APFCB Masterclass in Interpretative Commenting

Thyroid function test results -2

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Perth, Western Australia
Today’s Agenda

1. Interpretative commenting in Clinical Chemistry
   - Intro / recap

2. Series of more complex TFT results
   - Interpretative comments
     - Note these are not case studies or discussions
Recap summary

- Most clinicians welcome appropriately applied interpretative comments on Clinical Chemistry reports.
- TFT report comments may improve patient outcomes.
- Pathologists and Clinical Scientists have a duty to add value to reports where appropriate, including through interpretative comments.
RCPPath (UK) guidelines for provision of interpretative comments on biochemical reports

Comments might be appropriate when:

- a management / treatment decision is indicated by the results
- a result is unexpected
- a specific question has been posed but it is not obvious whether the results provide the answer
- a clinician has requested a test with which they are unlikely to be familiar
- Interpretation should be provided by an appropriately qualified person
- Comments more appropriate for GPs and junior doctors
  - but not always so - Ascertain user requirements
- Over-interpretation may be misleading
- RCPA (UK) Chemical Pathology Guidelines
Possible components of an interpretative comment

- The absence or presence of an abnormality and its degree or severity
- Possible implications of abnormality
  - diagnosis, prognosis, change in status etc
- Suggested action/follow-up
Communication with clinicians

- To:
  - Get feedback about the comments
  - Agree on test protocols & diagnostic criteria

- Unusual and interesting results could be triggers for direct (verbal) communication and discussion
Biotin interference comment

High dose Biotin (>5mg/d) may falsely decrease/increase reported serum x/y concentrations (Z Diagnostics assay)

Contact the laboratory for further information

Provide phone number

Be aware of assay updates!
TFT results
Patient: 39-year-old female

- Patient Location: General practice
- Clinical Notes: Amenorrhoea
- TFTs
  - TSH: 0.03 mU/L (0.50–4.0)
  - Free T4: 21 pmol/L (10–20)
Patient: 39-year-old female

- Patient Location: General practice
- Clinical Notes: Amenorrhoea
- TFTs
  - TSH: 0.03 mU/L (0.50–4.0)
  - Free T4: 21 pmol/L (10–20)
  - Free T3: 5.5 pmol/L (3.0-5.5)
Patient: 39-year-old female

- Patient Location: General practice
- Clinical Notes: Amenorrhoea

**TFTs**

- **TSH:** 0.03 mU/L (0.50–4.0)
- **Free T4:** 21 pmol/L (10–20)
- **Free T3:** 5.5 pmol/L (3.0–5.5)

**Comment:** The suppressed TSH and high/normal fT4 and fT3 suggest hyperthyroidism. TRAb may be useful. However, low TSH may be seen in pregnancy which should be excluded. These results are within reference intervals for first trimester. If pregnant, repeat TFTs in 6 weeks.

**Q:** Can the lab add on a test for hCG?
Patient: 39-year-old female

- Patient Location: General practice

- Clinical Notes: Amenorrhoea

- TFT s
  - TSH 0.03 mU/L (0.50–4.0)
  - Free T4 21 pmol/L (10–20)
  - Free T3 5.5 pmol/L (3.0–5.5)

**TSH reference intervals in pregnancy**
- 1st trimester 0.02 – 2.5
- 2nd and 3rd trimester 0.30 – 3.0
Patient: 53-year-old female

- Patient Location: General practice

- Clinical Notes: Annual check

- TFTs
  - TSH <0.01 mU/L (0.50–4.0)
  - Free T4 16 pmol/L (10–20)
  - Free T3 5.5 pmol/L (3.0-5.5)
Patient: 53-year-old female

- Patient Location: General practice
- Clinical Notes: Annual check
- TFTs
  - TSH <0.01 mU/L (0.50–4.0)
  - Free T4 16 pmol/L (10–20)
  - Free T3 5.5 pmol/L (3.0-5.5)

- Comment:
  - Clinical conditions associated with a suppressed TSH include non-toxic goitre, subclinical hyperthyroidism and glucocorticoid therapy.
  - Suggest repeat TFTs in six weeks time.
  - Other causes of this pattern: Excessive T4 therapy for hypothyroidism, treated 1ry hyperthyroidism. May also be seen in the elderly. Acute psychiatric illness may raise FT4 and/or lower TSH.
Patient: 53-year-old female (Cont’d in 6/12)

- Patient Location: General practice

- Clinical Notes: Previous suppressed TSH

- TFTs
  - TSH <0.01 mU/L (0.50–4.0)
  - Free T4 17 pmol/L (10–20)
  - Free T3 6.1 pmol/L (3.0–5.5)

