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Interpretative commenting in clinical chemistry with worked examples for thyroid function test reports

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ABSTRACT

Correct interpretation of pathology results is a requirement for accurate diagnosis and appropriate patient management. Clinical Pathologists and Scientists are increasingly focusing on providing quality interpretative comments on their reports and these comments are appreciated by clinicians who receive them. Interpretative comments may improve patient outcomes by helping reduce errors in application of the results in patient management. Thyroid function test (TFT) results are one of the areas in clinical chemistry where interpretative commenting is practised by clinical laboratories. We have provided a series of TFT reports together with possible interpretative comments and a brief explanation of the comments. It is felt that this would be of help in setting up an interpretative service for TFTs and also assist in training and continuing education in their provision.

1. Introduction

Accurate interpretation of pathology results is a requirement for appropriate patient management. The managing clinician needs to interpret the results correctly in order to arrive at the right diagnosis and manage the patient appropriately. These steps can be compromised in the instances of incorrect interpretation of laboratory results by the managing clinician [1,2]. Hence, clinical laboratories in Clinical Pathology disciplines are increasingly focusing on providing quality interpretative comments on their reports [3]. This is also increasingly expected by clinicians and where practised, by patients who receive these reports [4,5]. Additional drivers for provision of interpretative comments include patient safety which has led to the desirability of provision of interpretative comments being included in quality requirements for international standards for laboratory accreditation [6]. International Standard for laboratory accreditation (ISO 15189) requires laboratories to provide clinical advice in the interpretation of examination results, including the provision of interpretative comments on result where applicable. There is now significant evidence that incorrect interpretation of laboratory results occurs in both in-patient and out-patient setting, impacting on patient safety; interpretative comments in clinical laboratory reports would reduce the risk of occurrence of these errors and improve patient safety and outcomes [1,2,7,8]. There is consensus that interpretative comments should be monitored as a quality indicator of the post-analytical phase [6].

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1.1. Adding value

In traditional clinical laboratory practice, verbal (phoned or "corridor conversation") requests for interpretations of both common and routine tests [e.g., iron studies, liver function tests and renal profile (urea and electrolytes)], thyroid function tests and other hormone profiles are commonly fielded by Clinical Scientists and Pathologists [3]. Qualitative or semi-quantitative tests such as protein electrophoresis have always required a comment. Instances where comments can add value include unexpected results due to an interference (e.g., from macroproteins or heterophile antibodies in immunoassays) or suggestions for additional or reflexive testing.

1.2. Training in interpretation and commenting

The knowledge that doctors have about laboratory results and their interpretation varies considerably between regions and even between training institutions within the same country. There is a perception now among Pathologists that the focus of medical education on laboratory testing within the newer methods of undergraduate teaching has decreased in terms of time devoted to it and as a result, clinicians' knowledge of interpretation of laboratory tests has deteriorated in recent times [9,10]. Added to this, the number and varieties of tests, as well as their complexities, have increased over time. Surveys have indicated that junior doctors do not often feel confident in interpreting even some common laboratory tests [11]. In other surveys, health care staff (doctors and clinical nurses) have indicated their preference for the inclusion of interpretative comments in laboratory reports [9]. As regards Laboratory personnel qualified to comment on reports, Pathologists, and Clinical Scientists with appropriate training, qualification and credentialing generally perform this function in Clinical Chemistry [3,12]. In addition, scientists with a focus of expertise and experience in a specialised area comment on results generated by their specialised area only.

1.3. Competence of an individual to add interpretative comments

1.3.1. Best practice [12]

Proven knowledge in, and experience of, providing accurate interpretative comments in respect of the tests being validated is required. For junior staff, this should form part of their competency assessment while under supervision. For senior staff, this could be by formal peer assessment and demonstration of continuous professional development.

Participation and satisfactory performance in an interpretative comments EQA scheme.

