Alterations of thyroid function tests: not always the thyroid!
Case #1

- 36 year-old male, A. D.

- **Personal history:**
  - Smoker until 2005
  - Hypercholesterolaemia

- **Familial history:**
  - Thyroidectomy in grand-mother (benign disease)
  - Mother with goiter treated with L-thyroxine
Case # 1

- Headaches, chronic fatigue, dyspnea
- Biology:

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<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>TSH (µU/mL)</td>
<td>3.07</td>
<td>3.61</td>
<td>3.89</td>
</tr>
<tr>
<td>(N: 0.3-3.5)</td>
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<tr>
<td>fT4 (ng/dl)</td>
<td>0.61</td>
<td>0.62</td>
<td>0.52</td>
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<tr>
<td>(N: 0.6-1.6)</td>
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<tr>
<td>fT3 (pg/mL)</td>
<td>2.25</td>
<td>2.05</td>
<td></td>
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<td>(N: 2.1-4.2)</td>
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Case # 1

• 19/11/2009: Ac anti-TPO (+)

• Echography of the thyroid: no goiter. Mixed nodule 10 mm left lobe.

• Thyroid Scintigraphy: normal

• Diagnosis: primary hypothyroidism → R/ L-thyroxine
Case # 1

- ↑ L-thyroxine dose up to 100 µg/day
- R/ L-thyroxine 100 µg/day (3 months)
  - TSH : 0.01 µU/mL (0.20-3.50)
  - fT₄ : 0.8 ng/dl (0.6-1.4)
  - fT₃ : 3.0 pg/mL (2.2-4.0)
Case # 1

- Fatigue persisting
- Anorexia, weight loss (6 kgs in 6 months)
- Muscular and bone pain
- Headaches increase
- Loss of libido
Case # 1

- weight: 86 kg; height 182 cm, BMI 25.9 kg/m²
- BP 12/8 mmHg; HR 68/min
- Thyroid normal
- Loss of peripheral hair - small testes
- Neurological examination: normal
Case # 1: extensive hormonal biology

- **Somatotrope axis**
  - GH 0.13 ng/mL (< 1.50)
  - IGF-1 58 ng/mL (110-338)

- **Gonadotrope axis**
  - LH 1.0 mUI/mL (1.7-12.1)
  - FSH 1.1 mUI/mL (1.4-9.9)
  - Testosterone 1.4 nM (13.0 - 35.0)

- **Corticotrope axis**
  - ACTH 16 pg/mL (5-49)
  - Morning cortisol 71 nM (260-540)

- **Prolactin** 10366.0 ng/mL (< 12)
Case #1  pituitary MRI
Case # 1  pituitary MRI
Case # 1  ophtalmologic examination

- Normal visual acuity
- Bitemporal hemianopsy
Invasive macroprolactinoma with:

- complete pituitary insufficiency (including TSH deficiency)
- optic compression
Central hypothyroidism

81% normal TSH
11% low TSH
8% high TSH!
Central hypothyroidism

**Total T4**

- µg/dl
- (n=58)

**Free T4**

- ng/dl
- (n=63)
Central hypothyroidism

**Total T3**

- Units: ng/dl
- Range: 0 to 200
- Data points: (n=53)

**Free T3**

- Units: pg/ml
- Range: 0 to 6
- Data points: (n=54)
Case # 2

• 45 year-old male, A.B.

• **Personal history:**
  - Oesophagitis
  - HTA R/ Nobiten
  - Dyslipidaemia

• **Familial history:**
  - hyperthyroidism in the mother

• **Treatment:**
  - Zurcale 20 mg, Nobiten 5 mg
Case # 2

- Since 1 year: general alteration of health status, fatigue, muscular weakness of legs and insomnia
- **Biology March 2010:** diagnosis of hyperthyroïdism
  → R/Strumazol 2/day

