CLINICAL TREATMENT GUIDELINE FOR THE MANAGEMENT OF HYPOTHYROIDISM IN ADULTS

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1.0 INTRODUCTION

Hypothyroidism is the second most common endocrine disorder after diabetes mellitus, resulting from deficiency of endogenously produced thyroid hormone and can affect any time, including pregnancy. Thyroid hormone action is an important determinant of development and growth and plays a critical role in the regulation of the function and metabolism of every organ system in the body.[1]

Hypothyroidism is usually a primary process, in which the thyroid gland is unable to produce enough thyroid hormone. Hypothyroidism can also be secondary where the thyroid gland itself is normal, but it receives insufficient stimulation because of low secretion of thyroid-stimulating hormone (TSH) from the pituitary gland or inadequate secretion of thyrotropin-releasing hormone (TRH) from the hypothalamus leading to insufficient release of TSH, which in turn causes inadequate thyroid stimulation[2].
Hypothyroidism can also be subclinical, where serum TSH is above the normal reference limit in combination with normal free thyroxine.

Worldwide, iodine deficiency remains the foremost cause of hypothyroidism. In other areas of adequate iodine intake, autoimmune thyroid disease (Hashimoto disease) is the most common cause of hypothyroidism and has been estimated to be 5-10 times more common in women than men.[1]
Although studies and data are lacking, hypothyroidism happens to be a common condition among the adults in Maldives.
A survey done by UNICEF in 1995 showed the goiter rate in Maldives was 23.6% in a sample of 2834 children between 6-12 years of age. The survey also included evaluating iodine levels in 39 samples of salt of which only 8% had adequate iodine levels following which universal salt iodinization was proposed for the country.[1]
More research is needed to establish the prevalence and cause of hypothyroidism in the Maldives, where most people consume iodized salt in the diet.

2.0 SCOPE OF THE GUIDELINE

Hypothyroidism is a common endocrinological condition seen across all tiers of healthcare service delivery in the Maldives. To date, there is no national clinical guideline for the management of hypothyroidism in adults.

This clinical practice guideline is meant to be a guidance document for health care professionals and is based on the best available evidence at the time of guideline development. This guideline intends to ensure effective treatment of the condition and standardize the care across the country.

The guideline should be used as a guidance document by general medical practitioners, physicians, endocrinologists, and other health care professionals engaged in managing hypothyroid patients.
It is also intended to be used as a reference document by healthcare policy makers as an assistance in formulating health care policy decisions regarding the management of hypothyroidism.

3.0 CAUSES OF HYPOTHYROIDISM

3.1 Primary hypothyroidism

- The most prevalent cause of hypothyroidism is iodine deficiency in iodine deficient geographical areas worldwide.

Table 1: Causes of primary hypothyroidism

- Chronic lymphocytic (autoimmune) thyroiditis: Hashimoto's thyroiditis, Atrophic thyroiditis
- Iodine deficiency
- Postpartum thyroiditis
- Subacute (granulomatous) thyroiditis
- Drug-induced hypothyroidism (Table 2)
- Iatrogenic causes: Iodine treatment, thyroidectomy, external irradiation of neck cancer[19]
- Congenital hypothyroidism

- In areas of iodine sufficiency, the most frequent cause of acquired hypothyroidism is chronic lymphocytic (autoimmune) thyroiditis (Hashimoto thyroiditis). Most of the affected individuals will have circulating anti–thyroid peroxidase antibodies (TPOAb), which are the hallmark of this disease. It should be noted that antibody levels can vary over time, may not be present early in the disease process, and can disappear over time.

