Diseases of the thyroid

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Diseases of the Thyroid

• Normal function is the secretion of L-thyroxin (T4) and thriiodo-L-Thyroxin (T3) that influence a diversity of metabolic processes

• Qualitative and quantitative alterations in hormone secretion, and enlargement of thyroid (goiter), or both
Goiter

- Generalized
- Focal – neoplastic benign, or malignant
- Associated with increased, normal or decreased hormone secretion
Goiter
Diffuse goiter
Toxic multinodular goiter
Solitary hot nodule
Chest Xray – huge goiter
Function

• TSH
• FT4, FT3 level
Hyperthyroidism
Abstract

• Hyperthyroidism characterized by hypermetabolism and elevated levels of free thyroid hormones.
• Symptoms are many but include tachycardia, fatigue, weight loss, nervousness and tremor.
• Diagnosis is clinical with thyroid function tests.
• Treatment depends on cause.
Etiology

1. Increased synthesis and secretion of T4, T3 from the thyroid, caused by
   a. thyroid stimulators in the blood
   b. autonomous thyroid hyperfunction
2. Excessive release of T4, T3 without increased synthesis
3. Other rare clinical syndromes producing hyperthyroidism
1.a. Graves’ disease  
(toxic diffuse goiter)

The most common cause of hyperthyroidism, characterized by:

- **Goiter diffuse**
- Exophtalmos
- Infiltrative dermopathy
- **Thyroid stimulator**: autoantibody against the thyroid TSH receptor-continuous synthesis and secretion of T4, T3
- RAIU increased
Epidemiology, cause, pathology

- Most common
  Especially in women in the third and fourth decade (female/male 7/1)
- Unknown (HLA-b8d,rW3 haplotype, but no single factor)
- Thyroid hypertrophy, hyperplasia, usually accompanied by lymphocytic infiltration
Graves’ and concomittant autoimmune disorders

- Type 1 diabetes mellitus
- Pernicious anaemia
- Connective tissue diseases
- Polyglandular deficiencies

Clinical course: can remit as the other autoimmune diseases.
Ophtalmopathy

- Immunoglobulins directed against the receptors in the orbital fibroblast and fat- inflammation and accumulation of glycosaminoglycans
- Result: proptosis, ophtalmoplegia (muscular weakness), conjunctivitis, corneal ulceration, optic neuritis and atrophy.
- May be unilateral, or bilateral
- Onset before and as late as 20 years afterward the manifestation of hyperthyroidism.
Ophtalmopathy
CT scan of exophthalmos
Dermopathy

Pretibial myxoedema (confusing term, because suggest hypothyroidism)

- Nonpitting infiltration by proteinaceous substance usually in the pretibial area
- Often pruritic, and erythematous in early stages, subsequently becomes brawny
- Cause – unknown
- May appear years before or after hyperthyroidism
Pretibial myxedema
1.b. Toxic solitary or multinodular goiter

- It arises in long standing simple goiter
- It is the disease of the aging or elderly
- A functional autonomy (i.e. independence from TSH stimulation in one or more areas of the gland) develops. No stimulating antibodies, no autoimmune manifestations, usually do not remit.
- Cause is unclear (administration of iodides may lead to thyrotoxicosis=jodbasedow)
- RAIU increased
Toxic solitary goiter
2. Inflammatory thyroid diseases (thyroiditis)

Excessive release of stored T4, T3 without increased synthesis, because of inflammatory destructive changes in the gland. (RAIU decreased)

- **Subacute** (granulomatous, giant cell, or deQuervain’s) thyroiditis (pain, fever, nodularity, high ESR)
- **Chr lymphocytic thyroiditis** (no pain, no fever, no nodularity, no elevated ESR)
- **Hashimoto’s thyroiditis** - lycytic goiter (autoimmune factors play a prominent role, anti thyroglobulin AB, antithyroid peroxidase AB)
Various, rare forms of hyperthyroidism

