Understanding thyroid function tests

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Disclosures

No financial disclosure

I will present fictitious cases and thyroid function tests (TFTs) that are based on scenarios I commonly encounter. Any similarity to patients you may have is purely accidental.

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Learning objectives

- Identify tests used in evaluating thyroid disease and understand their limitations
- Choose correct test for the clinical scenario
- Interpret TFTs within the clinical context
- Recognise discordant tests and understand when referral is advisable
- Decide whether or not treatment of a patient with an abnormal test is necessary

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Introduction

- TFTs are straightforward most of the time, *but*
- they are sometimes discordant *resulting in*
- misinterpretation *leading to*
- incorrect diagnosis *resulting in*
- inappropriate treatment *and*
- unnecessary anxiety/ further unwellness on part of the patient

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

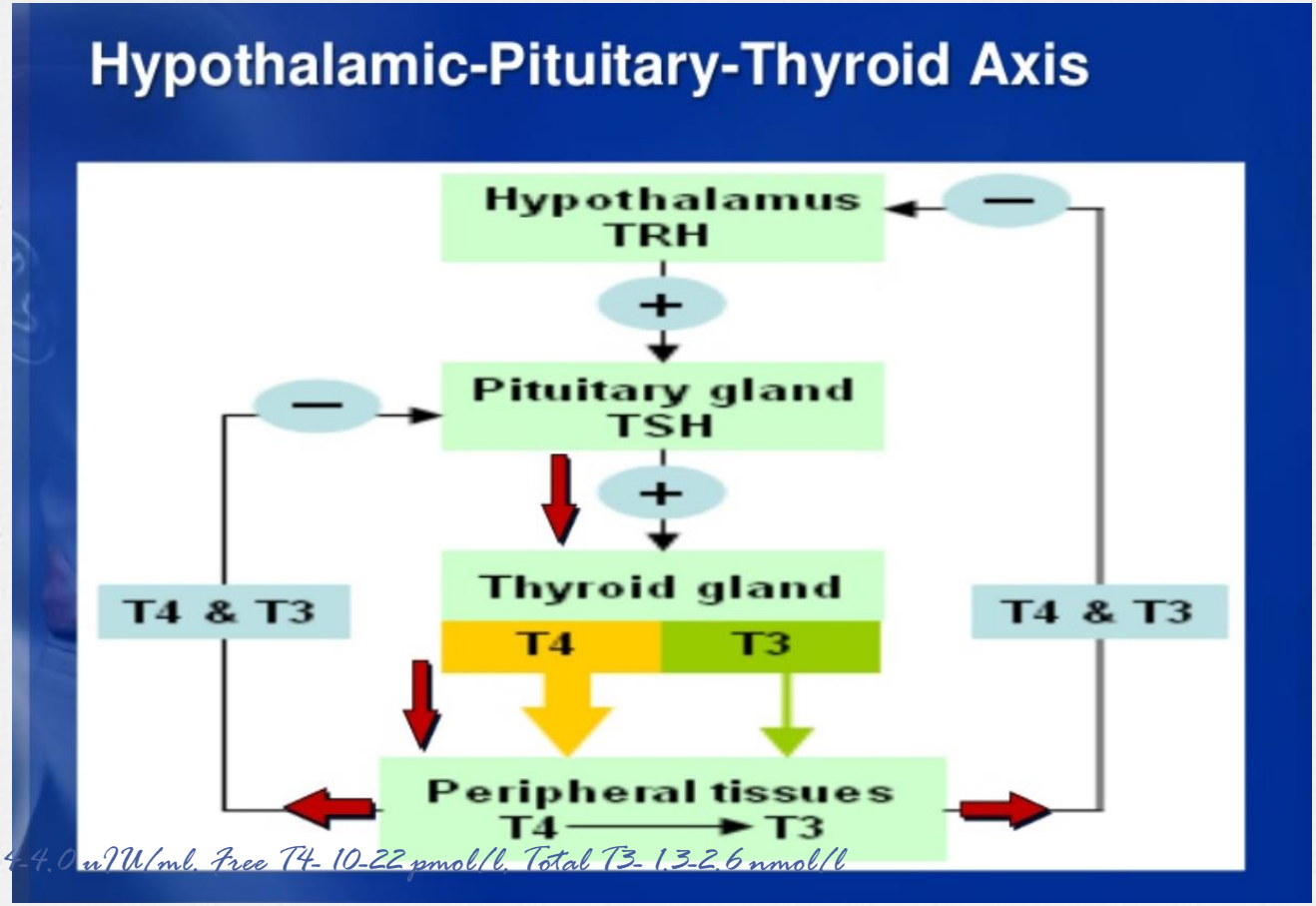
Our task as doctor

- We are faced with a patient who may or may not have symptoms but who has one or more abnormal test (TSH, T4 T3)