- Hypothyroidism may also occur due to postpartum thyroiditis which can occur in up to 10% of postpartum women in the 2-12 months after delivery. The frequency may be as high as 25% in women with type 1 diabetes mellitus. The condition is usually transient for over 2-4 months, however, patients with postpartum thyroiditis and TPOAb positive are at increased risk of permanent hypothyroidism or recurrence of postpartum thyroiditis with future pregnancies. [2,3]

- Subacute granulomatous thyroiditis, also known as de Quervain disease, though relatively uncommon, occurring most frequently in middle-aged women can also lead to hypothyroidism. Disease features include low grade fever, thyroid pain, dysphagia, and elevated erythrocyte sedimentation rate. It is usually self-limited and does not normally result in longstanding thyroid dysfunction. [3]

Table 2: Common medications reported with potential to cause hypothyroidism

• Amiodarone	• Interleukin (IL)-2
• Interferon alfa	• Ethionamide
• Thalidomide	• Rifampin
• Lithium	• Phenytoin
• Stavudine	• Carbamazepine
• Oral tyrosine kinase inhibitors – Sunitinib, imatinib	• Phenobarbital
	• Aminoglutethimide
	• Sulfisoxazole
• Perchlorate	
• *p* -Aminosalicylic acid	
• Ipilimumab	

- Hypothyroidism may also occur because of radioiodine or surgical treatment for hyperthyroidism including thyroid cancer, benign nodular thyroid disease and use of radioactive iodine for treatment of Graves' disease. External neck irradiation (for head and neck neoplasms, breast cancer, or Hodgkin disease) may also result in hypothyroidism. [5]

3.2 Secondary hypothyroidism

- Secondary hypothyroidism results when there is insufficient production of TSH due to disease conditions of the hypothalamic - pituitary axis (Table 3) [3]

Table 3: Causes of secondary hypothyroidism
• Hypopituitarism: Pituitary tumors, Sheehan's syndrome, pituitary surgery or pituitary irradiation and infiltrative disorders • Tumors impinging on the hypothalamus • Lymphocytic hypophysitis • Drugs (eg: dopamine, prednisone, or opioids) • Isolated TSH deficiency • TRH resistance or TRH deficiency

4.0 CLINICAL MANIFESTATIONS

- The patient's presentation may vary from asymptomatic to myxedema coma but commonly manifests as a slowing in physical and mental activity and symptoms may often be subtle or non-specific (Table 4 and 5).
  In symptomatic patients, dry skin, cold sensitivity, hair loss, fatigue, muscle cramps, voice changes, weight gain and constipation are among the most common symptoms. Women may present with menstrual disturbances and decreased fertility or infertility. [3,11]

Table 4: Symptoms of Hypothyroidism	
• Fatigue, loss of energy, lethargy • Weight gain • Decreased appetite • Cold intolerance • Dry skin • Hair loss • Sleepiness • Muscle pain, joint pain, weakness in the extremities • Depression • Emotional lability, mental impairment • Forgetfulness, impaired memory, inability to concentrate	• Constipation • Menstrual disturbances, impaired fertility • Decreased perspiration • Paresthesia and nerve entrapment syndromes • Blurred vision • Decreased hearing • Fullness in the throat, hoarseness

- With severe disease, additional findings such as delayed ankle reflex relaxation time, edema, obstructive sleep apnea (secondary to macroglossia), carpal tunnel syndrome, euvolemic hyponatremia and even myxedema coma may be seen. If left untreated it can cause elevation of lipids, cardiovascular and neuromuscular problems. [2]

- Myxedema coma is a life-threatening emergency requiring immediate intervention. It most commonly occurs in individuals with undiagnosed or untreated hypothyroidism who are subjected to external stress. Patients may have clinical manifestations of altered mental status, hypothermia, bradycardia, hypercarbia and hyponatremia. Cardiomegaly, pericardial effusion, cardiogenic shock, and ascites may also be present (Table 6).

Table 5: Signs of Hypothyroidism	
• Weight gain • Dry skin • Pallor • Coarse, brittle, straw-like hair • Loss of scalp hair, axillary hair, pubic hair, or a combination • Dull facial expression • Coarse facial features • Periorbital puffiness • Macroglossia • Slow speech and movements	• Goiter • Hoarseness • Decreased systolic blood pressure and increased diastolic blood pressure • Bradycardia • Pericardial effusion • Hypothermia (only in severe hypothyroid states) • Nonpitting edema (myxedema) • Pitting edema of lower extremities • Hyporeflexia with delayed relaxation, ataxia or both

