Abnormal Thyroid Function Tests (TFTs) Results in Adults Guidance

Which patients to undertake TFTs in?

- Symptoms present
- Suspected goitre or thyroid nodule
- Atrial fibrillation
- Type 1 diabetes
- Dyslipidaemia
- Osteoporosis
- Subfertility

There is no evidence for screening healthy populations

Target case finding in individuals with symptoms

NB. Congenital hypothyroidism (incidence 1:4000) is a common preventable cause of mental retardation in babies. The UK have a national screening programme in place.

Consider whether your patient is taking any drugs affecting thyroid hormone levels:

- **Lithium** can ↑ (rare) or ↓ thyroid hormone secretion - *Check TFT every 6-12 months whilst on treatment or earlier if goitre develops*
- **Amiodarone** can ↑ or ↓ thyroid hormone secretion - *Check TFT every 6 months including 12 months after treatment cessation*
- **Oestrogens** can ↑ T3, T4 and TBG
- **Androgens** can ↓ T3, T4 and TBG
- **Glucocorticoids** can ↓ TSH, T3, T4 and TBG
- **Methadone** can ↑ T3, T4 and TBG

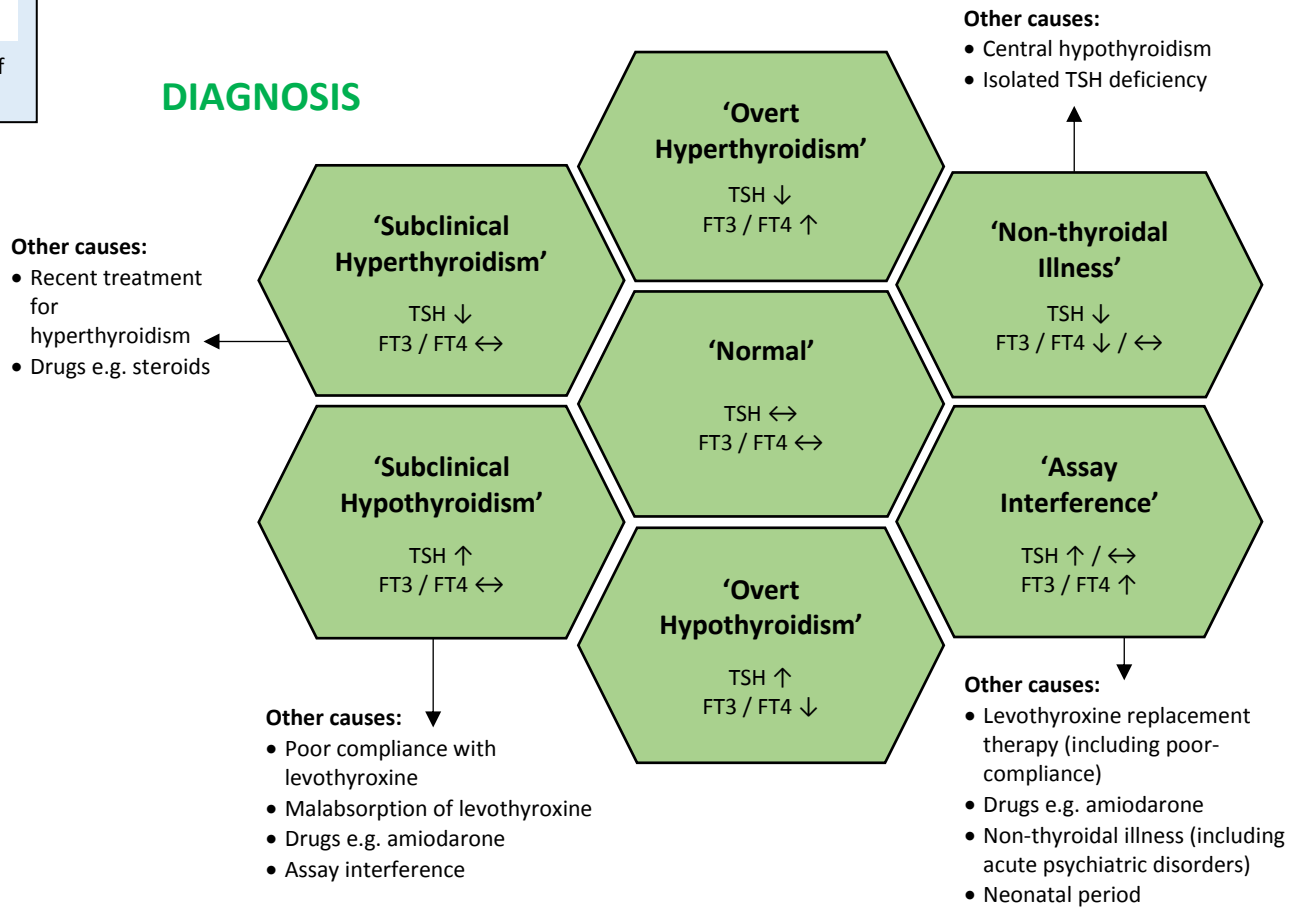
Check TFT annually in the following patients:

