THE THYROID deficiency diagnosis, clinical signs lab tests

Dr Benoit Claeys

claeysbenoit@hotmail.com
FUNCTION

To give energy and warmth, needed for development and conservation of our body.
Anatomy - embryology

• On the middle line, between the 1° and 2° branchia, the thyroid is developing herself. Then she operate a migration along the base of the tongue towards trachea.

• If the thyroid stay fixed somewhere on this traject, she will not work properly.
• Normal weight of thyroid is about 10 - 20 grams, but she can grow up if needed.
• Thyroid gland is made of follicles, containing follicle cells, which contains a colloidal liquid, called thyroglobuline.
Hypothalamus
TRH  Thyroid Released Factor

pituitary gland
TSH  Thyroid Stimulating Hormon

THYROID

R-T4  L-T4  (inactive)

R-T3  L-T3  (active)
The thyroid is producing Tétraïodothyronine (inactiv T4) and a little Triiodothyronine (T3, tha activ hormon). The main part of activ T3 active is coming from transformation of T4. This happen in the lever and the kidneys, wich contains 5’-deiodase. The T3 is then entering in the mitochondria of the peripheric cells to produce ATP.
The thyroid is producing 100 µgr of T4 a day, and 10 µgr of T3.

Half life of thyroxine (T4) is 8 days, half-life of triiodothyronine (T3) is about de 26 hours.

The feedback between TSH and the thyroid hormones is mainly made by T4, and a little bit by T3.
The production of T3 from T4 is function of the 5′-deiodase
Are necessary: Se, Vit E, Mg, Zn, Fe, Vit B2, Cortisol, Melatonine, Growth hormone, T3

Are working against the 5′-deiodase: lever insufficiency, renal insufficiency, fasting, poor intestinal resorption, diabetes I, olderness, oestrogens, contraceptives, beta-blockers, lithium, co-trimoxazole, amiodarone, phénylbutazone, strumasol.
If the body temperature of a rat is artificially raised up of 1 C degree, the concentration of 5’-deiodase is going down of 25 % in the lever, and of 20 % in the kydney; which is reducing the level of T3 in the serum. But administration of Vitamine E and Sélénium is restoring the situation.

Iodine is coming mainly from food. Iodine is transformed in Natrium iodide in the intestine, and is entering in the thyroid follicle cell by an activ way, thanks to the NIS (Natrium Iodide Symporter). This explains why the concentration of iodine is 100 times more important in the follicle cell than in the plasma.

The only way to check iodine of a patient is the 24-hours urine test.
Thyroid binding globulines

99.95 % of T4 and 99.50 % of T3 sont binded to proteins and are so inactifs.

The main of those proteins is

**TBG** (Thyroid Binding Globuline), produced by the lever.  
TBG is binding 75% of T4.  
**TTR** (Transthryretine), called also TBPA (Thyroid Binding Préalbumine) is binding 10 % of T4,  
**Albumine** is binding 12 %  
**Lipoprotéines** are binding 3 %.

The affinity of TBG for T4 is very high, and is lower for T3.  
On such a way, only 0.03 % of T4 remains free, but 0.3 % of T3 remains free ans active. Those bindings are reversible.
Incidence of pathology of the thyroid

A study made by the Mayo Clinic (1997)[i][6], was looking former studies of the 15 former years:

* 60 % of autopsia were showing thyroid anomalies.

• 50 % of echographies were showing the same.