Table 6: Symptoms and signs of Myxedema Coma	
• Hypothermia • Bradycardia • Hypotension • Hyponatremia • Hypoventilation, Hypercarbia • Decreased pulse pressure • Periorbital edema, swelling of face and lips, macroglossia • Non pitting edema of hands and feet • Coarse or thin hair, dry brittle nails	• Cardiomegaly, Pericardial effusion • Cardiogenic shock • Abdominal distension due to ascites or ileus • Hyporeflexia with delayed relaxation • Altered mental status / confusion /slow speech, seizures, coma

5.0 DIAGNOSIS

The diagnosis of hypothyroidism is based on clinical suspicion from the patient symptoms and signs at presentation, which is then confirmed by laboratory testing.

- All patients with clinical symptoms suggestive of hypothyroidism should undergo a comprehensive physical examination for signs of hypothyroidism. If there is clinical suspicion of hypothyroidism, it should prompt laboratory testing of thyroid function tests to establish the diagnosis.

5.1 Screening for Hypothyroidism

5.1.1 Routine screening for thyroid disease is not recommended for asymptomatic adults but screening should be considered in all those with high risk for hypothyroidism (Table 7).[3,5]

5.1.2 A measurement of serum TSH is the initial screening test done for hypothyroidism and if the TSH level is elevated then free T4 level should be measured.

5.1.3 If TSH level is elevated, then provision of "Reflex testing" of free T4 from the same blood sample should be available and triggered by the laboratory.

5.1.4 If patient is symptomatic initial screening should include both TSH and free T4.

Table 7: Indications for screening of hypothyroidism
• Those with an abnormal thyroid examination like the presence of a goiter or thyroid nodule • All Pregnant women • Women older than 60 years • Patients with type 1 diabetes or other autoimmune disease • Family history of thyroid disease • Patients with a history of head and neck irradiation • Previous radio iodine therapy • Treatment with drugs known to influence thyroid function • Those with psychiatric disorders • Those with a prior history of thyroid surgery

5.2 Investigations for Diagnosis of Hypothyroidism

5.2.1 Laboratory investigations

5.2.1.1 TSH and Free T4 (fT4) levels are sufficient for the diagnosis of hypothyroidism. An elevated TSH above the upper reference range of a 3rd generation assay of a given laboratory with low free T4 levels are characteristic for a diagnosis of overt primary hypothyroidism.

5.2.1.2 Routine measurements of Total T4, Total T3 and Free T3 are not required for diagnosis of primary hypothyroidism.

5.2.1.3 Normal or low TSH with low Free T4 is suggestive of secondary hypothyroidism and should be referred to endocrinologist for further evaluation and management.

5.2.1.4 Elevated TSH with a normal free T4 is diagnostic of subclinical hypothyroidism. Subclinical hypothyroidism should be diagnosed only when this TFT pattern (elevated TSH with normal T4) is persistent on 2 separate tests done 3 months apart or earlier if indicated.[11]

5.2.1.5 In patients with subclinical hypothyroidism anti–thyroid peroxidase antibodies (TPOAb) measurements should be done. [3]

- Assay for TPOAb may be helpful in determining the etiology of hypothyroidism or in predicting future hypothyroidism. However, once a patient has been found to be antibody positive, repeated antibody testing adds little to the clinical picture and is not recommended.

5.2.1.6 Thyroid function tests are not recommended in critically ill patients, unless thyroid dysfunction is strongly suspected, because the underlying illness may affect the test results. In non- thyroidal illness, serial measurement of thyroid function may be required .[11]

5.2.1.7 Some abnormalities in the complete blood count and metabolic profile (lipid profile, liver profile, renal profile with electrolytes) may be found in patients with hypothyroidism and performing these tests may contribute to overall management of the patient.

5.2.2 Imaging

5.2.2.1 Radiological Imaging of the thyroid gland has no role in diagnosis of hypothyroidism. However, ultrasonography (USG) of thyroid gland is indicated in the presence of a goiter or nodule in the thyroid gland and in the case of suspected absent or ectopic thyroid gland. [11]

5.2.2.2 Higher imaging modalities such as Computed Tomography, Magnetic Resonance Imaging and nuclear scans are not routinely recommended. Specific indications may warrant the use of these modalities.