1.4. Limitations

Clinical Chemistry laboratories produce a large number of results every day, and interpretative commenting on each of these is neither practical nor is it necessary. A major limitation to the provision of meaningful and useful interpretation on laboratory reports is the paucity of information about the patient and the context for the test requests, i.e. the reason for the test. In addition to the lack of knowledge of the clinical details, the laboratory is often unaware of pre-analytical factors that may interfere with or influence the results, including patient status and preparation at testing and medication history. Although the reason for the test, i.e., the clinical question, ought to be provided to the laboratory, this is rarely the case. Nor is it practical to manually obtain this information from the requesting clinician or the clinical information system for each request. The art of commenting which is acquired during training and enhanced with practice factors in these limitations; the comments should be limited to what can be offered with the limited knowledge of the patient details available to the laboratory [3]. Over-interpretation based on false assumptions can lead to inappropriate or misleading comments and also lead to loss of confidence among requesting clinicians in the laboratory advisory service [13].

Guidelines for the provision of interpretative comments on biochemical reports [3] state that whether a comment is required will depend on:

- the clinical details provided
- the clinical implication of the results
- the likely familiarity of the requesting clinician with the tests and their interpretation.

The guidelines suggest that comments might be appropriate when:

- a decision on management or treatment is indicated by the results in combination with the clinical details provided
- 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 not likely to be familiar [5,6].

The usual components of a comment include the following [15]:

1. The presence or absence of an abnormality and its degree or severity.
2. Possible clinical implications of the abnormality and/or a diagnosis.
3. Suggested follow-up, including further testing and, if required, specialist referral.

This review will provide a series of examples of thyroid function test (TFT) results with possible comments by way of introduction to the field of commenting. In the examples, TFTs refers to thyroid stimulating hormone (TSH) and free thyroxine (FT4) measurements. It is hoped that this will provide 'beginners' with a basic platform to build their comments database from which to individualise interpretative comments to TFTs reported by their laboratories. Note, the reference intervals quoted (in parenthesis in the example reports) would vary depending on the population served by the laboratory (not to mention age of the patient) as well as the assay used, and should be adapted accordingly.

1.4.1. Report 1

Patient: 28-year-old female.
Patient Location: General Practice.
Clinical Notes on Request Form: Lethargy.
Tests: TFTs.

TSH	0.67 mU/L	(0.50–4.0)
Free T4	16 pmol/L	(10–20)

Comment:
Normal T4 and TSH are consistent with a euthyroid state.
Explanation:
The comment addresses the results and not the patient about whom the laboratory knows little. Hence, the statement "the results are consistent with a euthyroid state", rather than stating that the patient is euthyroid. It is assumed the tests are done to exclude thyroid dysfunction, but the comment would still be correct if the patient is on antithyroid treatment or on T4 replacement.

1.4.2. Report 1b

Patient: 28-year-old female.
Patient Location: General Practice.
Clinical Notes on Request Form: Lethargy.
Tests: TFTs.

TSH	0.67 mU/L	(0.50–4.0)

Comment:
Normal TSH is consistent with a euthyroid state.
Explanation:
Similar sentiments apply as to the comment on the previous report. The drawback of measuring TSH only is that secondary hypothyroidism due to pituitary dysfunction may be missed by this strategy. A normal TSH on its own does not exclude the latter condition, which is rare, and the even rarer conditions such a T4 resistance syndrome. However, the statement that the results are consistent with an euthyroid state does not rule out other conditions which can present with a normal TSH and an abnormal FT4, which should be addressed if the clinical question on the form or other results indicate so.

1.4.3. Report 2

Patient: 36-year-old female.
Patient Location: General Practice.
Clinical Notes on Request Form: Weight loss.
Tests: TFTs.

TSH	0.74 mU/L	(0.50–4.0)
Free T4	8 pmol/L	(10–20)

Comment:
A mildly reduced FT4 with a normal TSH may be due to non-thyroidal illness or pituitary hypothyroidism.
Explanation:
Without further information about the patient the more common cause of non-thyroidal illness is mentioned as a likely cause; however, since pituitary disease is important not to miss, even if rare, it is useful to bring it to the clinician's attention.