Which symptoms to be attentive to?
PATHOLOGIES OF THE THYROID

By frequency order

Hypothyroidism
Thyroiditis
Hyperthyroidism
Cancer of thyroid
HYPOTHYROIDISM
ETIOLOGIES OF HYPOTHYROIDISM

*Hereditary origin
- anomalies of the – thyroglobulin receptors
  - TPO (Thyroid Per Oxydase)
  - NIS (Sodium Iodide Symporter)
  - Pendrin (iodine transporter)

*Acquired
- Thyroidectomie
- Intake of radioactiv iodine
  - Thyroiditis, viral or bacterial, or toxic (excessiv iodine intake, amiodarone, pesticides…)
- Traumatic
Familial

**Thyroid diseases** -

**Cholelithiasis** -

Hypercholesterolaemia - Tuberculosis - Mycosis - Allergy - Hay fever - Diabetes mellitus - Arteriosclerosis - Myocardial infarction < 50 years - Xanthelasmata - Vitiligo - Psoriasis - Deafness - Pernicious anaemia – Autoimmune disease.
Paediatrics

Flaccid pale children with hunched backs - Elderly look - Wide epicanthus - Turned-up nose due to a short skull base - Cretinism - Growth and intellectual retardation - Delayed ossification and dentition - Slowness, physical as well as mental - Drowsiness in daytime, but sleeplessness during the night - On the contrary, Hyperkinetism - Longstanding enuresis (over 2 years of age).
General

THE MAIN SYMPTOM:
Low basal temperature (<36.7° C)

(for women, on the second day of the periods)
(no ingestion of alcoholic drink the day before)

Cold hands, cold feet, cold nose –
Dead finger

Sensation of coldness - Intolerance to cold but also to heat
Fatigue (especially at waking up) - Impaired memory - Dullness and slow cerebration - Depression - Repetitive infections of sinus, respiratory and urinary tract – Unability to lose weight - Gain of weight but also loss of weight - Oedema not related to cardiac nor to renal failure –
Neck

*Thyroid hyperplasia* - or lack of any thyroid tissue - *Hoarseness* – Sensation of constriction of the throat.
Head

Pallor - *Hertoghe eye brow sign* - Hair loss - *Lock of bleached hair* - Scanty hair – Curled hair

*Prematurely grey* - Hair of poor quality - Dry - Thick or thinly structured - *Red hair* - *Headache* - Palpebral oedema – Pouched eyes - *Repetitive sneezing* - Allergy - *Teeth in staggered rows* - Aphthosis
Cardiovascular

Bradycardia (with or without palpitations) - Constrictive pain over the heart - Microvoltage on ECG - Enlarged heart on X-Ray - Bad circulation in the limbs - Cyanosis - Hypertension with elevated diastolic pressure.
Gastrointestinal

Constipation (especially women)

Dysphagia - Slow digestion -
Protuberant abdomen - Umbilical hernia - Gain of weight unrelated to food intake - but also loss of weight – even acute abdomen.
Orthopaedics

Generalised weakness - Arthritis -
Muscle cramps (pour Ca and Mg resorption)-
Burning or tingling pain in the extremities - Carpal tunnel syndrome.
Swollen hands and wrist (morning)
Neurology

Prolonged Achilles reflex – Depression – Postnatal depression – Anxiety - Phobia
Urogenital - women

Premenstrual tension - Dysmenorrhea
Amenorrhea - Delayed fertility -
Weightgain of more than 12 kg
during pregnancy - Heavy babies of
more than 4.5 kg at birth –
Miscarriages – Endometriosis –
Cysts of breast and ovaries
Breastcancer.
Urogenital - men

Enuresis > 2 years
prostatitis
Dermatology

Lack of perspiration - *Dry skin*, coarse, crackeled, with *cracks in thick heel* and finger skin - Scaling - Hyperkeratosis of the extensor side of the limbs - Chipped nails - Itching. 31
THE 8 MAIN SYMPTOMS

*FATIGUE : unusual, persistent, especially on awakening, less toward the evening, with slow recovery

*DEPRESSION : Psychological melancholia, with tendency towards suicide, postnatal.

COLDNESS : deep as well as peripheral (forehead, nose, hands, feet and knees, breasts), cyanosis, dead finger,

HEADACHE : migraine, tension headache.

MUSCLE CRAMPS : in calves, toes, fingers, diaphragm, also in thighs and upper-arms.

ARTHRITIS : rheumatoid pain, joint-, tendon- and muscle swelling and stiffness

ACHILLES REFLEX : Prolonged Achilles tendon reflex, especially the last relaxation phase. ((chronic neuropathy by alcoholics and diabetes)!