6.0 MANAGEMENT

6.1 Management of primary hypothyroidism

- The treatment goals for hypothyroidism are:
  - To reverse clinical progression and achieve an euthyroid state, with resolution of hypothyroid symptoms and correction of metabolic derangements, as evidenced by normal blood levels of serum TSH and free T4.
  - To avoid iatrogenic thyrotoxicosis or over treatment.

- Patients with hypothyroidism usually require treatment with lifelong thyroid hormone replacement in general, and hypothyroidism can be adequately treated with levothyroxine. [2,3,11]
- When deciding on a starting dose of levothyroxine, the degree of TSH elevation, age and weight of the patient and general clinical context, including the presence of cardiac disease and pregnancy status should be considered.
  Thyroid hormone therapy should be initiated as an initial full replacement or as partial replacement with gradual increments in the dose titrated upward to normalize TSH as the goal. TSH should be re-assessed 4-8 weeks after any dosage change.[2,3] If the clinical situation dictates, the clinician may re-assess TSH and fT4 earlier based on clinical judgement.

- In most patients, thyroid hormone treatment reverses the signs and symptoms of hypothyroidism. With treatment, other secondarily affected laboratory values such as lipid and prolactin levels should improve. Undertreatment leads to disease progression, with gradual worsening of symptoms and further metabolic derangements. Ultimately, untreated hypothyroidism can cause profound coma or even death

  6.1.1 Adults < 65 years, with no history of ischemic heart disease and TSH markedly elevated, should be started on an initial dose of full replacement, 1.6 mcg/kg/ day of levothyroxine (rounded to the nearest 25mcg) and titrated to achieve the target TSH level. [3]

  6.1.2 A starting dose of 25-50 mcg of levothyroxine with titration can be used for adults >65 years and those having milder degrees of hypothyroidism. [3]

  6.1.3 For those with known ischemic heart disease, caution is required when starting levothyroxine. In these patients, the starting dose should be reduced to 12.5 -25mcg daily and monitored for presence of anginal symptoms.

6.1.4 To get a consistent effect, it is recommended to use the same preparation of levothyroxine without switching between different brands as bioavailability differs with brands. Switching between different preparations of levothyroxine may lead to variations in the dose, and therefore, should be avoided. [2]

6.1.5 Levothyroxine should be taken, at least 30 to 60 minutes consistently before breakfast each day[2] because when co-administered with food, levothyroxine absorption is reduced compared with absorption in the fasting state.
For those patients having difficulty taking the medicine in the morning, or have missed the morning dose, it can be taken at bedtime, 3 to 4 hours after the last meal. [2,3.]

6.1.6 Liothyronine, alone or in combination with levothyroxine, is not routinely recommended for treating people with primary hypothyroidism as there is not enough evidence that it offers benefits over levothyroxine monotherapy. [3,11]
If liothyronine is indicated, the patient should be referred to the endocrinologist.

6.1.7 It is known that stability and potency problems with oral thyroxine preparations could potentially have adverse effects on health. It is therefore very important that thyroxine tablets should be kept in their original container and stored properly per product insert, out of sunlight, in a cool dry place.[3]

6.1.8 No adjustments in levothyroxine dosing are required in cases of cirrhosis or renal failure but Nephrotic syndrome, with its large urinary protein losses that include the thyroid hormone transport proteins, can be a cause of increased Levothyroxine requirement due to excessive urinary thyroid hormone losses.

6.1.9 Discuss with the patient, the lifelong nature of hypothyroidism, the need for lifelong levothyroxine therapy, the proper way to take medicine, and the need for TSH testing at least annually once thyroid function tests are stable. Emphasize proper compliance with medication, at each visit and the risks of over and under treatment and how thyroid disease and treatment may affect pregnancy and fertility.

6.1.10 If symptoms persist while on treatment, consider adjusting the dose of levothyroxine further to achieve optimal wellbeing, but avoid using doses that cause TSH suppression or thyrotoxicosis unless otherwise clinically indicated.

