Trust Guideline for the Management of Suspected Thyroid Emergencies

A Clinical Guideline

For Use in:	Endocrinology out patients, clinical investigation unit, acute medical unit, accident and emergency and all other clinical areas of the trust
By:	Medical staff
For:	Suspected thyroid emergencies in non- pregnant adults
Division responsible for document:	Medical Division (Including Emergency)
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If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?	N/A

This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

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Contents

1. Quick reference guidelines

Thyroid conditions are extremely common, with autoimmune thyroid disorders alone affecting 5% of adults in the UK. Complications of thyroid dysfunction and its treatment are therefore also surprisingly common, and it is essential that potential thyroid emergencies are recognised early and managed appropriately.

This guideline aims to bring together the emergency management of most of the common thyroid emergencies for use by specialists and non-specialists alike.
This guideline includes emergency management of:

- Hypothyroidism and myxoedema coma
- Hyperthyroidism (thyrotoxicosis) and thyroid storm
- Complications of anti-thyroid drug therapies
- Preparation for emergency thyroid surgery
- Preparation for emergency radioactive iodine therapy

2. Hypothyroid Crisis / Myxoedema Coma

Hypothyroidism is usually an autoimmune condition of insidious onset. Treatment is generally started with Levothyroxine 50mcg for 2 weeks, then increased to 100mcg with a repeat TSH performed after 6 weeks of treatment to guide future dose adjustment. Once treatment with Levothyroxine is established, annual monitoring of TSH alone is sufficient and this is usually performed in primary care.

However, hypothyroid crisis or myxoedema coma is a medical emergency and requires immediate specialist input. Hypothyroid crisis usually occurs in patients with long-standing hypothyroidism, in whom treatment has been interrupted or in whom the diagnosis has not yet been made. The crisis typically occurs in elderly female patients with climate-induced hypothermia and can also be precipitated by use of sedatives, phenothiazine treatment or other intercurrent illness such as stroke or pneumonia.

2.1 Diagnosis of hypothyroid coma

- Free thyroxine will be low or undetectable, TSH will usually be extremely high
- Patients will usually look classically hypothyroid with non pitting oedema, facial coarsening, loss of hair, cool dry skin etc
- Mental status will be affected though symptoms may vary between lethargy, stupor, delirium or coma
- Hypothermia is usual
- Bradycardia is usual, with hypotension and low output cardiac failure possible
- Electrocardiogram will confirm bradycardia, and may also exhibit small complexes, evidence of acute ischaemia, or “J” waves in hypothermia
- Type 2 respiratory failure with hypoventilation and respiratory acidosis may be present
- Slow relaxing reflexes will be present, though they may also be present in other causes of hypothermia
- Hyponatraemia, hypoglycaemia, and macrocytosis are common. These may indicate other coexistent autoimmune conditions such as Addison’s disease or pernicious anaemia.
- CK may be elevated indicating either hypothyroid myopathy or rhabdomyolysis.

2.2 Management

- IV access
- Take blood for TSH, free thyroxine (fT4), free liothyronine (fT3), U+E, FBC, cortisol, glucose, CK, arterial blood gases
- Perform a septic screen: chest radiograph, blood and urine cultures, and ECG
- Inform HDU and contact endocrinology team (weekdays 9-5pm: endocrinology registrar on bleep ****. Weekends, out-of-hours: endocrinology consultant/registrar on-call **********).
- Consider central venous monitoring to help guide fluid status
- Give hydrocortisone 100 mg intramuscularly when the diagnosis is first suspected, then intramuscularly every 6 hours

- Liothyronine (T3) 5-10mcg orally or via a nasogastric tube, if necessary. Liothyronine is only available in 20mcg tablets. These are scored and can be easily halved, but very low quantities will require preparation by pharmacy by crushing and weighing 20mcg tablets.
- DO NOT GIVE T3 INTRAVENOUSLY. IV T3 is associated with an increased risk of arrhythmia, tachycardia and other cardiac complications compared with enteral T3. It should therefore only be used in patients in whom oral or nasogastric treatment is not possible.
- Slow re-warming using a space blanket in a warm room – preferably with a continuous cardiac monitor
- Monitor capillary blood glucose 4 hourly and treat hypoglycaemia
- Assuming no ill effects (e.g. cardiac arrhythmias) within 6 hours of the first dose, continue liothyronine 10mcg PO/NG 12 hourly. The endocrinology team will advise on when to increase the liothyronine dose (typically to 20mcg bd by day 3) and when to introduce Levothyroxine (usually 25mcg on around day 3-5).
- Consider broad spectrum antibiotics and treat any underlying cause