CONSTIPATION : (especially women)
THE LAB TESTS

• **TSH IS A VERY POOR INDICATOR OF THE SYMPTOMS OF HYPOTHYROIDISM.**

• *In Europe, the value should be < 4.5, but following recent publications in the USA TSH shoule be < 2.0*

Firts of all, to consider the value of TSH, you need to be certain that the hypothalamus is working properly, that the pituitary gland is working properly, and that the receptors to the TSH in the thyroid are working properly.

In other words, it is only in primary hypothyroidism that TSH could have any value.

*Anyhow, TSH is giving an idea of the circulating inactive T4, but doesn’t at all gives any indication on the active T3.*
Other lab tests

CHOLESTEROL : 40 Years ago, a cholestérol > 300 mgr % was considered as a sign of hypothyroidism. A recent study [ii][11], published in 1990, showed a good correlation between a rising of T3 and diminution of cholesterol.

HOMOCYSTEINE : is increased in hypothyroidism et low in hyperthyroïdisim.

URIC ACID : is commonly to high in hypothyroidism


(Source : W. Baisier)
Other lab tests

- **T3 and T4 IN 24 HOURS URINE TEST**
  The best test today to have a correct idea of the real functioning of the thyroid.\[11][26] Goog relation with the symptoms, with the treatment, as well in hypothyroidism as hyperthyroidism.
  No influence of the binding proteins
  The value of creatinine allows a control of the test.

**IODINE IN 24 HOURS URINE TEST**

90% of belgian population is missing iodine

In the last guidelines of the National Academy of Clinical Biochemistry, published in 2002, the limit of TSH has been considered to be < 2.5 mI/L.
Only looking to TSH while giving thyroxine (only T4) could make you patient going worse.
WHY?
Indeed, 50 to 75 µg de thyroxine (T4) are enough to reduce the value of TSH to a very low value.

Since the feedback of the thyroid is related mainly to T4, and not to T3, the thyroid will stop producing T4, but also T3.

Since the clinical symptoms are related to T3, the patient will feel worse...

But the practitioner will be happy with conventionnal figures.
Hypothalamus

TRH  Thyroid Released Factor

Hypophyse

TSH  Thyroid Stimulating Hormon

THYROID

R-T4  L-T4  (inactive)

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Auto-immune diseases of the thyroid

Graves' disease in full-blown form is characterized by hyperthyroidism, goiter, and often exophthalmos. Hashimoto's thyroiditis (goitrous lymphocytic thyroiditis) was first described in 1912 by a Japanese physician named Hashimoto. Clinical manifestations of the disorder are variable and include euthyroidism, subclinical hypothyroidism, permanent hypothyroidism, and, less commonly, transition from hyperthyroidism to hypothyroidism or vice versa. Overlap of Hashimoto's thyroiditis with the extrathyroidal manifestations of Graves' disease is not unusual.

Subclinical hypothyroidism is defined as mild elevation of serum thyrotropin (TSH) levels and normal circulating thyroid hormone levels. Antithyroid antibodies are positive in 95% of affected patients.

(Source: Mayo Clinic)
In autopsy series, the frequency of lymphocytic infiltration of the thyroid gland ranges from 20% to as high as 40%. In a study conducted in the English town of Whickham, 8% of the women 35 years of age and older were found to have subclinical hypothyroidism, mostly due to autoimmune thyroid disease. The prevalence of thyroid antibody positivity in the general population is 15% to 25% in women and 5% to 10% in men. Graves' disease is less prevalent than Hashimoto's thyroiditis. However, it is the most common cause of spontaneous hyperthyroidism in all age-groups.