6.1.11 In general, levothyroxine dose adjustments of 12.5–25 mcg/day are made, either up or down, depending on whether the serum TSH is high or low, respectively.

6.1.12 Serum TSH measurements should be done at 4-8 weeks after initiation of treatment or after a change in dose until the TSH target has been reached (2 similar measurements within the reference range of a third generation TSH assay, 3 months apart).

6.1.13 Once the TSH target is reached, periodic measurements of serum TSH should be done at 6 months and then followed by 12-month intervals. If the clinical situation dictates TSH can be done earlier.[3]

6.1.14 If levothyroxine dose requirement is much higher than expected, rule out non-compliance. Other causes of failure to normalize TSH include improper storage of Levothyroxine, factors affecting absorption and concomitant use of drugs interfering in absorption or metabolism of levothyroxine.

6.1.15 Refer to endocrinologist for further evaluation if TSH does not normalize despite correction of all causes.

6.2 Management of secondary hypothyroidism

6.2.1 The treatment goals for secondary hypothyroidism are to achieve a state of euthyroid with resolution of hypothyroid symptoms and correction of metabolic derangements, as evidenced by normal blood levels of free T4 and to avoid iatrogenic thyrotoxicosis or over treatment.

6.2.2 Routine TSH measurement during monitoring of treatment is not required in secondary hypothyroidism.

6.3 Using Levothyroxine in the month of Ramazan

6.3.1 Levothyroxine ideally should be taken on an empty stomach, 30 to 60 minutes before having Suhoor in the month of Ramazan.

6.3.2 If the patient is unable to take levothyroxine at suhoor time, it is recommended to be taken 3 to 4 hours after the last meal and to remain empty stomach for at least 30 to 60 minutes.[21]

6.4 Use of other medication and supplements while on levothyroxine

6.4.1 Where feasible, levothyroxine should be separated from other potentially interfering medications and supplements (e.g., calcium salts, phosphate binders, proton pump inhibitors and ferrous sulfate).

6.4.2 Initiation and discontinuation of estrogen and androgens should be followed by reassessment of serum TSH, since such medications may alter the levothyroxine requirement.

6.4.3 Thyroid function tests should be done before starting amiodarone and at 3–6-month intervals after that. The patient should be monitored up to a year after stopping amiodarone. [11]

6.4.4 Serum TSH should also be reassessed in patients who are started on agents such as tyrosine kinase inhibitors that affect thyroxine metabolism and deiodination.

6.4.5 Serum TSH monitoring is also advisable when medications that have been shown to increase hepatic metabolism of T4 and T3 such as antiepileptics (phenobarbital, phenytoin, carbamazepine) or others such as rifampin, and sertraline are started.

6.4.6 Biotin, commonly used as a supplement, has shown interference with laboratory testing of TFT resulting in falsely high levels of T3 and T4 and low levels of TSH. It is recommended to stop biotin at least 2 days before TFT to avoid the risk of a misleading test.[18]

7.0 HYPOTHYROIDISM AND PREGNANCY

- Untreated or inadequately treated hypothyroidism in pregnancy can produce an array of obstetric complications both for the mother and the baby. It has been associated with increased risk of miscarriage, maternal anemia, myopathy, congestive heart failure, pre-eclampsia, placental abnormalities, and postpartum hemorrhage.
  Thyroid hormone is critical for brain development in the baby and children born with congenital hypothyroidism can have severe cognitive, neurological and developmental abnormalities if the condition is not recognized and treated promptly.

- Serum TSH remains the main determinant used to guide treatment decisions in hypothyroidism and the difficulties lie in the presence of substantial differences in the upper reference limits of pregnancy specific reference range for TSH between populations. Thyroid function tests should be interpreted using population based, pregnancy-specific reference intervals for each trimester of pregnancy.

7.1 All pregnant women should be screened for thyroid dysfunction at first contact with a healthcare professional by measuring thyroid function tests.