- Comment: The increased fT3 and suppressed TSH are consistent with T3 toxicosis
Patient: 84-year-old female

- Patient Location: Emergency Department
- Clinical Notes: Severe hypertension, sweating and palpitation
- TFTs
  - TSH <0.01 mU/L (0.50–4.0)
  - Free T4 45 pmol/L (10–20)
  - Free T3 18 pmol/L (3.0-5.5)
Patient: 84-year-old female

- Patient Location: Emergency Department
- Clinical Notes: Severe hypertension, sweating and palpitation
- TFTs
  - TSH <0.01 mU/L (0.50–4.0)
  - Free T4 45 pmol/L (10–20)
  - Free T3 18 pmol/L (3.0-5.5)
- Comment:
The severely increased fT4 and suppressed TSH are consistent with thyrotoxicosis. Suggest measure TRAb
  - These results may be phoned urgently given the clinical presentation
  - If TFTs were normal, I would suggest plasma metanephrines
Patient: 84-year-old female

- Patient Location: Emergency Department
- Clinical Notes: Severe hypertension, sweating and palpitation
- TFTs
  - TSH <0.01 mU/L (0.50–4.0)
  - Free T4 45 pmol/L (10–20)
  - Free T3 18 pmol/L (3.0-5.5)
  - TRAb 39 U/L (<1.8)

- Comment:
The severely increased fT4 and suppressed TSH and the high TRAb are consistent with Graves’ disease.
- This patient was diagnosed with "thyroid storm"
Patient: 46-year-old female

- Patient Location: General Practice

- Clinical Notes: Started carbimazole therapy recently for Graves’

- TFTs
  - TSH <0.01 mU/L (0.50–4.0)
  - Free T4 7 pmol/L (10–20)
Patient: 46-year-old female

- Patient Location: General Practice

- Clinical Notes: Started carbimazole therapy recently for Graves’

- TFTs
  - TSH <0.01 mU/L (0.50–4.0)
  - Free T4 7 pmol/L (10–20)

- Comment:
The reduced fT4 is consistent with excessive anti-thyroid treatment. The suppressed TSH may take many months to normalise following commencement of ant-thyroid treatment.

- Anti-thyroid therapy initially is guided by fT4 level until TSH normalises.
Patient: 57-year-old female

- Patient Location: Nuclear Medicine
- Clinical Notes: Thyroid cancer. Pre I-131 therapy
- TFT s
  - TSH 120 mU/L (0.50–4.0)
Patient: 57-year-old female

- Patient Location: Nuclear Medicine
- Clinical Notes: Thyroid cancer. Pre I-131 therapy
- TFTs
  - TSH: 120 mU/L (0.50–4.0)
  - Comment: History noted

[Post Thyrogen (thyrotropin alpha = recombinant human TSH)]
Patient: 61-year-old female

- Patient Location: Oncology Clinic

- Clinical Notes: Thyroid cancer. Post thyroidectomy, monitoring

- **TG/ATG**
  - Thyroglobulin: 31 ug/L

Ref Interval
Thyroglobulin

- Tumour marker for thyroid cancer
- Post thyroidectomy, detectable serum Tg indicates presence of remnant or tumour thyroid tissue
- hTSH stimulated Tg testing is recommended to unmask occult disease in such patients
- Highly sensitive serum Tg assays may render TSH stimulation unnecessary
- Anti-TG Antibodies, if present, interfere with Tg immunoassays
- When Tg is measured by immunoassay, Anti-TG Ab should also be measured
Patient: 61-year-old female

- Patient Location: Oncology Clinic

- Clinical Notes: Thyroid cancer. Post thyroidectomy, monitoring

- **TG/ATG**
  - Thyroglobulin: 31 ug/L (*see below)
  - Anti-Thyroglobulin < 1 kU/L (< 4)

  *In athyrotic patients on suppressive thyroxine therapy for differentiated thyroid cancer, thyroglobulin < 0.1 ug/L would suggest minimal risk of recurrent cancer. Results should be interpreted in the context of serial measurement.*
Patient: 61-year-old female

An alternative scenario

- Patient Location: Oncology Clinic

- Clinical Notes: Thyroid cancer. Post thyroidectomy, monitoring

- **Tg and TgAb**
  - Thyroglobulin: <0.1
  - Anti Thyroglobulin antibody: 14 (<4 kU/L)
Patient: 61-year-old female

- Patient Location: Oncology Clinic
- Clinical Notes: Thyroid cancer. Post thyroidectomy, monitoring

**Tg and TgAb**

<table>
<thead>
<tr>
<th>Test</th>
<th>Ref Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroglobulin</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Anti Thyroglobulin antibody</td>
<td>14 (&lt;4 kU/L)</td>
</tr>
</tbody>
</table>

- Comment: The positive anti thyroglobulin antibodies may interfere with this thyroglobulin immunometric assay and cause a false negative result making the thyroglobulin result unreliable.