(source: Mayo Clinic)
Histopathologic findings

Hashimoto's thyroiditis is characterized by destruction of follicular cells, varying degrees of lymphocytic infiltration, and fibrosis. In Graves' disease, the degree of lymphocytic infiltration may vary, but follicular cells are hyperplastic and the thyroid gland is hypervascular. Activation of fibroblasts and immune cascade in the extrathyroidal tissues (orbital tissues in patients with ophthalmopathy and the pretibial area in those with dermopathy) can be demonstrated in affected patients.
diagnosis of Hashimoto's thyroiditis

This diagnosis is made when positive antithyroid antibodies are present or spontaneous hypothyroidism develops. The presence of serum antithyroid antibodies with or without thyroid dysfunction or goiter is usually adequate.

The antithyroid peroxidase (TPO) antibody test is more sensitive than the antithyroglobulin antibody assay. Results of scintigraphy and ultrasonography are highly variable in goitrous Hashimoto's thyroiditis and usually not helpful. In some cases, ultrasound-guided biopsy of small, clinically suspicious nodules may be required.

(source: Mayo Clinic)
Graves' disease,

In Graves' disease, the combination of suppressed levels on "sensitive" thyrotropin testing, high thyroidal uptake of radioiodine, and elevated serum levels of thyroid hormones in patients with a diffuse goiter is diagnostic. Measurement of radioiodine uptake is essential for differentiating between Graves' disease and conditions involving very low radioiodine uptake

(source: Mayo Clinic)
Autoimmune thyroiditis, specifically Hashimoto's thyroiditis, is more prevalent in persons with various autoimmune and non-autoimmune disorders and some genetic conditions. In addition, underlying overt hypothyroidism may provoke depression, which can be reversed with hormonal replacement. There is some evidence that treatment of subclinical hypothyroidism may improve depressive symptoms.

(source: Mayo Clinic)
Conditions associated with increased incidence of autoimmune thyroiditis

Alopecia areata
Autoimmune liver
Autoimmune polyglandular syndromes (eg, Addison's disease, hypoparathyroidism, type 1 diabetes, ovarian failure)
Celiac disease
Chronic ulcerative colitis
Crohn's disease
Down syndrome
Hepatitis C infection
Idiopathic thrombocythemia
Idiopathic thrombocytopenic purpura
Klinefelter's syndrome
Mixed connective tissue disease
Myasthenia gravis
Polymyalgia rheumatica
Primary biliary cirrhosis
Rheumatoid arthritis
Scleredema
Sjögren's syndrome
Systemic lupus erythematosus
Turner's syndrome
Vitiligo

(source: Mayo Clinic)
Treatment of autoimmune thyroid disease

Treatment varies widely, depending on the specific disorder.

Euthyroid autoimmune goiter
Small goiters should be monitored. Treatment is indicated for larger goiters, symptomatic goiters, and those that cause cosmetic concerns. Evidence shows that suppressive therapy can shrink goiter in Hashimoto's thyroiditis. However, goiters that are hard and fibrotic do not respond.

Transient postpartum thyroiditis
Therapy for transient disease is usually not needed. However, beta blockers can alleviate thyrotoxic symptoms in the hyperthyroid phase, and short-term therapy is appropriate for the hypothyroid phase.
Treatment of hypothyroidism

Novothyral    synthetic    T4/T3 : 100/20%
Armour Thyroid animal origin    T4/T3 : 100/23 %
Elthyrone,    synthétique :    T4     : 100/00 %

**Motif d'admission :**
Patiente admise pour des douleur thoracique médiatothoracique augmentant à l'inspiration profonde, non irradiée avec difficulté à respirer. Pas de toux, pas de température.

**Antécédents**
- greffe rénale en 95 (herbes chinoises)
- hypertension artérielle
- ostéonécrose des 2 hanches opérées 2006
- hernie hiatale
- cholécystectomie.

**Examen physique**
- TA : 13/8 mm Hg.
- RC : 84 /min.
- Température : 36.1°c.
- Membres : absence d'oedème des membres inférieurs. Dermite ocre au niveau des membres inférieurs.
TSH 1.2

testosterone 0

DHEA <150

Ac AT 0

Ac PO 37

Urine : T3 253  T4 6800

ECHO Thyroide 2005 N