- TSH secreting anterior pituitary adenoma. 
  α-subunit of TSH is high.
- Molar pregnancy, choriocarcinoma and hyperemesis gravidarum- 
  human chorionic gonadotropin(hCG) a week thyroid (FT4) 
  stimulator. (High hCG serum and urin level)
- Drug induced- from amiodaron, interferon, lithium 
  can induce thyroiditis
- Excess iodine ingestion (amiodaron, contrast agents, expectorans)- 
  nontoxic goiter with autonomous areas- FT4 production
- Extrathyroid source of hormone: 
  Thyrotoxicosis factitia (overingestion of thyroid hormon) 
  Struma ovarii- ovarian teratomas contain thyroid tissue- 
  RAIU in the pelvis, thyroid is suppressed
Symptoms and Signs

Most symptoms are the same regardless of the cause. Exceptions are infiltrative ophtalmopathy and dermopathy which occur only in Graves’ disease.

- Common symptoms: nervousness, palpitations, hyperactivity, increased sweating, fatigue, increased appetite, weight loss, insomnia, weakness, bowel movements (occasionally diarrhea). Hypomenorrhoea.

- Signs: warm, moist skin, tremor, tachycardia, widened pulse pressure, atrial arrhythmias.
Symptoms and signs

- **Elderly patients**: may present with atypical symptoms: apathetic, no tremor. Atrial fibrillation, syncope, heart failure and weakness are more often.

- **Thyroid storm**: acute form of HYT. Abrupt, florid symptoms with one or more of the following: fever, marked weakness and muscle wasting, extreme restlessness with wide emotional swings, confusion, coma, nausea, vomiting, diarrhoea, hepatomegaly, jaundice. May present with cardiovascular collapse and shock. *Emergency, prompt treatment!*
Diagnosis

Thyroid cause of HYT:
  Low TSH, high FT4, FT3, increased RAIU
  (Care of T3, and T4 toxicosis!)
Hormon overproduction - RAIU increased
Graves’: clinical picture + TSH receptor antibodies
Thyrotox. Fact.: Se thyroglobulin level low or normal - unlike in all causes of HYT
TSH secreting tu: high TSH, high FT4, FT3
Treatment depends on cause

- Medical therapy
  - Propylthiouracil or methimazol
  - $\beta$ receptor blockers (BB)
  - Iodine
- Radioactive iodine
- Surgery
Propylthiouracile and methimazole

- Block thyroid peroxidase (decreasing organification of iodid).
- P. in high doses inhibit periferal conversion of T4 to T3
- Starting dose P.: 100-150mg po q8h
  M.: 5-20 mg po tid
- Maintenance dose P. 50mg tid., M. 5-20mg once/d
- Adverse effects: rush, allergic reactions, reversible agranulocytosis (M. < 40mg/day agran. less common, P. agran. may occur at any dosage)
- P. is indicated in pregnancy (does not cross the placenta or enter breast milk)
Beta blockers

Adrenerg stimulation respond to BB.

• (tachycardia, tremor, mental symptoms, sweating, heat intolerance, proxymal myopathy)

• Propranolol decreases peripheral conversion of T4 to T3. Atenolol or metoprolol may be preferable. Esmolol for iv.
Iodine

- Inhibits the release of T3 and T4
- Transitory effect lasting from a few days to a week
- Emergency management for thyroid storm
- For hyperthyroid patients undergoing emergency nonthyroid or thyroid surgery, decrease the vascularity of the gland as well.
- Dosage 2-3 drops of Lugol po tid or qid for 10 days
Radioactive sodium iodine 131

- Most common treatment for Graves’, toxic nod. goiter including children.
- Not used in pregnancy.
- There is no proof that I 131 increases the incidence of tumors, leukemia, thyroid cancer.
Surgery

• For patients with Graves’ whose hyperfunction has recurred after courses of AT drugs and refuse I131 therapy
• Patients with very large goiters
• Patients with toxic adenoma and multinodular goiter
• Complications: vocal cord paralysis, hypoparathyroidism (uncommon), Hypothyroidism.
Treatment of thyroid storm

- Propycil 600mg pos before iodine, then 400mg q 6h
- Iodine 10 drops Lugol po tid or
  1gr Na iodide slowly by iv drip over 24 h
- Propranolol 40mg po qid
- Iv dextrose solutions
- Correction of dehydration and electrolyte imbalance
- Antiarrhythmic drugs (verapamil, adenosin, BB for atrial fibrillation
- Corticosteroid: hydrocortison 100mg iv q 8h or
dexamethasone 8mg iv once/day
- Definitive therapy after control of the crisis via ablation of thyroid with I131 or surgical treatment.
Case 1. Mrs P.M.