- Anti-Tg Ab trends may be used as a surrogate tumour marker
Patient: 50-year-old male

- **Patient Location:** General Practice

- **Clinical Notes:** Family history of thyroid disease

- **TFTs**
  - TSH: 4.2 mU/L (0.50–4.0)
  - Free T4: 11 pmol/L (10–20)
  - fT3: 5.6 pmol/L (3.0-5.5)
  - TPO Ab (Abbott): 876 kU/L (< 6)
Patient: 50-year-old male

- Patient Location: General Practice

- Clinical Notes: Family history of thyroid disease

- TFTs

  - TSH: 4.2 mU/L (0.50–4.0)
  - Free T4: 11 pmol/L (10–20)
  - fT3: 5.6 pmol/L (3.0-5.5)
  - TPO Ab (Abbott): 876 kU/L (< 6)

- Comment

  The mildly increased TSH with normal fT4 and raised TPO antibodies indicate subclinical hypothyroidism due to autoimmune thyroid disease. fT3 measurement is helpful only in hyperthyroidism.

*[we are assuming patient is not on T3 replacement]*
Patient: 62 year-old male

- Patient Location: General Practice
- Clinical Notes on Request Form: On amiodarone.

- TFTs
  - TSH  < 0.01 mU/L (0.50-4.00)
  - Free T4  23 pmol/L (10-20)
  - Free T3  5.0 pmol/L (3.0-5.5)
Patient: 62 year-old male

- Patient Location: General Practice
- Clinical Notes on Request Form: On amiodarone.

**TFTs**
- **TSH**  < 0.01 mU/L  (0.50-4.00)
- **Free T4**  23 pmol/L  (10-20)
- **Free T3**  5.0 pmol/L  (3.0-5.5)

**Comment:**
- Amiodarone inhibits T4 to T3 conversion as well as presenting the thyroid with a large iodine load.
- The suppressed TSH and raised fT4 may suggest amiodarone-induced hyperthyroidism but should be interpreted in the light of clinical findings.
Patient: 62 year-old male - 2

- Patient Location: General Practice
- Clinical Notes on Request Form: On amiodarone.

- TFTs
  - TSH $< 0.01$ mU/L (0.50-4.00)
  - Free T4 23 pmol/L (10-20)
  - Free T3 5.0 pmol/L (3.0-5.5)

- Comment 2:
  - Amiodarone inhibits T4 to T3 conversion as well as presenting the thyroid with a large iodine load.
  - Suggest consider Specialist Endocrine referral.
Patient: 51-year-old male

- Patient Location: General Practice
- Clinical Notes: Diabetes
- TFTs
  - TSH: 1.3 mU/L (0.50–4.0)
  - fT4: 26 pmol/L (10–20)
Patient: 51-year-old male

- Patient Location: General Practice
- Clinical Notes: Diabetes
- TFTs
  - TSH: 1.3 mU/L (0.50–4.0)
  - fT4: 26 pmol/L (10–20)

Comment

Normal TSH indicates an euthyroid state. Causes of a raised FT4 with reduced T4/T3 conversion include non-thyroidal illness, drugs (beta-blockers, amiodarone, heparin, radiocontrast) and treated thyroid disease.

Suggest measure fT3 if not on treatment
Patient: 51-year-old male

- Patient Location: General Practice
- Clinical Notes: Diabetes

- TFTs
  - TSH: 1.3 mU/L (0.50–4.0)
  - fT4: 26 pmol/L (10–20)
  - fT3: 6.1 pmol/L (3.0-5.5)
Patient: 51-year-old male

- Patient Location: General Practice

- Clinical Notes: Diabetes

- TFTs
  - TSH: 1.3 mU/L (0.50–4.0)
  - fT4: 26 pmol/L (10–20)
  - fT3: 6.1 pmol/L (3.0–5.5)

- Comment
  Results confirmed by alternative method.
  Heterophile antibody excluded for TSH.
  Consider specialist Endocrine referral to test for TSH secreting tumour or thyroid hormone resistance.
Previous TFTs 3 years ago