1.4.4. Report 3

Patient: 57-year-old female.
Patient Location: General Practice.

Clinical Notes on Request Form: Weight gain.
Tests: TFTs.

TSH	7.3 mU/L	(0.50–4.0)

Comment:
Mildly increased TSH may be found in patients with subclinical hypothyroidism or sick euthyroid syndrome. Suggest measurement of FT4, TSH and thyroperoxidase (TPO) antibodies in 6 weeks.
Explanation:
A mildly raised TSH due to subclinical hypothyroidism or sick euthyroid syndrome is one of the commonest TFT abnormality and can usually be differentiated by repeat testing and the measurement of TPO antibody. It is important to measure FT4 with TSH in the repeat test, to exclude rare abnormalities which will be addressed further down.

1.4.5. Report 3b

Patient: 57-year-old female.
Patient Location: General Practice.
Clinical Notes on Request Form: Weight gain.
Tests: TFTs.

TSH	7.3 mU/L	(0.50–4.0)
Free T4	13 pmol/L	(10–20)

Comment:
Mildly increased TSH with a normal FT4 may be found in patients with subclinical hypothyroidism or sick euthyroid syndrome. Suggest repeat measurement with TPO antibodies in 6 weeks.
Explanation:
Similar sentiments apply as to the comment on the previous report.

1.4.6. Report 4

Patient: 76-year-old male.
Patient Location: General Practice.
Clinical Notes on Request Form: Routine check.
Tests: TFTs.

TSH	4.5 mU/L	(0.50–4.0)
Free T4	15 pmol/L	(10–20)

Comment:
Mildly increased TSH with a normal FT4 can be seen in the euthyroid elderly.
Explanation:
The upper reference limit for TSH may be higher in the elderly, even though the reference intervals quoted in the elderly are often the same as for younger adults.

1.4.7. Report 5

Patient: 62-year-old female.
Patient Location: General Practice.
Clinical Notes on Request Form: Constipation.
Tests: TFTs.

TSH	14.0 mU/L	(0.50–4.0)
Free T4	13 pmol/L	(10–20)

Comment:
A moderately increased TSH with a normal FT4 is consistent with (mild) primary hypothyroidism.
Explanation:
A TSH >10.0 is considered to signify hypothyroidism even if the FT4 is within reference intervals [14].

1.4.8. Report 6

Patient: 27-year-old female.

Patient Location: Obstetric clinic.
Clinical Notes on Request Form: Period of amenorrhea 12/40 weeks.
Tests: TFTs.

TSH	0.05 mU/L	(0.50–4.0)
Free T4	13 pmol/L	(10–20)

Comment:
TSH reference intervals in pregnancy.

1st trimester	0.02–2.5
2nd and 3rd trimester	0.30–3.0

Explanation:
TSH is lower in early pregnancy than in non-pregnant women due to the action of human chorionic gonadotropin, and returns to the pre-pregnancy levels towards the end of pregnancy [15,16] and this should be accommodated in the report for the TFTs to be interpreted appropriately.

1.4.9. Report 7

Patient: 32-year-old female.
Patient Location: General Practice.
Clinical Notes: Trying for a baby.
Tests: TFTs.

TSH	4.6 mU/L	(0.50–4.0)
Free T4	13 pmol/L	(10–20)
TPO Antibodies	33 kU/L	(<6)

Comment:
The mildly increased TSH and raised TPO antibodies indicate subclinical hypothyroidism due to autoimmune thyroid disease.
Suggest confirming subclinical hypothyroidism by repeat testing. Poor pregnancy outcomes have been described in women with a raised TSH. If raised TSH confirmed, consider thyroxine replacement.
Explanation:
Thyroid dysfunction during pregnancy can result in complications for both mother and foetus. This is recognised by guidelines which suggest treatment of subclinical hypothyroidism with low dose T4 replacement both pre-conception and during pregnancy [15].

1.4.10. Report 8

Patient: 55-year-old male.
Patient Location: General Practice.
Clinical Notes: Feeling very tired.
Tests: TFTs.