• 43 years old, when disease started: tremor, weight loss, nervousness. Exophtalmos.
• Struma
• TSH 0,08 miU/L (N 0,3-4,5)
  FT4 43,6 (N 20)  FT3 16,5 (N 5) pM/L
  TRAK >40 U (N 2)
• Scintigraphy: enlargement, diffuse acitivity uptake
Mrs. P.M.

2004. 2x20mg thiamazol /day
   3x40mg Propranolol
6 month later TSH 0.06 FT4 20.3 FT3 4.2
TRAK 29 Therapy 10mg thiamazol/day
2006. 10mg or 15/mg thiamazol/day, 2x20mg
   Propranolol
TRAK 24. She refused I131 therapy or surgery
2009. Therapy and TRAK the same. Exophthalmos
does not progressed. Sunglasses, liquifilm drops
Case 2. Mr. F.L. 56 years old

- 2006. Atrial fibrillation, heart failure, weight loss, asymmetric exophtalmos, diffuse goiter.
- TSH: 0.002 FT4 60 FT3 22 TRAK 48
- Scintiscan: diffuse activity uptake
- Thiamazol 2x20mg/d and 3x40mg Propranololol for rate controll and acenocoumarol for anticoagulation.
- 3 month later TSH normalized- DC cardioversion-SR.
Mr. F.L.

• 6 month later partial strumectomie.
• 2 month later: TSH, TRAK NOT NORMAL
• 2009. 5mg thiamazol /day
• No complaints
• Sinus rhythm
• Exophtalmos regressed
Case 3. Mrs. K.I. 54 years old

- 1994. Moderate diffuse goiter - no complaints - normal TSH
- TSH 0.01 FT4 66, FT3 5.2, TRAK 82
- Scintigraphy: diffuse activity uptake
- Therapy: 3x10mg thiamazol/ die 3x40mg Propranolol
  FT4 gradually decreased, dose of thiamazol gradually decreased to 10mg/die
For month later TRAK 3, thiamazol ex.
Mrs. K.I.

- 1998. No complaints, TRAK 3
- 2008. Nervousness, weight loss, tachycardia. TSH 0.01 FT4 60 TRAK 78
- After for month of thiamazol, propranololol therapy TSH, TRAK normalized. Therapy stopped.
- 2009. No complaints. Normal TSH, TRAK.
Case 4. Mrs. X.Y. 48 years old

- 2008. Exophthalmos, diplopia, starbismus
- TSH normal
- CT demonstrated characteristic thickening of the extraocular muscles
- Diuretic to reduce edema
- Elevating head at night, tinted glasses for protection from sun, wind and foreign bodies. 1% methylcellulose and plastic shields during sleep for prevention of corneal drying
- 100-120mg prednisolon/die for 2 weeks-no regression
- She is on orbital irradiation- If it will not help, orbital decompression (i.e. removal of part of the bony orbit) is required.
Case 5. Mrs. H. K. 68 years old

- History of hypertension for 10 years.
- Obesity from her childhood. Present weight 110kg and height 165cm.
- Multinodular goiter.
- Horseness and dyspnoe.
- TSH 0.1  FT4 33 FT3 3  TRAK 3 (normal)
- Scintiscan: multinodular goiter with hot nodules
- Short thiamazol therapy (2x10mg/d), than partial strumectomie
- 10 years later: 50ug L-Thyroxin/die because of hypofunction
Case 6. Mr. V.E. 51 years old

- In 1999, DCM was diagnosed (LVEF 30%) Parox PF- DC cardioversion- TSH normal- Amiodaron treatment.
- Regular TSH control. Last in 02.05. 2002. 5.5 miU/L.
- 13.10.2002. Palpitation. TSH 0.01 FT4 51pM/l Scintiscan.: decreased uptake
  Amiodaron stop. Thiamazol 3x20mg/die, but FT4, FT3 increased.
  Hormon leakage because of inflammation- Medrol therapy
- 2003.06. TSH normalized, thiamazol, medrol ex.
- 2003.11. Weight gain, sleepiness- TSH 8-
  L-Thyroxin substitution
- 2009. 75ug LThyroxin- TSH normal. No complaints.
Hypothyroidism
Introduction

• Common endocrin disorder resulting from deficiency of thyroid hormon.