- Patient Location: General Practice

- Clinical Notes: Diabetes

- TFTs
  - TSH 1.1 mU/L (0.50–4.0)
  - fT4 17 pmol/L (10–20)

- Comment
  Normal TSH and T4 are consistent with an euthyroid state
Patient: 51-year-old male

- Patient Location: General Practice
- Clinical Notes: Diabetes
- TFTs
  - TSH: 1.3 mU/L (0.50–4.0)
  - fT4: 26 pmol/L (10–20)
  - fT3: 6.1 pmol/L (3.0-5.5)
- Comment
  Results confirmed by alternative method.
  Heterophile antibody excluded for TSH.
  Previous normal TFTs noted making thyroid hormone resistance less likely. Consider specialist Endocrine referral to investigate for TSH secreting tumour.
Patient: 51-year-old male

- Patient Location: General Practice
- Clinical Notes: Diabetes

- TFTs
  - TSH 1.3 mU/L (0.50–4.0)
  - fT4 26 pmol/L (10–20)
  - fT3 6.1 pmol/L (3.0-5.5)

- [alpha subunit measurement may be useful]
Patient: 39-year-old male

- Patient Location: Emergency Dept.

- Clinical Notes on Request Form: General weakness

- TFTs

  - TSH  < 0.01 mU/L  (0.50-4.00)
  - Free T4  43 pmol/L  (10-20)
  - Free T3  22 pmol/L  (3.0-5.5)
Patient: 39-year-old male

- Patient Location: Emergency Dept.
- Clinical Notes on Request Form: General weakness
- TFTs
  - TSH < 0.01 mU/L (0.50-4.00)
  - Free T4 43 pmol/L (10-20)
  - Free T3 22 pmol/L (3.0-5.5)

Before commenting look at other results!
Patient: 39-year-old Asian male

- Patient Location: Emergency Dept.
- Clinical Notes on Request Form: General weakness

**Electrolytes**

- Sodium 143 mmol/L (134-146)
- Potassium 2.4 mmol/L (3.4-5.0)
- Bicarbonate 18 mmol/L (22-32)
- Urea 6.0 mmol/L (3.0-8.0)
- Creatinine 62 umol/L (60-110)
- eGFR > 90 mL/min/1.73m^2
Patient: 39-year-old Asian male

- Patient Location: Emergency Dept.

- Clinical Notes on Request Form: General weakness

- **TFT s**
  - TSH  < 0.01 mU/L  (0.50-4.00)
  - Free T4  43 pmol/L  (10-20)
  - Free T3  22 pmol/L  (3.0-5.5)
  - TRAb  14.7 kU/L  (< 1.0)

Comment:

Thyrotoxicosis with hypokalaemia and muscle weakness may be consistent with thyrotoxic periodic paralysis
Patient: 51 year-old male

- Patient Location: General Practice
- Clinical Notes on Request Form: Previous raised TSH.

- TFTs
  - TSH 4.5 mU/L (0.50-4.00)
  - Free T4 8 pmol/L (10-20)
Patient: 51 year-old male

- Patient Location: General Practice
- Clinical Notes on Request Form: Previous raised TSH.

- **TFT s**
  - TSH 4.5 mU/L (0.50-4.00)
  - Free T4 8 pmol/L (10-20)

- **Comment:**
  The presence of a low fT4 with only a marginal increase in TSH may suggest pituitary insufficiency, although these results may also be seen in non-thyroidal illness.

Suggest further pituitary investigations or Specialist Endocrine referral if abnormalities persist.
Patient: 67 year-old female

- Patient Location: General Practice
- Clinical Notes on Request Form: Pituitary failure. On T4

- TFT s
- TSH: 0.02 mU/L (0.50-4.00)
- Free T4: 8 pmol/L (10-20)
Patient: 67 year-old female

- Patient Location: General Practice
- Clinical Notes on Request Form: Pituitary failure. On T4

- TFTs
  - TSH 0.02 mU/L (0.50-4.00)
  - Free T4 8 pmol/L (10-20)

- Comment:
  FT4 should be maintained in the upper reference interval in patients on thyroxine for 2ry hypothyroidism,
  Suggest review T4 dose (and adherence to therapy) based on clinical assessment.
## Patient: 66 year-old female

- **Patient Location:** Emergency Department
- **Clinical Notes on Request Form:** Semicoma