3. Thyrotoxicosis

The commonest cause of thyrotoxicosis is nodular thyroid disease, with the second commonest in the UK being autoimmune thyroid stimulation (Graves' or Hashimoto's disease).Other causes may include acute thyrotoxicosis following a large iodine load (e.g. following contrast CT scan or radioactive iodine therapy), or rarely hyperemesis in pregnancy, choriocarcinoma, or TSH-secreting pituitary tumours.

3.1 Management of thyrotoxicosis:

1. Thyrotoxicosis suspected:
   Check thyroid function: TSH, fT4, fT3
2. Thyrotoxicosis confirmed:
   Refer all cases to endocrinology – in patients should be referred via the endocrinology STR on DECT 2763during working hours, out patients via a faxed referral to **********Emergency out of hours cases can be discussed with the endocrinology consultant on call **********, however, unless thyroid storm is diagnosed, these can usually be referred as above the next working day.
3. Check FBC, U+E, LFTs, calcium prior to starting treatment
   Start carbimazole 20mg bd orally
   Consider beta blocker: e.g. propranolol 40mg-80mg tds for rapid relief of symptoms in severe thyrotoxicosis
   Give patient carbimazole / propylthiouracil information sheet (appendix 1) and warn them of potential side effects of rash, neutropaenia and abnormal liver function

3.2 Thyroid Storm

Severe thyrotoxicosis can occasionally present with an acute exacerbation as a true thyrotoxic emergency or "thyroid storm". This is usually triggered by infection, on a background of severe long standing thyrotoxicosis. Other recognised causes include recent manipulation of the thyroid during surgery, an iodine load from CT contrast media or radioactive iodine treatment, or other severe intercurrent illnesses or recent surgery. It is useful to document the severity and duration of thyrotoxic symptoms e.g. weight loss, palpitations, tremor, diarrhoea, and heat intolerance, as well as to seek evidence of

possible triggers of thyroid storm to help confirm the diagnosis and to help guide future treatment.

True thyroid storm is a medical emergency and carries a mortality of 20-30% – call the on-call endocrinologist as soon as this diagnosis is suspected. The cardinal features of thyroid storm are fever above 38°C, tachycardia above 110 (+/- atrial fibrillation), heart failure and agitation.If none of these features are present, the patient does not have thyroid storm. However, if some of these features are present, a scoring system is useful to help differentiate between severe thyrotoxicosis and true thyroid storm.

3.3 Diagnosing thyroid storm

The diagnostic criteria for thyroid storm in a patient with confirmed biochemical thyrotoxicosis, are listed below (adapted from Burch & Wartofsky). Scores above 45 confirm thyroid storm. Scores between 25-45 suggest impending thyroid storm and so should be treated as for thyroid storm. Scores below 25 exclude thyroid storm and should be managed as for thyrotoxicosis.

Diagnostic parameters for thyroid storm	**Scoring points - >45 = storm**
Thermoregulatory dysfunction: temperature °C	
37.2-37.7	5
37.8-38.2	10
38.3-38.8	15
38.9-39.2	20
39.3-39.9	25
≥ 40.0	30
Central nervous system effects	
Mild agitation	10
Moderate e.g. delirium, psychosis, extreme lethargy	20
Severe e.g. seizures/coma	30
Gastrointestinal-hepatic dysfunction	
Moderate (diarrhoea, nausea/vomiting, abdominal pain)	10
Severe (unexplained jaundice)	20
Cardiovascular dysfunction	
Tachycardia (beats/minute)	
90–109	5
110–119	10
120–129	15
130–139	20
>/= 140	25
Congestive heart failure	
Mild (pedal oedema)	5
Moderate (bibasal crackles on examination)	10
Severe - clinical pulmonary oedema	15
Atrial fibrillation absent	0
Atrial fibrillation present	10
Precipitating event identified	
Precipitating event absent	0
Precipitating event present	10