- Down's syndrome
- Turner syndrome
- Previous postpartum thyroiditis
- Previous neck irradiation or surgery
- Type 1 diabetes
- Addison's disease
- Radioiodine or surgery for hypothyroidism

Glossary

TSH - Thyroid stimulating hormone
FT4 - Free thyroxine
FT3 – Free tri-iodothyronine
FBC - Full blood count
LFTs - Liver function tests
HbA1c - Glycated haemoglobin
TPOAb - Thyroid peroxidase antibodies
PPT - Postpartum thyroiditis
TBG – Thyroxine-binding globulin

DIAGNOSIS



References

British Thyroid Association - UK guidelines for the use of thyroid function tests (2006)
NICE Clinical Knowledge Summaries (CKS) – Hypothyroidism (June 2018) and Hyperthyroidism (June 2016)
Clinical Endocrinology. What should be done when thyroid function tests do not make sense? Mark Gurnell, David J. Halsall, V. Krishna Chatterjee. 21st Feb 2011
THYROID. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. E K Alexander et al. Volume 27, Number 3, 2017

Clinical Contact for this pathway for queries: camden.pathways@nhs.net

Pathway created by: Alex Warner & Sarah Morgan, March 2013
Reviewed: June 2015, February 2019 (with thanks to Dr Bernard Khoo, RFH)
Review due: Feb 2022

Please refer to the Summary of Product Characteristics (SPC) of any drug considered. This pathway has been developed from published guidance in collaboration with local endocrinologists. This guidance is to assist GPs in decision making and is not intended to replace clinical judgement.

Causes of hypothyroidism include:

Primary causes
- Iodine deficiency (most common)
- Autoimmune thyroiditis e.g. Hashimoto's
- Drugs
- Post-ablative therapy or surgery
- Transient thyroiditis e.g. subacute or postpartum

Secondary causes
- Pituitary dysfunction due to e.g. tumours, surgery
- Hypothalamic dysfunction due to e.g. tumours, surgery

Hypothyroidism

(TSH ↑, FT4 ↓ or ↔, TPO antibody -/+)

History - Consider in anyone with the following non-specific signs & symptoms:

- Dry skin
- Constipation
- Menstrual irregularities
- Weight gain
- Cold intolerance
- Non-specific weakness
- Fatigue/lethargy
- Bradycardia
- Depression
- Hoarseness
- Oedema
- Memory loss

Arrange emergency admission for patients presenting with suspected **myxoedema coma**. (Presents with typical features of hypothyroidism with hypothermia, coma and occasional seizures)

Refer 2ww if red flag symptoms/signs
Patients presenting with a goitre, nodule or structural change in the thyroid gland and suspected malignancy.