TSH	0.02 mU/L	(0.50–4.0)	
Free T4		18 pmol/L	(10–20)

Comment:
The suppressed TSH and normal FT4 are consistent with subclinical hyperthyroidism.
Suggest measure free triiodothyronine (FT3).
Explanation:
The measurement of FT3 is suggested in subclinical hyperthyroidism since FT3 is more sensitive for the diagnosis of hyperthyroidism than FT4 [17].

1.4.11. Report 8b

Patient: 55-year-old male.
Patient Location: General Practice.
Clinical Notes: Hyperthyroid?

Tests: TFTs.

TSH	0.02 mU/L	(0.50–4.0)
Free T4	18 pmol/L	(10–20)
FT3	6.1 pmol/L	(3.0–5.5)

Comment:

The increased FT3 and suppressed TSH (with a normal FT4) are consistent with T3 toxicosis. Suggest measure TSH-receptor antibodies (TRAb).

Explanation:

Thyrotoxicosis is commonly due to Graves' disease; less common causes are thyroiditis or nodular thyroid disease. In hyperthyroidism due to excess T4 therapy or surreptitious thyroxine intake, FT3 is not as raised as in innate thyrotoxicosis. The presence of raised TRAb favours the diagnosis of Graves' disease [17].

1.4.12. Report 9

Patient: 74-year-old male.

Patient Location: General Practice.

Clinical Notes: Hypothyroid?

Tests: TFTs.

TSH	59 mU/L	(0.50–4.0)
Free T4	<5 pmol/L	(10–20)

Comment.

The severely increased TSH with a very low FT4 is consistent with primary hypothyroidism. Suggest measure TPO antibodies.

Explanation:

Raised TPO antibodies would indicate the presence of autoimmune thyroid disease as the cause of the hypothyroidism [14].

1.4.13. Report 9b

One week later.

Patient Location: General Practice.

Clinical Notes: Hypothyroid, started T4 replacement 1 week ago.

Tests: TFTs.

TSH	40 mU/L	(0.50–4.0)
Free T4	8 pmol/L	(10–20)

Comment:

Suggest repeat TFT measurement at least 4–6 weeks after commencement of T4 replacement.

Explanation:

TFTs take 4–6 weeks to stabilise after initiation of Thyroxine replacement; earlier testing can mislead regarding adequacy of thyroxine dose [14].

1.4.14. Report 10

Patient: 43-year-old female.

Patient Location: General Practice.

Clinical Notes on Request Form: On T4 replacement.

Tests: TFTs.

TSH	0.72 mU/L	(0.50–4.0)
Free T4	16 pmol/L	(10–20)

Comment:

The normal TSH and FT4 are consistent with adequate thyroid hormone replacement.

Explanation:

The aim of thyroxine replacement therapy is to normalise TSH and stabilise it in the lower half of the reference interval [14].

1.4.15. Report 11

Patient: 54-year-old female.

Patient Location: General Practice.
Clinical Notes on Request Form: On T4 replacement.
Tests: TFTs.

TSH	5.6 mU/L	(0.50–4.0)
Free T4	12 pmol/L	(10–20)

Comment.
Increased TSH suggests inadequate thyroid hormone replacement if the dose has not been changed for at least 6 weeks and patient has been taking the medication regularly.
Suggest review dose and repeat TFTs in 6 weeks.
Explanation:
As indicated previously, 4–6 weeks should elapse after any change in thyroxine dose before testing.

1.4.16. Report 12

Patient: 61-year-old female.
Patient Location: General Practice.
Clinical Notes on Request Form: On T4 replacement.
Tests: TFTs.

TSH	0.02 mU/L	(0.50–4.0)
Free T4	19 pmol/L	(10–20)

Comment: Suppressed TSH is consistent with excessive thyroid hormone replacement.
Explanation:
TSH below the lower reference limit in a patient on thyroxine replacement would suggest excessive thyroxine dose.

1.4.17. Report 13

Patient: 51-year-old female.
Clinical Notes on Request Form: Previous total thyroidectomy for thyroid cancer. On thyroxine.
Tests: TFTs.