7.2 All pregnant women with hypothyroidism should be managed in conjunction with an endocrinologist.

7.3 In hypothyroid women on levothyroxine who are planning a pregnancy, serum TSH should be evaluated preconception, and levothyroxine dose adjusted to achieve TSH

level between lower reference limit and 2.5mU/L and maintain this throughout the pregnancy.

7.4 Women who are already on treatment for hypothyroidism should be counselled to empirically increase their dose of levothyroxine by 25 -30% in the event of a positive pregnancy test. [11,20] This may be done by doubling the dose on 2 days of each week or by a dose increment of 25mcg per day for those taking ≤ 100mcg levothyroxine daily or 50mcg for those taking >100mcg daily.[20]
Once TSH is done, the dosage should be titrated to attain the trimester specific TSH target.

7.5 For women with existing subclinical hypothyroidism, treatment with levothyroxine should be considered starting preconception with titration to achieve a preconception TSH ≤2.5mIU/L, especially those with TPOAb [9, 20]

7.6 Women undergoing assisted reproductive technologies should receive levothyroxine to achieve a TSH ≤2.5mIU/L.[8]

7.7 The normal reference range for TSH during pregnancy is lower than the normal reference range for the general population. Ideally, the trimester-specific TSH reference range for the population should be used. Until trimester specific country data is available for Maldives, following are the recommendation for treatment naive patient.

TSH levels	TPOAb	Levothyroxine Therapy
>10mU/L	Positive	Recommended
	Negative	Recommended
>4-10mU/L	Positive	Recommended
	Negative	Can be considered*
2.5-4mU/L	Positive	Can be considered
	Negative	Not recommended
*Weak evidence: local expert consensus is to treat *Ideally, sample should be taken in the morning while fasting in a standardized lab		

7.8 The following are the recommended trimester specific reference ranges for TSH to be followed in guiding treatment decisions[22]:

- 1st Trimester: 0.1-3.0mIU/L
- 2nd Trimester: 0.2-4.0mIU/L
- 3rd Trimester: 0.3-4.0mIU/L

7.9 In women newly diagnosed at any time in pregnancy, with overt hypothyroidism and subclinical hypothyroidism should receive levothyroxine therapy with the dose titrated to achieve a TSH concentration within the trimester-specific reference range[12,13,9,20]

7.10 Serial serum TSH levels should be assessed every 4 weeks up to 20 weeks gestation and at 28-30 weeks gestation [8, 20]

7.11 In women with isolated hypothyroxinemia, levothyroxine therapy is not recommended. Thyroid function tests should be checked 4-6 weeks later to ensure they remain stable [20]

7.12 After delivery, for those already on levothyroxine before conception, the dose can be reduced to the pre pregnancy level at two weeks of postpartum[20].TSH can be checked in 6 weeks post-partum.[8,13,20]

7.13 For those women not taking levothyroxine before conception, levothyroxine can be stopped following birth and Thyroid function test checked six weeks post-partum. [20]

8.0 HYPOTHYROIDISM AND SURGERY

- Hypothyroidism due to its effect on multiple organ systems, can predispose patients to perioperative complications.

8.1 In hypothyroid patients planned for a surgical procedure, the preoperative assessment should include measurement of serum TSH to see if the thyroid treatment is adequate to ensure that the treatment is optimized before surgery.[17]

8.2 In elective surgery, surgery should be postponed until adequate treatment with thyroid hormones has achieved an euthyroid state.

8.3 In cases where surgical procedure is urgent, levothyroxine should be started/ adjusted as soon as possible and surgery proceeded without delay with the awareness of possible post operative complications.

8.4 If urgent surgery is required in a patient who is severely hypothyroid such as in myxedema coma or with severe complications (pericardial effusion or heart failure or very low levels of free T4), free T4 levels should be normalized rapidly using IV levothyroxine in a loading dose of 200-500mcg followed by 50-100mcg IV daily. Glucocorticoids should be administered if adrenal insufficiency is suspected. [17]
Surgery should proceed with invasive intraoperative and careful post operative monitoring.