• The patient’s presentation may vary from asymptomatic to, rarely coma with multisystem organ failure.

• The frequency increases with age. 5.9% of women, 2.9% of men older than 60 years have hypothyroidism
Pathophysiology

• Because all metabolically active cells required thyroid hormone, the effects of deficiency vary. Systemic effects are either due to derangements in metabolic processes or direct effects by myxedematous infiltration, accumulation of glucosaminoglycans in the tissues.

• Myxedematous changes
  in the heart: decreased contractility, cardiac enlargement, pericardial effusion
  in the GI tract: achlorhydria, stasis.

• Anovulation, menstrual irregularities, infertility

• Increased level of total cholesterol and LDL (change in metabolic clearance)

• Increased insulin resistance
Causes/primary
(95% of cases)

- **Autoimmune (Hashimoto)** is the most frequent cause.
  Antimicrosomal (anti-TPO 95%) and antithyroglobulin (antiTG 60%) antibodies are found. Ly infiltration and progressive gland destruction.

- **Iatrogenic** (after radioactive iodine treatment, thyroidectomy, external neck irradiation)

- **Iodine deficiency** (worldwide is the most common cause)
  or excess.
  (Excess J inhibits J organification- abnormal thyroid glands may not escape from this effect)

- **Drugs**: amiodaron, interferon-alfa, thalidomid, lithium

- **Postpartum thyroiditis**
  (10% of postpartum women may develop lymphocytic th-itis, 2-10month after delivery. Usually transient)

- **Subacute granulomatous thyroiditis** (de Quervain or painful)
  transient hyperth. followed by transient hypoth.

- **Rare**: inborn errors of thyroid hormon synthesis.
Causes/ Central

• Pituitary adenoma (secondary)
• Tumors impinging on the hypothalamus (tertiary)
• History of brain irradiation
• Drugs (dopamine, lithium)
Causes/ hormon resistance

Very rare

- TSH ineffective.
- T4 ineffective.
Clinical spectrum of congenital hypothyroidism

After delivery (1/4000 newborns):

- Icterus neonatorum prolongatus
- Inactive succling, movements
- Constipation
- Umbilical hernia
Congenital hypothyroidism
Clinical spectrum of congenital hypothyroidism

Later

• Growth retardation, delayed puberty
• Bone age, teeth age are delayed.
• Cretinism, mental retardation
• Hardness of hearing, logopathy
Congenital hypothyroidism

Diagnosis:
5 days after delivery TSH screen
(3 weeks delay, irreversible mental retardation!)
Therapy: hormone replacement
14 years old girl before and after L-thyroxin therapy
Clinical signs of adult hypothyroidism

Symptoms:
Weakness, lethargy, fatigue, memory impairment, cold intolerance, weight gain, constipation, loss of hair, hoarseness, deafness, dyspnea, myalgia, arthralgia, paresthesias, precordial pain, menstrual irregularity
Physical signs of adult hypothyroidism

- Dry, coarse, cold skin
- Periorbital, peripheral edema
- Coarse thin hair, pallor, vitiligo
- Thick tongue
- Slow speech
- Decreased reflexes
- Hypertension, bradycardia
- Pleural-, pericardial effusion, ascites
Myxedema coma

• Extremely rare, frequently fatal. Precipitated by stress (infection, alcohol, drugs, cold exposure)
• Hypothermia
• Respiratory failure (hypoventilation-hypercapnia, CO2 narcosis)
• Bradycardia, hypotonia
## Labor diagnosis