<table>
<thead>
<tr>
<th></th>
<th>TSH (mU/L)</th>
<th>fT4 (ng/dl)</th>
<th>fT3 (pg/mL)</th>
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<tbody>
<tr>
<td>March 2010</td>
<td>0.06</td>
<td>1.1</td>
<td>2.6</td>
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<tr>
<td>May 2010</td>
<td>0.34</td>
<td>0.6</td>
<td>3.0</td>
</tr>
<tr>
<td>August 2010</td>
<td>0.64</td>
<td>1.0</td>
<td>4.2</td>
</tr>
<tr>
<td>Sept 2010</td>
<td>0.29</td>
<td>0.5</td>
<td>2.3</td>
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Case # 2

• Thyroid Antibodies (-)

• **Thyroid echo and scintigraphy:**
  normal
Case # 2

- fatigue and proximal muscular weakness
- weight gain (5 kg in 1 year)
- swelling of the face and ankles
- easy bruising of the skin
- loss of libido
Case # 2

- **Thyroid function tests**
  - total T4  4,2 µg/dl (4,8-12)
  - free T4  0,8 ng/dl (0,8-1,8)
  - free T3  2,3 pg/ml (2,4-4,0)
  - TSH      0,12 µU/ml (0,2-3,5)
Case # 2 extensive hormonal biology

- **Somatotrope axis**
  - GH 1,03 ng/mL (< 1,50)
  - IGF-1 123 ng/mL (110-338)

- **Gonadotrope axis**
  - LH 0,9 mUI/mL (1,7-12,1)
  - FSH 4,3 mUI/mL (1,4-9,9)
  - Testosterone 3,5 nM (13,0 - 35,0)

- **Prolactin** 8,6 ng/mL (< 12)

- **Corticotrope axis**
  - ACTH 89 pg/mL (5-49)
  - Cortisol 868 nM (8h:260-540)
  - 24h-urinary free cortisol: > 1500 µg/L
Case # 2 extensive hormonal biology

- **Cortisol - ACTH profile**

<table>
<thead>
<tr>
<th></th>
<th>8h</th>
<th>12h</th>
<th>16h</th>
<th>20h</th>
<th>24h</th>
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</thead>
<tbody>
<tr>
<td>Cortisol (nM)</td>
<td>675</td>
<td>708</td>
<td>674</td>
<td>739</td>
<td>642</td>
</tr>
<tr>
<td>ACTH (pg/mL)</td>
<td>81</td>
<td>70</td>
<td>88</td>
<td>101</td>
<td>98</td>
</tr>
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</table>
Case # 2 extensive hormonal biology

• **Dexamethasone suppression tests**

  - 4 x 0.5 mg dexamethasone/day for 2 days
    - Cortisol (8h): 559 nM (nl < 140)

  - dexam at 23h00
    - Cortisol (8h): 313 nM (nl ↓ de 50%)
Case # 2 pituitary MRI
Case # 2 conclusions

- Cushing's disease related to a pituitary microadenoma

- Chronic cortisol excess often induces:
  - a low TSH concentration with euthyroidism
  - a hypogonadotrope hypogonadism
  - a glucose intolerance
  - a dyslipidaemia
  - high blood pressure
Causes of low TSH

- All causes of primary hyperthyroidism
  - Basedow/grave’s disease, multinodulaire goiter, autonomous adenoma, thyroiditis, « iod-Basedow », facticious hyperthyroidism, amiodarone, lithium, gestational hyperthyroidism, struma ovarii, ...

- 1st trimester of pregnancy (hCG peak)

- Pituitary disease with TSH deficiency (isolated/multiple pit def)

- Severe malnutrition, cachexia, prolonged fasting

- Infectious diseases and cancers

- Cushing’s syndrome

- Drugs → low TSH with euthyroidism

- (assay interference : very uncommon)
Low TSH

- **Drugs**
  - Dopamine and dopamine agonists, dobutamine
  - Somatostatine et somatostatine analogues
  - Glucocorticoids
  - cytokines, interferon
  - phenylhydantoin
  - metformine ? (only 1 publication...)