8.5 If there is a delay in restarting oral thyroxine by more than 5-7 days due to patient being kept nil per oral post-surgery, then IV levothyroxine should be administered at a dose of 60-80% of the oral dose. [2,16]

9.0 MYXEDEMA COMA

- Myxedema coma is a medical emergency that consists of severe hypothyroidism with decompensation and requires prompt diagnosis and treatment. It is diagnosed clinically in patients presenting with hallmarks of reduced conscious level and hypothermia.
  It usually occurs in patients with a history of undiagnosed or long-standing untreated hypothyroidism, typically precipitated by a systemic illness.

- Complications of myxedema coma include metabolic decompensation (hypoglycemia, hyponatremia), cardiovascular (bradycardia, hypotension, pericardial effusion, and heart failure), neurological (psychosis, seizures, altered consciousness), respiratory (hypoventilation, hypercapnia, sleep apnea) complications, renal failure and anemia.

9.1 Patients diagnosed with myxedema coma, are critically ill and should be managed in intensive care units under the care of an endocrinologist in conjunction by a multi-disciplinary team.

9.2 Absorption of oral medications is reduced in myxedema coma due to multiple factors and require intravenous thyroxine[2,3.]

9.3 Concurrent hypoadrenalism maybe present, thus Intravenous hydrocortisone 200 mg stat, then 50 mg, 6 hourly should be administered prior to levothyroxine. Ideally a serum cortisol is done prior to administration of intravenous hydrocortisone.

9.4 Initial intravenous levothyroxine of 200–400 mcg followed by 1.6 mcg/kg/day (75% if administered intravenously) should be given. If intravenous levothyroxine is not available, oral levothyroxine to be given as 500 mcg loading followed by maintenance dose.[2,3,5.]

9.5 Intravenous liothyronine (when available) may be given in addition to levothyroxine. Loading dose recommended is 5–20 mcg followed by 2.5–10 mcg every 8 hours till patient regains consciousness. [2]

9.6 As with all critically ill patients, multi-organ parameters should be monitored including mental status cardiovascular parameters, respiratory parameters, renal function, and metabolic parameters. Frequent free T4 monitoring is needed.

10.0 SUBCLINICAL HYPOTHYROIDISM

- Subclinical hypothyroidism is defined as an elevated serum TSH with normal freeT4 levels. Most people with subclinical hypothyroidism will have minimal or no specific symptoms. It can be challenging to determine the extent to which mild thyroid dysfunction is causing a patient's symptoms because of the high rate of some complaints such as cold intolerance, weight gain, constipation, fatigue and hair loss in the general population.

  10.1 Thyroid function tests should be repeated after 3 months to establish the diagnosis or earlier if clinically indicated.

- Spontaneous recovery has been seen in some people with subclinical hypothyroidism and is more likely in those with negative anti-thyroid antibodies and having serum TSH levels less than 10.0mIU/L.

  10.2 Measure anti-TPO antibodies in all patients diagnosed with subclinical hypothyroidism[11.]

  10.3 Patients with subclinical hypothyroidism whose TSH levels are higher than 10.0mIU/L should be treated with levothyroxine irrespective of anti-TPO antibodies status.[19]

  10.4 In patients with subclinical hypothyroidism, initial levothyroxine dosing is lower than what is required in the treatment of overt hypothyroidism. A daily dose of 25–75 mcg should be considered, depending on the degree of TSH elevation. Further adjustments should be guided by clinical response and follow-up thyroid function tests.[3]

  10.5 All patients with TSH levels between 4.5 and 10.0mIU/L, having symptoms compatible with hypothyroidism, underlying goiter, preconception, pregnant women, or those with positive anti-TPO antibodies should be considered for treatment. [19]

  10.6 It is advisable to decide whether to treat subclinical hypothyroidism depending on the risks and benefits involved in each case individually. Untreated patients should be monitored annually, and treatment should be started if symptoms develop or serum TSH increases to greater than 10.0mIU/L.