<table>
<thead>
<tr>
<th>Type</th>
<th>FT4 (12-31pM/L)</th>
<th>Basal TSH (0.3-4.5mIU/L)</th>
<th>After TRH TSH</th>
<th>Struma:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary thyreogen</td>
<td>low</td>
<td>High</td>
<td>increase</td>
<td>+/-</td>
</tr>
<tr>
<td>Secundary hypophyser</td>
<td>low</td>
<td>Low</td>
<td>No answer</td>
<td>Struma: never</td>
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<td></td>
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<td>Gonado tropin: low</td>
</tr>
</tbody>
</table>
Other laboratory abnormalities

- CPK elevated (modest cardiac isoenzyme increase may occur)
- hypercholesterinaemia
- HypoNa (relative ADH excess)
- Anaemia-normocytic, normochromic (but vitamine B12 deficiency also occur/autoimmunity/, or microcytic because of menorrhagia)
- ECG: bradycardia, variable degree of heart block, low voltage, aspecific ST-T changes
Other abnormalities

Autoimmun Hashimoto thyreoiditis:
anti- TBG antibodies and anti-thyreoida peroxidase antibodies( anti-TPO) increase

• Biopsy showes lymphocytic thyreoiditist
• Thyroid radionuclide uptake is diminished, or absent
Autoimmunity in thyroid gland

Genetic factors

- Stimulating factors
  - TSAb
  - Direct lymphocyte stimulation?
  - Cytokine?
  - Graves' Disease

- Blocking or inhibitory factors
  - TSBAb
  - Cytokines
  - IFN-γ, IL-1, INF-α

Environmental factors

- Destructive factors
  - ADCC
  - Cytotoxic T lymphocyte
  - TNFβ (Lymphotoxin)
  - Cytotoxic antibody
  - Hashimoto's Disease

Humoral and Cellular immunity

Remission

Myxedema
Differential diagnosis

• Nephrosis sy, cirrhosis- low TBG-low totalT4, totalT3, but free FT4 and FT3 normal, TSH normal

• Severely nonthyroid illnesses can induce the same abnormalities. During recovery transient TSH elevation

• TSH elevated, T4, T3 normal- subclinical hypothyroidism.
Therapy

Myxedema coma: 200 ug thyroxin iv bolus followed by 100ug hours later, and than 50ug daily

- Respiratory support
- Glucocorticoid, glucose infusion, electrolyt and fluid replacement
- Underlying event must be corrected (infection)

Manifest hypothyroidism: 25-50ug LT4/die with an incremental dose of 25ug every two to four weeks (75-150ug/die)

Latent hypothyroidism (FT4 FT3 at lower part of normal values, TSH slight increase or TRH test positive): treatment only in special cases (pregnancy)
72 years old women before and after thyroid hormon therapy
Adult man with the “obese form” of hypothyroidism before and after therapy
27 years old female before and after Lthyroxin and estrogen therapy
M.I. 60 year old female

Case report
Past history

• 1980. Cholecystectomy
• 1997. Hysterectomy
• Since 1997. treatment of hypertension
• In 2003. Examinations because of angina pectoris
• 2 month ago radioisotope treatment of hyperfunctioning struma.
Present complaines

- For 2 weeks exertional back pain, pain in both arms and legs. Dyspnoe, and palpitation at exertion.
- Neurological examination was negative for spinal radicular compression.
- No fever, cough, or abdominal complaines.
- Therapy: diuretic and ACE inhibitor for hypertension.
Physical examination.

- Normal skin, conjunctivae. Moderate edema on both legs. RR 140/80 P:70/min Negative cardiopulmonary status. No abdominal abnormality.
ECG
Laboratory results

- Wbc 6.42 Hb 127g/L Ht 0.37  creatinin 83uM/l glucose 6.9 Se Na 139 K 4.2 , Sebi 1.62 SGOT 99 GPT 40 LDH 442 CK 2457 U/L, cholesterin 7.08 mM/L
- TroponinT 0.017ug/L , D-dimer 0.22ug/ml
- CRP 2.9mg/L
- Normal urine sediment
Echocardiography

• EF 55% no wall motion abnormality.
• Mild aortic root calcification, central AI-I
• Normal atrial, and ventricular dimensions.
• Normal pericardium.
TSH

• 68 mIU/L