Significance of the thyroid profile

Thyroid hormones affect the regulation of every body organ, mainly through nuclear receptors (expression of genes through transcription), but also other receptors (membrane, mitochondria, etc.) or actions linked with other hormones. Consequently, any dysfunctioning in the thyroid system results in a large number of general symptoms indicating:

- either excess synthesis of thyroid hormones (hyperthyroidism)
- or insufficient production (hypothyroidism).

Main general symptoms associated with thyroid dysfunction:

- asthenia (hypo),
- apathy (hypo) or excitement (hyper),
- slow (hypo) or rapid (hyper) pulse rate,
- slow (hypo) or rapid (hyper) heart rate,
- weight gain (hypo) or loss (hyper),
- long (hypo) or short (hyper) intestinal transit times,
- in children: growth disorders.

Who requires a thyroid profile?

1. All patients with a combination of symptoms suggesting a thyroid dysfunction, and/or with a morphological anomaly of the thyroid gland.
   N.B. Since the role of thyroid hormones is essential for maturation and development, a profile is carried out for all newborns and children with a growth disorder.

2. Patients treated for a thyroid pathology either using synthetic anti-thyroid drugs (SAT), or thyroxin (T4).

3. Patients treated with drugs which may induce thyroid pathologies (cordarone, interferon, lithium, etc.)

4. Patients with non-thyroid auto-immune diseases (dominant role of autoimmunity in thyroid pathologies and frequent associations with various auto-immune diseases).
The hormones

**TSH**
TSH is a pituitary hormone, which is the centerpoint of the thyroid profile, since it acts as a "modulator" for variations in thyroxinemia (T4, contrary to T3, being exclusively produced by the thyroid).

**FT4 (Free T4 fraction).**
FT4 acts as an indicator of thyroid production and is used to confirm the diagnosis suggested by TSH.

**FT3 (Free T3 fraction).**
In some cases, FT3 can be produced by the thyroid gland, in preference over T4 (e.g. in cases of iodine deficiency). However, in most cases, FT3 is an indicator of peripheral deiodination of T4.
Main causes of discrepant profiles other than thyroid pathologies:

- **Decreased TSH**
  - Early stage of pregnancy (HCG)
  - Glucocorticoids, dopamine and dopaminergics (bromocriptine), serotonin, opiates, dextrogyral T4 (DT4), triiodoacetic acid.
  - Severe non-thyroid illnesses (NTI, psychiatric disorders).

- **Decreased FT4**
  - Kidney disorders, diphenyl-hydantoin, phenobarbital, carbamazepine.

- **Decreased FT3**
  - Fasting, cordarone, propanolol, severe non-thyroid illnesses (NTI), hepatic cirrhosis.

- **Moderate TSH increase**
  - Dopamine antagonists and neuroleptics (metoclopramide, chlorpromazine, haloperidol, domperidone, sulpiride), lithium, amiodarone (especially at the beginning of treatment).

- **Increased FT4**
  - Amiodarone, propanolol, active acute and chronic hepatitis, DT4.

- **Increased FT3**
  - Triiodoacetic acid, DT4.

- **Increased TSH**
  - Where there is little clinical context, eliminate a thyroid pathology from diagnosis using only the TSH assay.

- **Confirm diagnosis by associating TSH-FT4** (TSH may be affected by non-thyroid factors).

- **When monitoring treated patients, an FT4 or FT3 assay may be performed in addition to the TSH assay, if necessary.**

When monitoring treated cases of secondary hypothyroidism, the TSH assay is of no significance. FT4 or FT3 assays should be used for monitoring these patients.

**Which tests to prescribe?**

- Presence of anti-hormone antibodies (anti-T3, anti-T4) or mouse anti-gammaglobulins (HAMA), or abnormal albumin levels (dysalbuminemia).
- Hypothalamo-pituitary disorders.
- Thyroid hormone resistance syndromes.