Investigations to confirm diagnosis
Undertake TFT levels: TSH, FT4, TPOAb (if required)

If primary hypothyroidism is suspected:
- Check FBC – check for associated anaemia
- HbA1c – check for associated type 1 diabetes
- Serum lipids – if elevated, this may improve with treatment of hypothyroidism

Subclinical Hypothyroidism with TSH 4-10mU/L (FT4 within reference range)

Repeat TSH and FT4 (ideally at the same time of day) 3–6 months after initial result to exclude non-thyroidal illness/drug effects and to confirm the diagnosis

No symptoms

Observe and repeat TFTs in 6 months

If TSH remains elevated, arrange repeat TFTs every 6 months for the first 2 years and then annually

Check serum TPOAb

TPOAb positive or goitre present

Arrange annual TFTs

TPOAb negative

Monitor TFT every 3 years

Symptoms present

If TSH normalised - Check serum TPOAb

If asymptomatic, TPOAb negative and no goitre - **no further testing needed**

Subclinical Hypothyroidism with TSH >10mU/L (FT4 within reference range)

Start treatment with levothyroxine (even if asymptomatic) if aged ≤ 70 years

If <65 years - consider trial of levothyroxine on individual patient basis (see dosage instructions in 'treat with levothyroxine' box). Assess response to treatment 3-4 months after TSH stabilises within reference range.

If >80 years - follow a 'watch and wait' strategy. If a decision is made to treat, prescribe levothyroxine and recheck TSH after 2 months and adjust the dose accordingly.

If after 3-6 months, **symptoms have improved**, consider lifelong treatment

Once TSH has normalised, measure TFTs at least annually

If after 3-6 months, **symptoms have not improved/ adverse effects reported,** stop levothyroxine. **Refer to specialist.**[Δ]

Overt Hypothyroidism
TSH >10mU/L (FT4 < reference range)

Treat with levothyroxine

- **Most patients -** Start at 50-100micrograms once daily, then increase every 3-4 weeks in 25-50 microgram increments according to clinical and biochemical (TFTs) response. Usual maintenance dose is 100-200 micrograms once daily.
- **If older (>50 years) AND cardiac disease or severe hypothyroidism present** - Consider starting at 25micrograms once daily, then adjust dose every 4 weeks in 25microgram increments according to clinical and biochemical (TFTs) response (to avoid any sudden increase in metabolic demands). Maintenance dose 50-200 micrograms once daily.
- **If >80 years** - follow a 'watch and wait' strategy. If a decision is made to treat, prescribe levothyroxine and recheck TSH after 2 months and adjust the dose accordingly.

(Expert opinion suggests that age dependent titration may not be required or the 'watch and wait' strategy in

Once TSH is stable and adequate dose determined, monitor TSH every 4-6 months, and then annually (or earlier if symptoms develop)

If serum lipids were elevated at initial assessment, recheck to see if levels have adequately improved or if there is a need for dyslipidaemia treatment

Refer the following patients for specialist input:

- Secondary hypothyroidism – Suggested by low, normal or slightly raised TSH and low T4.

NB. Secondary hypothyroidism can be differentiated from non-thyroid causes by history, TSH, FT4, FT3 and other tests of other anterior pituitary hormones

- [Δ]Unresponsive to therapy
  - TSH not in normal range despite >200micrograms of levothyroxine *and* compliant with treatment **OR**
  - Symptoms continue despite apparently adequate thyroid replacement (TSH within reference range)
- Planning a pregnancy, pregnant or postpartum
- Undergoing fertility investigation / treatment
- Other pituitary disease
- Pre-existing cardiac disease
- Drug treatment e.g. lithium etc.
- Suspected subacute thyroiditis
- Adverse reaction to levothyroxine therapy
- Are suspected of having associated endocrine disease
- Nodule, goitre or structural change in thyroid gland – if malignancy suspected, refer as **2ww**

Liothyronine prescribing is restricted to certain indications within North Central London (NCL). Please see the local liothyronine position statement for further details.

Causes of hyperthyroidism

Primary causes include:

- Graves disease (NB. TPOAb test not required for diagnosis)
- Toxic multinodular goitre
- Toxic thyroid nodule (adenoma)
- Drugs e.g. iodine (i.e. in drugs such as amiodarone), lithium

Secondary causes include:

- Pituitary adenoma (rare)
- Thyroid hormone resistance syndrome (rare)
- High levels of human chorionic gonadotrophin

Non-thyroidal causes

TFT results: Usually ↓ TSH and FT3, although usually FT3 alone is low

If the person is clinically euthyroid, they do not require treatment. Abnormalities in TFTs typically resolve with resolution of the underlying illness.