1. What is the significance, if any, of the abnormal test?
2. Is this patient hypo hyper or euthyroid?
3. Can the symptoms really be ascribed to the abnormal test or is there an alternative explanation?
4. If hypo or hyper thyroid is it primary or secondary?

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Hypothalamic-Pituitary-Thyroid Axis



TSH- 0.4-4.0 uIU/ml. Free T4- 10-22 pmol/l. Total T3- 1.3-2.6 nmol/l

The bundle

- TSH
- Total T4, Free T4
- Total T3, Free T3
- TPO antibodies
- TSH receptor antibodies
- TG antibodies
- Thyroglobulin
- RAI uptake test

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

TSH

- Levels change dramatically in response to changes in thyroid hormone levels
- The most sensitive screening test in detecting primary disease of the thyroid
- The recommended test of choice to determine a patient's clinical thyroid status
- One should be very careful in diagnosing hyper or hypothyroidism in a patient with normal TSH

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Generations of TSH assays

- 1st
  - Can detect down to 1 uIU/ml
- 2nd
  - can detect down to 0.1uIU/ml
- 3rd
  - can detect down to 0.01 uIU/ml
- 4th
  - Can detect down to 0.004 uIU/ml

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Uses of TSH

- Screening of a normal population
- Confirmation of normal thyroid function
- Evaluation of thyroid hormone suppression and replacement therapy
- Detection of subclinical thyroid disease
- Detection of cases of inappropriate secretion of TSH (thyroid hormone resistance, TSH secreting pituitary tumours)

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Cautions

- TSH when used as a screening test is really an indirect measure of thyroid function
- Abnormal value found should lead to T4 +/- T3 being done
- There are limitations to its use in certain situations

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Limitations to use of TSH alone

- Central hypothyroidism
- Non thyroidal illness
- Recent treatment of hyperthyroidism or longstanding hypothyroidism
- Thyroid hormone resistance
- TSH secreting adenoma
- Assay interference

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Causes of a suppressed TSH

- Thyrotoxicosis- (endogenous or exogenous)
- Subclinical hyperthyroidism
- 3-6 months after resolution of a hyperthyroid state
- Pituitary/hypothalamic hypothyroidism

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Causes of a suppressed TSH

- Severe illness
- Pregnancy related
  - 1st trimester
  - Hyperemesis gravidarum
  - Hydatidiform mole/choriocarcinoma
- Drugs
  - Corticosteroids
  - Dopamine
  - Beta blocker

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Causes of an elevated TSH

- Primary hypothyroidism
- Iodine deficiency
- Secondary hyperthyroidism
- Thyroid hormone resistance
- Adrenal insufficiency
- Non thyroidal illness

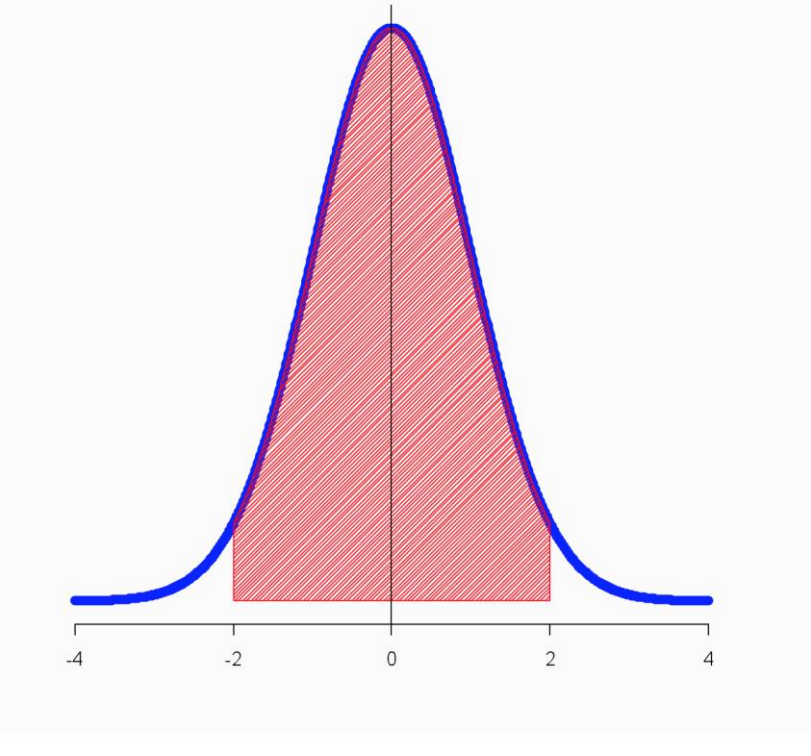
TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Free T4