TSH	0.12 mU/L	(0.50–4.0)
Free T4	19 pmol/L	(10–20)

Comment:
Previous history of thyroid cancer noted. Low TSH may be appropriate depending on treatment targets for this patient.
Explanation:
In a patient with a history of thyroid cancer, the aim is to suppress TSH to a level commensurate with the level risk of recurrence of disease [18]. The TSH target is best left to the specialist managing the patient.

1.4.18. Report 14

Patient: 56-year-old female.
Clinical Notes: Subclinical hypothyroidism, follow-up.
Tests: TFTs.

TSH	3.6 mU/L	(0.50–4.0)
Free T4	12 pmol/L	(10–20)

Previous Results 6 months ago:

TSH	4.3 mU/L	(0.50–4.0)
Free T4	13 pmol/L	(10–20)

Comment.
Borderline TSH persists. Suggest repeat in one year with thyroid autoantibodies (TPO antibodies).
Explanation:
The serial change in TSH in this patient is within its biological variation despite the two measurements being on either side of the

upper reference limit. Monitoring will reveal if there is a serial increase [14].

1.4.19. Report 15

Patient: 37-year-old female.
Patient Location: General practice.
Clinical Notes: Amenorrhea.
Tests: TFTs.

TSH	0.03 mU/L	(0.50–4.0)
Free T4	20 pmol/L	(10–20)

Comment: The suppressed TSH and high-normal FT4 may suggest hyperthyroidism. FT3 and 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.

Explanation:

As noted previously, the reference intervals for TSH are lower in pregnancy and results should be interpreted appropriately [15,16]. However, the presence of gestational thyrotoxicosis should also be considered.

1.4.20. Report 16

Patient: 53-year-old female.
Patient Location: General practice.
Clinical Notes: Annual check.
Tests: 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 include: Excessive T4 therapy for hypothyroidism, treated primary hyperthyroidism. Acute psychiatric illness may raise FT4 and/or lower TSH.

Explanation:

The paucity of clinical information may mean the comment would have to cover many possibilities.

1.4.21. Report 16b

Six weeks later.
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. Suggest measure TRAb.

1.4.22. Report 17

Patient: 84-year-old female.
Patient Location: Emergency Department.
Clinical Notes: Severe hypertension, sweating and palpitation.
Tests: 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 FT4and FT3 and suppressed TSH are consistent with thyrotoxicosis. These results together with the clinical

presentation may indicate thyroid storm. Suggest measure TRAb.

Explanation:

Thyroid storm may be suspected in a patient with severe thyrotoxicosis and accompanying suggestive symptoms and signs [19].

1.4.23. Report 18

Patient: 46-year-old female.

Patient Location: General Practice.

Clinical Notes: Started carbimazole therapy recently for Graves' disease.

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.

Explanation:

Anti-thyroid therapy is initially guided by FT4 level until TSH normalises [17].

1.4.24. Report 19

Patient: 59-year-old female.

Patient Location: Nuclear Medicine.

Clinical Notes: Thyroid cancer. Pre I-131 Thyrogen therapy.

Tests: TFTs.

TSH	120 mU/L	(0.50–4.0)

Comment:

Thyrogen [thyrotropin alpha (recombinant human TSH)] in blood is measured by the TSH assay.

Explanation:

The recombinant TSH administered before thyroid scan cross-reacts with the TSH assay and will lead to a raised TSH measurement. Alternatively, thyroxine withdrawal prior to the scan will also lead to an increased endogenous TSH concentration [18].

1.4.25. Report 20

Patient: 64-year-old female.

Patient Location: Oncology Clinic.

Clinical Notes: Thyroid cancer. Post thyroidectomy, monitoring.

Tests: Tg/TgAb		
Thyroglobulin:	31 μg/L	(*see below)
Anti-Thyroglobulin	<1 kU/L	(<4)

*In athyrotic patients on suppressive thyroxine therapy for differentiated thyroid cancer, thyroglobulin <0.1 μg/L would suggest minimal risk of recurrent cancer.