### Chemistry

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Unit</th>
<th>Reference Range</th>
</tr>
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<tbody>
<tr>
<td>Na</td>
<td>107</td>
<td>mmol/L</td>
<td>137 - 143</td>
</tr>
<tr>
<td>K</td>
<td>2.2</td>
<td>mmol/L</td>
<td>3.2 - 4.3</td>
</tr>
<tr>
<td>CL</td>
<td>68</td>
<td>mmol/L</td>
<td>102 - 111</td>
</tr>
<tr>
<td>HCO3</td>
<td>26</td>
<td>mmol/L</td>
<td>22 - 31</td>
</tr>
<tr>
<td>Urea</td>
<td>3.4</td>
<td>mmol/L</td>
<td>3.0 - 8.0</td>
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<tr>
<td>Creat</td>
<td>96</td>
<td>umol/L</td>
<td>70 - 100</td>
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<tr>
<td>Glu</td>
<td>7.9</td>
<td>mmol/L</td>
<td>3.0 - 5.5</td>
</tr>
<tr>
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<td>U/L</td>
<td>&lt; 150</td>
</tr>
<tr>
<td>Chol</td>
<td>8.7</td>
<td>mmol/L</td>
<td>&lt;5.5</td>
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Patient: 66 year-old female

- Patient Location: Emergency Department
- Clinical Notes on Request Form: Semicoma

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Comment: This pattern of abnormalities [hyponatraemia, hypercholesterolaemia and a raised CK due to myopathy] may be seen in severe hypothyroidism. Suggest measure TFTs.
Patient: 66 year-old female

- Patient Location: Emergency Department
- Clinical Notes on Request Form: Semicoma

TFTs

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<tbody>
<tr>
<td>TSH</td>
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<tr>
<td>fT4</td>
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Patient: 66 year-old female

- Patient Location: Emergency Department
- Clinical Notes on Request Form: Semicoma

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Diagnosis: Myxoedema coma
Thyroid Function Analysis in 50 Patients with COVID-19: A Retrospective Study

Min Chen,* Weibin Zhou,* and Weiwei Xu
Results: TSH lower than the normal range was present in 56% (28/50) of the patients with COVID-19. The levels of TSH and serum total triiodothyronine (TT3) of the patients with COVID-19 were significantly lower than those of the healthy control group and non-COVID-19 pneumonia patients. The more severe the COVID-19, the lower the TSH and TT3 levels were, with statistical significance ($p < 0.001$). The degree of the decreases in TSH and TT3 levels was positively correlated with the severity of the disease. The total thyroxine (TT4) level of the patients with COVID-19 was not significantly different from the control group.

Table 1. Comparison of Serum TSH, TT3, and TT4 Between COVID-19 and Healthy Control Group and Non-COVID-19 Pneumonia Patients

<table>
<thead>
<tr>
<th></th>
<th>COVID-19 (n = 50)</th>
<th>Healthy control (n = 54)</th>
<th>Non COVID-19 (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alb (g/L)</td>
<td>38.15 [34.57, 43.10]**</td>
<td>46.15 [43.98, 48.05]</td>
<td>38.70 [33.67, 40.95]</td>
</tr>
<tr>
<td>TSH (mIU/L)</td>
<td>0.30 [0.15, 0.86]**##</td>
<td>1.57 [1.03, 1.97]</td>
<td>1.18 [0.68, 1.91]</td>
</tr>
<tr>
<td>TT3 (nmol/L)</td>
<td>0.98 [0.84, 1.22]**#</td>
<td>1.58 [1.49, 1.73]</td>
<td>1.28 [0.82, 1.43]</td>
</tr>
<tr>
<td>TT4 (nmol/L)</td>
<td>97.41 [78.71, 113.73]</td>
<td>97.11 [85.73, 108.76]</td>
<td>90.37 [69.16, 105.83]</td>
</tr>
</tbody>
</table>
Thyroid Function Analysis in 50 Patients with COVID-19: A Retrospective Study

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<tr>
<th></th>
<th>TSH (mIU/L)</th>
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<tbody>
<tr>
<td>Control (n = 54)</td>
<td>1.57 [1.03, 1.97]</td>
</tr>
<tr>
<td>Moderate (n = 15)</td>
<td>0.50 [0.22, 1.58]</td>
</tr>
<tr>
<td>Severe (n = 23)</td>
<td>0.286 [0.13, 0.77]</td>
</tr>
<tr>
<td>Critical (n = 12)</td>
<td>0.23 [0.085, 0.42]</td>
</tr>
</tbody>
</table>

All the patients did not receive thyroid hormone replacement therapy. After recovery, no significant differences in TSH, TT3, TT4, free triiodothyronine (fT3), and free thyroxine (fT4) levels were found between the COVID-19 and control groups.
Thank you!