3.4 Management of thyroid storm

- IV access
- Take blood for TSH, T4, T3, U+E, FBC, liver function, calcium, glucose
- Perform a septic screen: chest radiograph, blood and urine cultures, and ECG
- Inform HDU and contact endocrinology team (weekdays 9-5pm: endocrinology STRonDECT 2763. Weekends, out-of-hours: endocrinology StR on DECT 2763 or on call consultant **********).
- Consider central venous monitoring to help guide fluid status.
- Propranolol 80mg tds PO to reduce heart rate and block effects of thyroid hormones. Alternatively, propranolol 2mg iv over 10 minutes can be used in a very unstable patient or one who cannot take oral medication. NB: beta blockade is NOT contraindicated in acute, severe thyrotoxic heart failure and is often the definitive treatment. Calcium channel blockers may be considered if beta blockade is contra-indicated e.g. in patients with asthma.
- Propylthiouracil 200mg tds PO / NG / PR to stop release and production of thyroid hormones. This is more suitable than carbimazole in emergency situations as it also prevents peripheral T4 - T3 interconversion.
- IV Hydrocortisone 200mg, followed by prednisolone 20mg tds PO. This prevents peripheral conversion of T4 to T3 and is particularly effective in Graves' disease.
- Chlorpromazine 50-100mg im may be given if emergency sedation is required.
- Cholestyramine 3g po tds may also be given to aid clearance of thyroid hormones by blocking their enterohepatic circulation.
- 60 minutes following the first dose of propyl-thiouracil give Lugol's iodine 5 drops qds PO in milk or orange juice. This is kept in stock in pharmacy and on Coltishall ward. Iodine must only ever be given once organification has been blocked by propylthiouracil, otherwise it may exacerbate thyrotoxicosis. After propylthiouracil treatment, iodide will prevent further release of pre-formed thyroid hormones.
- Monitor blood glucose levels 4 hourly.
- Supportive care e.g. cooling and iv fluids.
- Aggressively seek and treat precipitants eg infection or dehydration.

3.5 Complications of Anti-Thyroid Drug Therapies

3.5.1 Neutropaenia secondary to anti-thyroid drug use

Mild neutropaenia <1.5x10^9 is commonly observed in people with Graves' disease, certain racial groups and with anti-thyroid drug use. A baseline neutrophil count prior to starting therapy is therefore useful. Otherwise, routine full blood count (FBC) or neutrophil monitoring is not recommended for patients with thyrotoxicosis, as the development of agranulocytosis (neutrophil count <0.5 x10^9) is rare and idiosyncratic. Most cases occur within 90 days of starting treatment, and this is most dangerous in elderly patients.

- All patients starting treatment should be given verbal and written warnings regarding possible side effects of treatment – appendix 1.
- All patients should be warned to stop therapy and have a blood test if they develop a fever, sore throat or mouth ulcers.

3.5.2 Neutrophil count 1-1.5

- Continue therapy, but institute close monitoring of blood count.

3.5.3 Neutrophil count <1.0

- Stop anti-thyroid drug and monitor FBC daily.

3.5.4 Neutrophil count <1.0 with suspected sepsis / an unwell patient

- Stop anti-thyroid drug.
- Admit and follow sepsis care bundle.
- Monitor FBC every 12 hours initially and discuss results with haematology. Bone marrow biopsy may be useful to determine response.
- Discuss with haematology and microbiology regarding most appropriate antibiotic to continue. Pseudomonas is a common infective organism in this group.
- Haematology will consider treatment with granulocyte-colony stimulating factor (G-CSF) depending on results of monitoring $^{+}/_{-}$ bone marrow biopsy. G-CSF may hasten recovery in patients not responding to withdrawal of the offending drug, though this treatment does not necessarily alter outcome.
- Do not rechallenge patient with the same or alternative anti-thyroid drug as there is significant cross reactivity and this is a life threatening complication.
- Recommend radioactive iodine or surgery as definitive treatments for the thyrotoxicosis with adequate medical preparation as below.

4. Other complications of anti-thyroid drug therapy:

4.1 Rash

Itch is a common feature of untreated thyrotoxicosis. Typical drug rashes are also common with anti-thyroid drugs and usually respond to topical treatments, antihistamines or switching to an alternative anti-thyroid drug.