Comment:

Results should be interpreted in the context of serial measurement.

Explanation:

Modulation of TSH suppression depending on risk of thyroid cancer recurrence is best left to the managing specialist.

1.4.26. Report 20b. An alternative scenario

Tests: Tg and TgAb.

Thyroglobulin	<0.1 μg/L	
Anti Thyroglobulin antibody	14 kU/L	(<4)

Comment:

The positive anti thyroglobulin antibodies may interfere with this thyroglobulin immunometric assay and cause a falsely low result making the thyroglobulin result unreliable. Anti-Tg Ab trends may be used as a surrogate tumour marker for monitoring.

Explanation:

Thyroglobulin measurement should always be accompanied by measurement of anti thyroglobulin antibody which, if present, can interfere with, and negate the usefulness of, thyroglobulin measurement [18].

1.4.27. Report 21

Patient: 50-year-old male.

Patient Location: General Practice.

Clinical Notes: Family history of thyroid disease.

Tests: TFTs.

TSH	4.2 mU/L	(0.50–4.0)
Free T4	11 pmol/L	(10–20)
Free T3	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 diagnosing hyperthyroidism (or in monitoring FT3 supplementation).

Explanation:

FT3 measurement is not useful in diagnosis and management of hypothyroidism; it is best used for the diagnosis of thyrotoxicosis, where it is often more sensitive than FT4 [14,17].

1.4.28. Report 22

Patient: 63-year-old male.

Patient Location: General Practice.

Clinical Notes on Request Form: On amiodarone.

Tests: 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.

Alternative comment:

Amiodarone inhibits T4 to T3 conversion as well as presenting the thyroid with a large iodine load. Suggest consider Specialist Endocrine referral.

Explanation:

Amiodarone (an antiarrhythmic) can cause thyroid dysfunction due to several mechanisms and these should be considered in interpreting TFTs in patients treated with this medication [20].

1.4.29. Report 23

Patient: 53-year-old male.

Patient Location: General Practice.

Clinical Notes: Diabetes.

Tests: TFTs.

TSH	1.3 mU/L	(0.50–4.0)
FT4	26 pmol/L	(10–20)

Comment:

Normal TSH indicates a 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.

1.4.30. Report 23b

Tests: 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:

FT4 and TSH results confirmed by alternative method. Heterophile antibody excluded for TSH. Consider specialist Endocrine referral to test for TSH secreting tumour or thyroid hormone resistance.

Alternative scenario comment:

FT4 and TSH 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. Alpha subunit measurement may be useful.

Explanation:

Persistently raised FT4 with an "inappropriately" normal TSH may justify further investigations to elucidate the cause which can be analytical or clinical. Liaison with the managing clinician is warranted in these cases [21,22].

1.4.31. Report 24

Patient: 39-year-old male.

Patient Location: Emergency Dept.

Clinical Notes on Request Form: General weakness.

Tests: 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)

Additional results:

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 μmol/L	(60–110)
eGFR	>90 mL/min/1.73 m∧2	

Comment:

The raised FT4 and FT3 with suppressed TSH are consistent with thyrotoxicosis. Hyperthyroidism with hypokalaemia and muscle weakness may be consistent with thyrotoxic periodic paralysis.

Explanation:

Thyrotoxic periodic paralysis is a genetic condition often found in Asian males and should be considered when clinical electrolyte and TFT abnormalities are present together [23].

1.4.32. Report 25

Patient: 60-year-old male.

Patient Location: General Practice.

Clinical Notes on Request Form: Previous raised TSH.

Tests: TFTs.

TSH	4.5mU/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.

Explanation:

TSH is generally more sensitive than FT4 for the diagnosis of hypothyroidism. By the time FT4 decreases below the lower reference limit, TSH is usually well above the upper reference limit in primary hypothyroidism [14]. A mismatch in this relationship may

indicate pituitary dysfunction or sick euthyroidism.