Hyperthyroidism

(TSH ↓, FT4 and/or FT3 ↑ or ↔)

History - Consider in anyone with the following non-specific signs & symptoms:

- Warm moist skin
- Fatigue
- Palpitations
- Diarrhoea
- Muscle weakness
- Insomnia
- Irritability
- Anxiety
- Breathlessness, dysphagia, neck pressure
- Heat intolerance
- Polyuria, thirst, generalised itch
- Infertility, oligomenorrhoea, amenorrhoea
- Increased appetite with weight loss (or occasional weight gain)

Arrange emergency admission for patients presenting with **thyroid storm.** Clinical features include tachycardia, fever, atrial fibrillation, heart failure, fever, diarrhoea etc.

Refer 2ww if red flag symptoms/signs

Patients presenting with a thyroid nodule or goitre and suspected malignancy. NB. TFTs are usually normal in people with thyroid cancer.

Investigations to confirm diagnosis

Check TSH level

If TSH within reference range – further investigations usually not needed, as hyperthyroidism is very unlikely

Subclinical hyperthyroidism

TSH 0.1 – 0.4mU/L (FT4 and FT3 within reference range)

Recheck TSH, together with FT4 and FT3 after 1-2 months to exclude non-thyroidal illness and drug effects

NOT on levothyroxine

If other causes have been excluded, repeat TFTs in 3-6 months (or earlier if patient is elderly, has underlying cardiovascular disease, or if non-thyroidal illness may have caused initial TFT abnormalities), to determine if subclinical hyperthyroidism persists.

Long term - continue to check TFTS every 6-12 months, depending on clinical judgement to exclude progression to overt hyperthyroidism (or sooner if patient develops symptoms)

Refer to specialist if patient has:

- Persistent subclinical hyperthyroidism
- Presents with symptoms (palpitations/weight loss)
- Presence of cardiac disease or osteoporosis

ON levothyroxine

Indicative of 'over-treatment'
- Reduce levothyroxine dose to normalise TSH

TSH < 0.1mU/L

Check FT4 and FT3 to exclude overt hyperthyroidism

If FT4 and/or FT3 above reference range, diagnose **overt hyperthyroidism**

Overt hyperthyroidism

TSH < 0.05mU/L (FT4 and/or FT3 > reference range)

Refer to an endocrinologist for further investigations and management

Whilst awaiting review, consider initiating a beta-blocker to treat adrenergic symptoms (e.g. tremor, tachycardia), where clinically appropriate and if no contraindications:

- Propranolol 10-40mg 3 x day
- Metoprolol 50mg 4 x day

Titrate the dose according to clinical response. Taper and stop treatment once asymptomatic and euthyroid.

+ On advice and guidance of an endocrinologist, consider initiating an anti-thyroid drug i.e. carbimazole in the following patients:

- Distressing symptoms present despite treatment with a beta-blocker or if beta-blocker is not tolerated / contraindicated
- At risk of complication from hyperthyroidism
- Taking certain medication e.g. lithium, amiodarone

Ensure FBC and LFTS are checked prior to starting anti-thyroid treatment. Patient should be counselled on adverse effects of carbimazole to look out for including rash, agranulocytosis symptoms.

If taking carbimazole, monitor TSH & FT4 every 2-6 weeks (depending on clinical need) until stable. Once on maintenance dose, monitor every 3 months.

Other secondary care treatment options:

- Alternative anti-thyroid drugs/regimes
- Radioiodine
- Surgery

Thyroid dysfunction in pregnancy

Monitoring - Ideally measure TFTs:

- At pregnancy confirmation
- At antenatal booking
- At least once in 2nd and 3rd trimesters
- 2-4 weeks post-partum

Refer 2ww if red flag symptoms/signs
Patients presenting with a thyroid nodule or goitre and suspected malignancy.