4.2 Arthralgia and vasculitis

Arthralgia and vasculitis are very rare with carbimazole but are seen more frequently with propylthiouracil treatment. Stop the anti-thryoid drug. Perform an autoantibody screen, particularly a full ANCA screen, for drug-induced lupus and discuss with rheumatology and/ or renal medicine.

4.3 Hepatitis

Mild abnormalities of liver function are common with thyrotoxicosis, so a baseline assessment prior to treatment is useful. Mild hepatitis with an increase in transaminases to 1.6x upper limit of normal also commonly occurs after around 3 months treatment with propylthiouracil. This is usually transient and requires no treatment so routine monitoring is not recommended unless the baseline function was abnormal.

However, allergic hepatitis causing submassive hepatic necrosis occurs in ~0.1-0.2% of patients treated with propylthiouracil. Stop propylthiouracil and involve hepatology immediately if this condition is suspected.
Carbimazole is not associated with allergic hepatitis. However, carbimazole treatment may be associated with the development of a cholestatic pattern of abnormal liver function.

Withdraw the drug and inform hepatology if this condition is suspected, though complete recovery is usual after the drug is withdrawn.

4.4 Emergency Preparation for Thyroid Surgery

Patients undergoing thyroid surgery for nodular disease or suspected thyroid cancer require no special preparation.
Patients undergoing elective surgery (or radioactive iodine therapy) for Graves' disease are also usually well prepared with medical pre-treatment and so do not require any special preparation. However, patients requiring emergency surgery for example due to complications of medical treatment of thyrotoxicosis usually require optimisation prior to surgery.

- Normal fT4 and fT3 levels – no special precautions are required. Assuming these parameters are within or close to normal limits, the TSH result will not affect management in this situation.
- All abnormal elevated free T4 or fT3 levels should be discussed with the referring endocrinology consultant or bleep the endocrinology registrar on 1200. Severe thyrotoxicosis eg fT4 >28pmol/l or fT3 >10pmol/l will require full treatment as below, though lesser degrees of elevation should be considered on an individual case basis.
- Optimise dose of carbimazole or propylthioracil in patients able to continue anti-thyroid therapy. Doses of up to 80 mg per day carbimazole can be used under specialist supervision and within short periods of time can produce very useful reductions in fT4 levels pre-operatively.
- Propranolol 40-80mg tds po for at least 48 hours pre op, or diltiazem 60mg tds if beta blockade is contraindicated.
- Prednisolone 20mg bd po for up to 1 week pre op to reduce T4-T3 interconversion. This is particularly effective in Graves' disease.
- Lugol's iodine 5 drops qds given in milk or orange juice for one week prior to surgery to block hormone release. (Lugol's iodine is also known as Aqueous Iodine Oral Solution, 5 drops providing approximately 32.5mg iodine.)
- Consider cholestyramine 3g tds po to reduce circulating thyroid hormone levels by reducing their enterohepatic circulation.
- Consider lithium 250mg tds po as a direct antithyroid treatment, though this typically takes 1-2 weeks to be effective and will require serum monitoring of lithium levels.

4.5 Post-operative treatment – see also guideline CA4072v2

All patients undergoing total thyroidectomy for benign disease should be started on Levothyroxine 100mcg po daily from day 1 post op.

All patients undergoing total thyroidectomy for suspected thyroid cancer should be started on Levothyroxine 125 mcg from day 1 post op. If the cancer diagnosis is confirmed they may require radioactive iodine ablation and so should continue on Levothyroxine until they are seen by oncology. Subject to grading of the thyroid, long term suppressive Levothyroxine therapy maybe recommended
All patients will require a blood test for TSH 6 weeks post-operatively to guide future replacement therapy.
See post-operative hypocalcaemia prevention and management guideline CA4072v2 for guidance on peri-operative calcium management.

4.6 Emergency Treatment with Radioactive Iodine Therapy

Patients undergoing elective radioactive iodine therapy for thyrotoxicosis are also usually well prepared with medical pre-treatment. They require no further preparation, and tolerate the planned withdrawal of anti-thyroid medication for 1 week prior to radioactive iodine well. However, patients requiring emergency radioactive iodine, for example due to complications of medical treatment of thyrotoxicosis, may require optimisation prior to treatment which will be discussed with the endocrinology consultant in all cases.