- T4 set point is relatively constant
- Changes in T4 is usually associated with concordant change in TSH
- Large population reference range for T4

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Normal distribution



TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Free T4

- Changes in T4 that can lead to change in TSH and hypo or hyperthyroidism may not be reflected as abnormal based on population reference range

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Uses of T4

- To help determine the abnormality if any following after obtaining an abnormal TSH
- To monitor response to treatment of primary hyperthyroidism
- To monitor effectiveness of thyroxine treatment in central hypothyroidism

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

T3

- Not a good indicator of patient's thyroid status
- Should not be used to diagnose hypothyroidism
- Should not be used for monitoring patients on thyroxine treatment

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Uses of T3

- Suspected T3 thyrotoxicosis- suppressed TSH but normal T4
- Together with T4 to monitor response to treatment in hyperthyroidism. Particularly useful if it was a T3 toxicosis
- In diagnosing non thyroidal illness

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Patterns of TFTS

- In most cases there is concordance
- FT4 high TSH low
- FT4 low TSH high
- FT4 normal TSH normal

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

TSH	**High**	**PRIMARY HYPOTHYROIDISM (Some cases of central hypothyroidism)**	**Subclinical hypothyroidism** Poor compliance with thyroxine Malabsorption of thyroxine Drugs Non thyroidal illness Assay interference TSH resistance	TSH secreting adenoma Assay interference Thyroid hormone resistance Thyroxine therapy ?compliance Drugs (Amiodorone, heparin)
	Normal	Assay interference Central hypothyroidism Non thyroidal illness Isolated TSH deficiency Normal variation Recovery phase of thyroiditis	**NORMAL**	Assay interference Normal variation TSH secreting adenoma Thyroid hormone resistance Thyroxine therapy Drugs (Amiodorone, heparin)
	Low	Central hypothyroidism Non thyroidal illness Isolated TSH deficiency Assay interference	**Subclinical hyperthyroidism** Recent treatment for hyperthyroidism Drugs (steroids, dopamine) Non thyroidal illness Assay interference	**PRIMARY HYPERTHYROIDISM**
		Low	**Normal**	**High**
		Free T4		

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Case studies

- There will be clinical scenarios with thyroid function tests
- For each state consider what is the MOST LIKLEY clinical thyroid state of the patient
- Reference ranges are below

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment ?

- 58 year old woman who was investigated because of high cholesterol
- TSH- 34.5 mIU/ml
- Free T4- 5.4 pmol/l

- Primary hypothyroidism

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment ?

- 32 year old woman complaining of weight loss and palpitations.
- TSH- 0.02 uiu/ml
- FT4- 69.2 pmol/l
- Total T3- 6.9 nmol/l
- Primary hyperthyroidism

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment?

- 62 year old woman with fast irregular pulse
- TSH- 0.01
- Free T4- 14.6
- Total T3 - 3.5
- T3 toxicosis

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment ?

- 30 year old woman whose mother has Graves' disease

- FT4 -11.1 pmol/l
- TSH- 10.21 uIU/ml

- Subclinical primary hypothyroidism

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment?