**TSH** is always the first screening test to be performed.

The following approach could then be used:

1. Where there is little clinical context, **eliminate** a thyroid pathology from diagnosis using only the TSH assay.
2. In cases of a clinically suspected thyroid dysfunction, **confirm** diagnosis by associating TSH-FT4 (TSH may be affected by non-thyroid factors).
3. When monitoring treated patients, an FT4 or FT3 assay may be performed **in addition to** the TSH assay, if necessary.

**Effect of age:**
- TSH peak during first days of life
- FT4 levels higher in newborns than in adults (with lower FT3)
- FT3 levels higher in children and adolescents than in adults
- FT3 levels reduced in the elderly

**Situations inducing thyroid pathologies:**
- Treatment with lithium, interferon, amiodarone, ingestion of substances leading to excess iodine exposure.

**Other parameters for investigation of the thyroid function**

TSH anti-receptor antibody
Anti-thyroglobulin antibody
Anti-thyroxoperoxidase antibody
Thyroglobulin
Thyrocaltitonin
A considerable time period (at least 2 to 3 weeks) should separate the biological follow-up from the initiation or modification of treatment.

Initial biological investigation of thyroid disorders

**Patient not receiving treatment**

- **TSH**
  - **normal**
  - **increased**
    - **FT4**
      - **normal or decreased**
        - **HYPOTHYROIDISM**
        - **EUTHYROID** (if confirmed by clinical examination)
      - **increased**
        - **FT4**
          - **normal or decreased**
            - **HYPOTHYROIDISM**
            - **EUTHYROID** (if confirmed by clinical examination)
  - **low**
  - **decreased**
    - **FT4**
      - **normal or decreased**
        - **HYPOTHYROIDISM**
        - **EUTHYROID** (if confirmed by clinical examination)
      - **increased**
        - **FT4** and or **FT3**
          - **increased**
            - **HYPERTHYROIDISM**
            - See clinical examination (NTI*, therapeutic drugs, pregnancy...). Complete the investigation by performing an immunological profile, or iodine profile, or scintigraphy.
          - **normal**
            - **HYPERTHYROIDISM**
            - See clinical examination (NTI*, therapeutic drugs, pregnancy...). Complete the investigation by performing an immunological profile, or iodine profile, or scintigraphy.
          - **decreased**
            - **SECONDARY HYPOTHYROIDISM**
            - **NTI***

* NTI = non-thyroid illness

**Biological monitoring***

**Patients treated with thyroxin as a substitute**

- **TSH**
  - **decreased**
    - **Hypothyroid state persists. Increase dosage**
  - **normal**
    - **Hypothyroid state persists. Increase dosage**
  - **increased**
    - **Reduce dosage**

**Patients treated with synthetic anti-thyroid drugs**

- **TSH**
  - **decreased**
    - **Hypothyroid state persists. Increase dosage**
  - **normal**
    - **Continue same dosage**
  - **increased**
    - **Reduce dosage**

* A considerable time period (at least 2 to 3 weeks) should separate the biological follow-up from the initiation or modification of treatment.
These difficulties are based on the following observations:

1. The non-thyroid origin of TSH (physiological or pathological disorders of the hypothalamo-pituitary axis),
2. Difficulty in determining the free fraction of thyroid hormones,
3. Difficulty in defining a normal range,
4. Repercussions possibly due to a deficiency or excess of iodine (although no pathology is detected),
5. The inevitable possibility of interference due to analytical (in vitro), medicinal (in vivo and sometimes in vitro) or biological (associated pathologies) factors.

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**What should be done in the case of a discrepant profile?**

1. Check that results are valid (by controlling the assay giving an apparently abnormal result).
2. Study the information given on treatments being taken which may interfere with the parameters being tested (see page 4).
3. Perform several simple tests to eliminate the possibility of analytical interference (dilutions, spiking tests).

After these controls, it may be helpful to perform an immune profile and/or an iodine profile.

Repeating a profile at a later date may often be useful in clarifying the situation (return to normal or evolution).