- Consider propranolol 40-80mg tds po or diltiazem 60mg tds if beta blockade is contra-indicated.
- Consider cholestyramine 3g tds po to reduce circulating thyroid hormone levels by reducing their enterohepatic circulation.
- Consider lithium 250mg tds as direct antithyroid treatment. Thyroid hormone levels are expected to fall by 40% within 1-2 weeks.
- Prednisolone 20mg bd po to reduce T4-T3 inter-conversion in Graves' disease.
- Lugol's iodine or Potassium iodide must never be given prior to radioactive iodine therapy. Radioactive iodine will not be effective within 3 months of iodine containing contrast medium given for CT scans.

5. Objective/s

The aim of this guideline is to ensure that all patients with thyroid emergencies are discussed appropriately and early with the endocrinology team, and to ensure that their emergency management by non specialists is in keeping with international best practise in endocrinology.

6. Rationale

Most non specialists will rarely encounter thyroid emergencies. For that reason, clear guidance should be available to ensure that medical and nursing staff understand the importance of these conditions, and to ensure that their emergency management is appropriate.

7. Broad recommendations

If in doubt, please call the endocrinology SPR **********during working hours or the consultant on call **********at any time for advice on suspected thyroid emergencies.

8. Clinical audit standards

Patients with confirmed or suspected thyroid emergencies should always be discussed with the endocrinology team.

In patients should be reviewed by the endocrinology team within 24 hours, and out patient referrals seen within 27 days.

9. Summary of development and consultation process undertaken before registration and dissemination

The authors listed above drafted this guideline on behalf of the Directorate of Endocrinology, which has agreed the final content at a clinical governance meeting. During its development it has been circulated for comment to all consultants and specialist endocrine nurses in the endocrinology directorate, plus all consultants in accident and emergency, the acute medical unit, intensive care, Dr Matthew Gray medical physicist and the thyroid surgeons Mr Pain, Mr Tassone, Mr Burrows and Mr Nassif for comments.

This version has been endorsed by the Clinical Guidelines Assessment Panel.

10. Distribution list/ dissemination method

By email to interested parties listed above and via trust intranet.

11. References/ source documents

In house guidelines on the management of thyroid emergencies have been developed in various endocrine centres in the UK. These were loosely based on those written by Professor Will Drake at St Barts hospital in London, and by Dr Amit Allahabadia at the Sheffield Teaching Hospitals. Other source documents and guidance are listed below.

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Appendix 1 – Carbimazole and propylthiouracil information sheet for patients

You have been started on tablets to control your overactive thyroid gland. These tablets are very safe, but do occasionally cause the side effects of a rash, changes in liver blood tests or a fall in the white blood cell count. Please take the following action if you experience these symptoms while on either carbimazole or propylthiouracil (PTU) therapy:

Rash

If you develop a rash, please stop your medication and see your GP, bringing this letter with you. Your GP may prescribe you with an anti histamine drug to control the itching or rash if necessary. They may also switch you to an alternative drug to do the same job.

Sore throat, fever, jaundice (yellow tinge to the eyes) or mouth ulcers

If you develop any of these symptoms, please stop your medication immediately and bring this letter with you to see your GP or go to an emergency department. You will need to have a blood test performed. Do not start taking your medication again until you have been told that your blood test is ok.

Carbimazole and propylthiouracil information for health care professionals
Rash

This patient is taking carbimazole/propylthiouracil (PTU) for their thyroid condition. If they have developed a rash, please consider switching to an alternative agent. If they are taking carbimazole, please prescribe PTU in its place. The dose of PTU is 10 times the dose of carbimazole (for example 20mg carbimazole = 200mg PTU). PTU doses should be divided and given two or three times a day (for example 100mg bd). Antihistamines may be given for associated pruritus if necessary. If the patient has had both carbimazole and PTU, or you are concerned about the patient or require further information, please contact the endocrinology doctor on call via the hospital switchboard 01603 286286.

Sore throat, fever, jaundice or mouth ulcers

If the patient attends with a fever, flu-like symptoms, mouth ulcers or a sore throat, this may indicate the development of neutropaenia. Please ensure that they have stopped their medication, and check their full blood count urgently. If the patient develops any features of liver disease e.g. jaundice, please also ensure they have stopped their medication and check their liver function tests. If their blood tests are normal, the patient can continue the drug. If the white cell count is low, or liver function is abnormal please contact the endocrine team immediately.