local invasion and lymph node spread / most common / lobectomy or thyroidectomy
- Follicular : more aggressive than papillary / can spread by local invasion of lymph nodes or hematogenously to bone, brain or lung / lobectomy or thyroidectomy
- Anaplastic : older people / very aggressive / painful / causes dysphasia and hoarseness
- Medullary : derived from calcitonin producing parafollicular cells and is more malignant than papillary or follicular / multifocal / spreads both locally and distally / can be autosomal dominant familial / Elevated basal serum calcitonin levels confirm the diagnosis