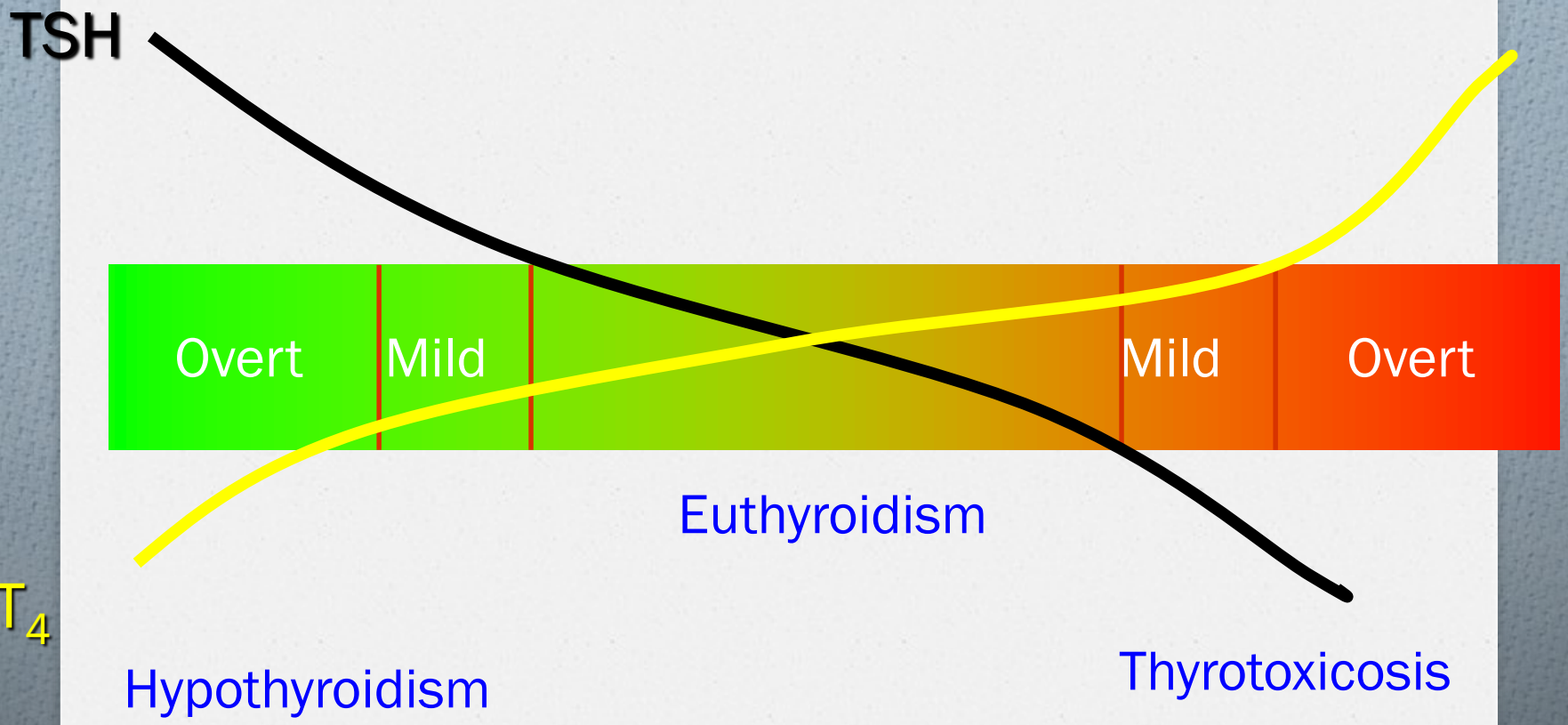
- 52 year old early post-menopausal woman complains of feeling hot and mood swings and weight loss

- TSH- 0.01ulU/ml
- Free T4- 17.2 pmol/l
- Total T3- 2.4 nmol/l

- Subclinical primary hyperthyroidism

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Mild Hypothyroidism & Mild Thyrotoxicosis
Definitions



TSH 0.4-4.0 u/IU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment?

- 31 year old woman with history of hyperthyroidism (At diagnosis, TSH 0.01muIU/ml, FT4- 54.6pmol/l). Has been on Carbimazole 20 mg po bd for 2 months.

- TSH- 0.01uIU/ml
- FT4- 16.8 pmol/l
- Total T3- 1.5 nmol/l

- Euthyroid. TSH is lagging in response. Inappropriate to use in this scenario and a waste of money

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment?