If overt or subclinical hypothyroidism present

Urgently refer to antenatal and endocrinology clinics

Check TSH and FT4 immediately and discuss with specialist whilst patient is awaiting assessment

On specialist advice:
Whilst awaiting review, discuss initiation of levothyroxine or if already taking levothyroxine, discuss changes to current dosage and monitoring requirements.
NB. An increase in the levothyroxine dose may be required (by 30-50%) from as early as 4-6 weeks gestation to maintain normal serum TSH levels.

Postpartum

- If patient was taking levothyroxine during pregnancy, **discuss with specialist** if any changes to the dose are required and the frequency of TFT monitoring.
- If patient was taking levothyroxine prior to pregnancy, the dose will need to be decreased back to pre-pregnancy dose **as advised by a specialist.** Check TFTs at 6 weeks postpartum.

If overt or subclinical hyperthyroidism present

Arrange emergency admission if the woman has severe signs and symptoms of hyperthyroidism (e.g. thyroid storm) or intractable vomiting suggesting hyperemesis gravidarum.

Urgently refer ALL patients (including women who are euthyroid) to antenatal and endocrinology clinics

Seek advice from an endocrinologist if the patient has adrenergic symptoms (e.g. tremor or tachycardia) which requires symptomatic treatment while awaiting specialist assessment.

Check TSH, FT4 and FT3 immediately and send results to specialist

Specialist treatment
If the patient is already taking anti-thyroid treatment, ongoing blood monitoring should be arranged and managed in secondary care.

Propylthiouracil is usually used in pregnant women due to the increased possible risk of congenital abnormalities with carbimazole therapy (see MHRA alert). The lowest possible dose should be used to maintain euthyroidism.

NB. The potential risks vs benefits of individual anti-thyroid treatments should be considered before prescribing in pregnancy.

Postpartum

- There is a significant chance of relapse.
- Check TFTs after delivery. Check TSH and FT4 6-8 weeks postpartum, particularly in patients with the following: goitre, non-specific symptoms suggestive of thyroiditis, history of PPT or autoimmune thyroid disease or TPOAb positive

Refer to endocrinologist if TFT results are abnormal (urgency depending on clinical judgement)

Postpartum thyroiditis (PPT) present

PPT usually resolves spontaneously within 1 year postpartum.

Thyrotoxic pattern
If initial TFTs show thyrotoxic pattern - **Refer to a specialist** for further tests to differentiate from Grave's disease. After resolution of thyrotoxic phase, monitor TFTs after 4-8 weeks (or if new symptoms develop) to screen for hypothyroid phase.

Hypothyroid pattern
If TFTs indicate a hypothyroid pattern, **seek advice from specialist** on whether to start levothyroxine treatment.

History of PPT (which has resolved)

- Offer annual TFT monitoring
- Screen woman prior to future pregnancy
- 6-8 weeks after pregnancy

(Due to high risk of permanent hypothyroidism and recurrence in subsequent pregnancies)

Women with type 1 diabetes
3 x more at risk of PPT. Therefore, TSH, FT4 and TPOAb status should be checked:

- Prior to pregnancy
- At diagnosis of pregnancy
- 3 and 6 months postpartum

Thyroid dysfunction in pregnancy

- ↑ oestrogen production and TBG concentrations lead to ↑ FT4 and FT3.
- Fall in TSH is normal in the 1st trimester.

Trimester-related reference ranges should be applied for TSH and for total and free thyroid hormones (FT4 and FT3).

Alterations in immune function occur, which can influence course of existing autoimmune thyroid disease.

After delivery, levels of thyroid hormones and TSH normally return to the pre-pregnant state.

Undetected subclinical hypothyroidism:
During pregnancy, this may adversely affect neuropsychological development & survival of foetus. Associated ovulatory dysfunction & infertility.

If maternal hyperthyroidism is inadequately controlled: This may increase risk of miscarriage, pre-eclampsia, intrauterine growth restriction, pre-term delivery, low birth weight, fetal death.