1.4.33. Report 26

Patient: 67-year-old male.
Patient Location: General Practice.
Clinical Notes on Request Form: Pituitary failure. On T4.
Tests: TFTs.

SH	0.02 mU/L	(0.50–4.00)
Free T4	8 pmol/L	(10–20)

Comment:
FT4 should be maintained within the upper reference interval in patients on thyroxine for secondary hypothyroidism. Suggest review T4 dose (and adherence to therapy) based on clinical assessment.
Explanation:
TSH measurement is not useful in managing T4 replacement in secondary hypothyroidism which should be guided by the FT4 level [14].

1.4.34. Report 27

Patient: 66-year-old female.
Patient Location: Emergency Department.
Clinical Notes on Request Form: Semi-coma.
Tests: Serum Chemistry.

Na	107 mmol/L	(137–143)
K	2.2 mmol/L	(3.2–4.3)
CL	68 mmol/L	(102–111)
HCO3	26 mmol/L	(22–31)
Urea	3.4 mmol/L	(3.0–8.0)
Creat	96 μmol/L	(70–100)
Glu	7.9 mmol/L	(3.0–5.5)
CK	888 U/L	(<150)
Chol	8.7 mmol/L	(<5.5)
Trig	1.8 mmol/L	(<1.8)

Comment:
This pattern of abnormalities [hyponatraemia, hypercholesterolaemia and a raised CK due to myopathy] may be seen in severe hypothyroidism. Suggest measure TFTs.
Explanation:
Severe (and longstanding) hypothyroidism can present with myxoedema coma, with the patient exhibiting hypothermia [14]. The combination of the other metabolic abnormalities present in this patient may be a clue to the presence of severe hypothyroidism.

1.4.35. Report 27b

Tests: TFTs.

TSH	>100 mU/L	(0.50–4.00)
Free T4	8 pmol/L	(10–20)

Comment:
The low FT4 and profoundly raised TSH are in keeping with severe hypothyroidism.
Explanation:
These results confirm the cause of the clinical presentation and metabolic abnormalities in this patient.

2. Discussion

Pathology results are estimated to inform 70% of clinical decisions [24]. This is particularly true of endocrine disorders where measurements of paired tropic and effector hormones provide objective evidence of dysfunction and provide clues to the underlying pathology. Correct interpretation of laboratory results is thus crucial for accurate and timely diagnosis and appropriate management of patients. Clinicians rely on the laboratory not only to perform and report on tests in a timely and accurate manner but also, to a varying extent, to provide an interpretative service [9]. The dependence of clinicians on the laboratory interpretative service will be influenced

by their knowledge of the test and ability in interpreting the results themselves, but also by the availability and quality of the laboratory interpretative service [4,11]. The laboratory should input where needed in the interpretation of the results they produce in order to improve patient outcomes. It has been shown in the case of interpretative commenting on thyroid function test reports, that this can in fact be achieved [7].

In addition to training Pathologists and Clinical Scientists in the art of interpretative commenting, continuing professional development should also include interpretative commenting within its scope [25]. ISO 15189 requires that quality assessment should include the entire examination process including post analytical procedures, meaning interpretative commenting too. Quality assurance programs for interpretative commenting provide opportunity for laboratory professionals to compare and share their expertise and knowledge in this area as well as maintain and develop their skills [26,27]. The examples of TFT reports and interpretative comments provided in this paper are meant to help in this regard. Some of these comments may be amenable to automation using rule-based algorithms and built into the knowledge base of the laboratory information system. Integration with the hospital or clinical information systems may provide avenues for these comments to be better informed and individualised to the patient's context. Interpretative commenting on Clinical Chemistry reports is still in its infancy; there is much scope for improvement and development of this field in conjunction with developments in electronic data management and artificial intelligence.

In conclusion, we have provided a series of thyroid function test reports with examples of interpretative comments which may be applied to these reports. We trust these examples may be useful in the training of Pathologists and clinical Scientists and may also help laboratories in developing their interpretative service for thyroid function test reports.

Declaration of competing interest

We have no conflict of interest to declare.

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The authors have none to declare.

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