- 22 year old woman 8 weeks amenorrhoea with positive pregnancy test. C/o heart racing, mood swings, tiredness. Has been vomiting a lot.
- FT4 19.0
- TSH 0.08
- Total T3- 2.8

- Early pregnancy effect

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Pregnancy

- Increased TBG leads to increase in **total** T4 and total T3
- Beta hCG has TSH like activity
- Rise in hCG associated with fall in TSH
- Population based trimester specific reference ranges should be uses: e.g.

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Trimester specific ranges

Table 2.

Sample Trimester-Specific Reference Intervals for Serum TSH

	Trimester[a]		
Reference	***First***	***Second***	***Third***
Haddow *et al.* (13)	0.94 (0.08–2.73)	1.29 (0.39–2.70)	—
Stricker *et al.* (14)	1.04 (0.09–2.83)	1.02 (0.20–2.79)	1.14 (0.31–2.90)
Panesar *et al.* (15)	0.80 (0.03–2.30)	1.10 (0.03–3.10)	1.30 (0.13–3.50)
Soldin *et al.* (16)	0.98 (0.24–2.99)	1.09 (0.46–2.95)	1.20 (0.43–2.78)
Bocos-Terraz *et al.* (17)	0.92 (0.03–2.65)	1.12 (0.12–2.64)	1.29 (0.23–3.56)
Marwaha *et al.* (18)	2.10 (0.60–5.00)	2.40 (0.43–5.78)	2.10 (0.74–5.70)

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment?

- 22 year old woman 8 weeks amenorrhoea with positive pregnancy test. C/o heart racing, and weight loss
- FT4 37.2
- TSH 0.00
- Primary hyperthyroidism in pregnancy

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment?

- 35 year old woman with history of postpartum haemorrhage 1 year ago. Lethargic, cold intolerance, slow tendon reflexes.
- TSH- 0.70 uIU/ml
- Free T4- 8.5 pmol/L

- Central hypothyroidism

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment?

- 17 year old boy with a history of epilepsy on Phenytoin. Has been a bit tired. Also studying for exams.
- TSH- 0.70 uIU/ml
- Free T4- 8.5 pmol/L

- Euthyroid- effect of medication on drug assay

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment?

- 35 year old woman with being seen for a routine physical. Asymptomatic

- TSH- 0.62 uIU/ml
- Free T4- 9.3 pmol/L

- Likely euthyroid

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment?

- 54 year old woman. Depressed with mood swings for past 3 years.

- TSH 0.54
- Free T4 13.5
- Total T3 1.10

- Euthyroid- do not use T3 value to diagnose hypothyoidism

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

What is your assessment?

- 64 year old man complaining of anxiety and weight loss. History of anxiety. No goitre, normal pulse rate.

- TSH- 1.24 uIU/ml
- FT4- 23.1pmol/L

- Euthyroid

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Importance of clinical context

- TSH- 0.02 uIU/ml (0.32 – 5.00)
- FT4- 17.2 pmol/L (9.0 24.0)
- Total T3- 1.39 pmol/l

- Subclinical hyperthyroidism
- Recent treatment for hyperthyroidism
- Recovery from thyroiditis
- Patient on steroids or dopamine

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Importance of clinical context

- TSH- 1.02 uIU/ml
- FT4- 9.2 pmol/L

- Central hypothyroidism
- Normal variation
- Drug effect- e.g patient on phenytoin/carbamezepine
- Recovery from thyroiditis

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Importance of clinical context

- TSH- 5.62 uIU/ml
- FT4- 27.2 pmol/L

- Central hyperthyroidism- TSH secreting adenoma
- Assay interference
- Patient on Thyroxine and not very compliant
- Thyroid hormone resistance
- Drugs e.g Amiodorone

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Summary

- TSH is the best indicator of thyroid function but there are limitations to its use
- Be careful about diagnosing hyper/hypothyroidism if TSH is normal. If you do so then you are diagnosing central (pituitary) disease and further evaluation is necessary before embarking on treatment

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

Summary

- One pattern on TFTs might have different meanings in different clinical scenarios and the importance of clinical context cannot be overemphasized
- Ultimately treating a patient with a thyroid abnormality will be determined not just by an abnormal test but in conjunction with the clinical context

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l

- Happy independence
- Thank you for listening

TSH- 0.4-4.0 uIU/ml, Free T4- 10-22 pmol/l, Total T3- 1.3-2.6 nmol/l