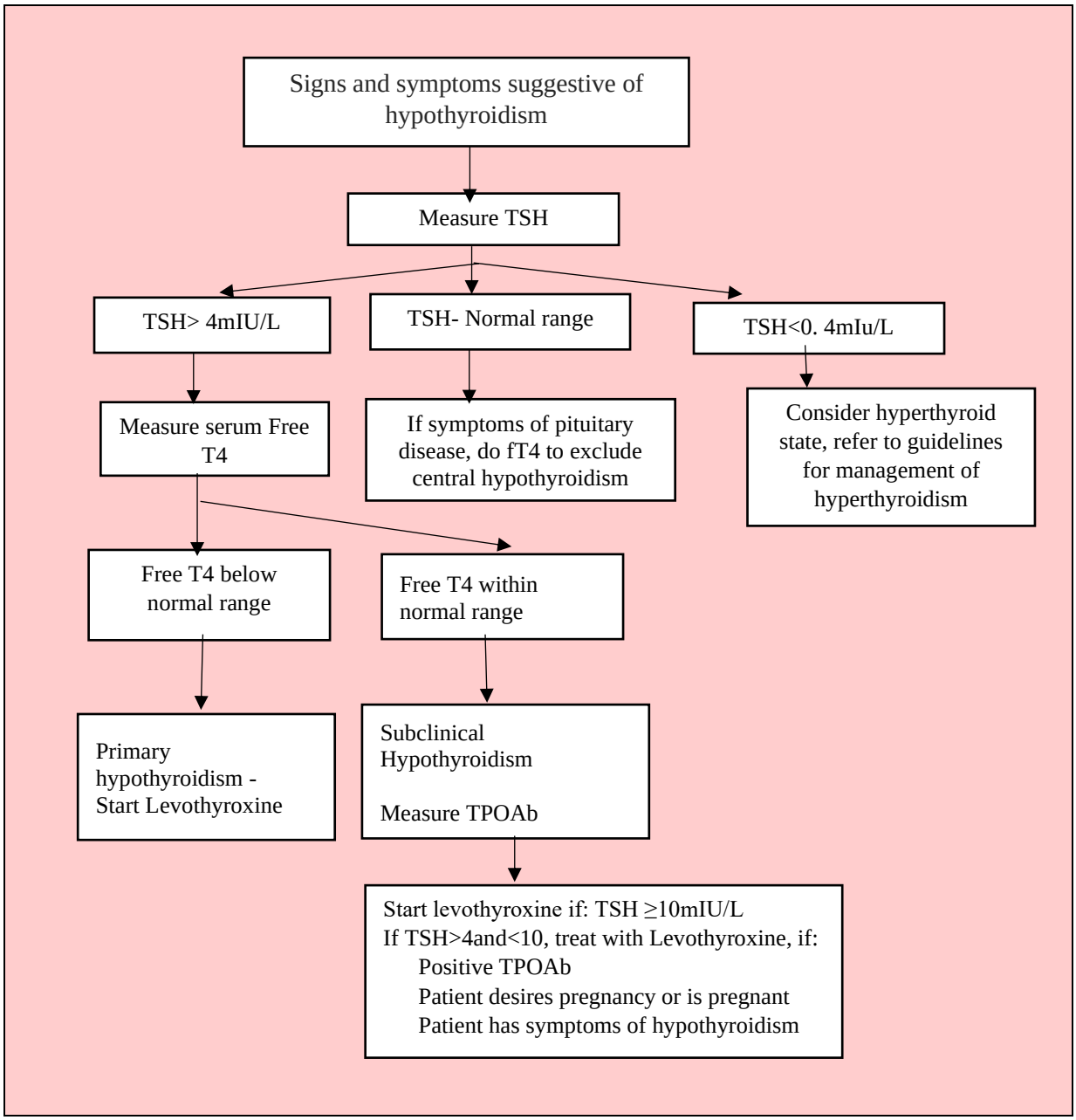
11.0 REFERRAL TO ENDOCRINOLOGIST

11.1 In general, most patients with uncomplicated hypothyroidism can be managed by physicians, but referral to an endocrinologist or management of the patient in conjunction with an endocrinologist is recommended in some conditions for better patient care and optimization of treatment [3,11.] Such patients include:

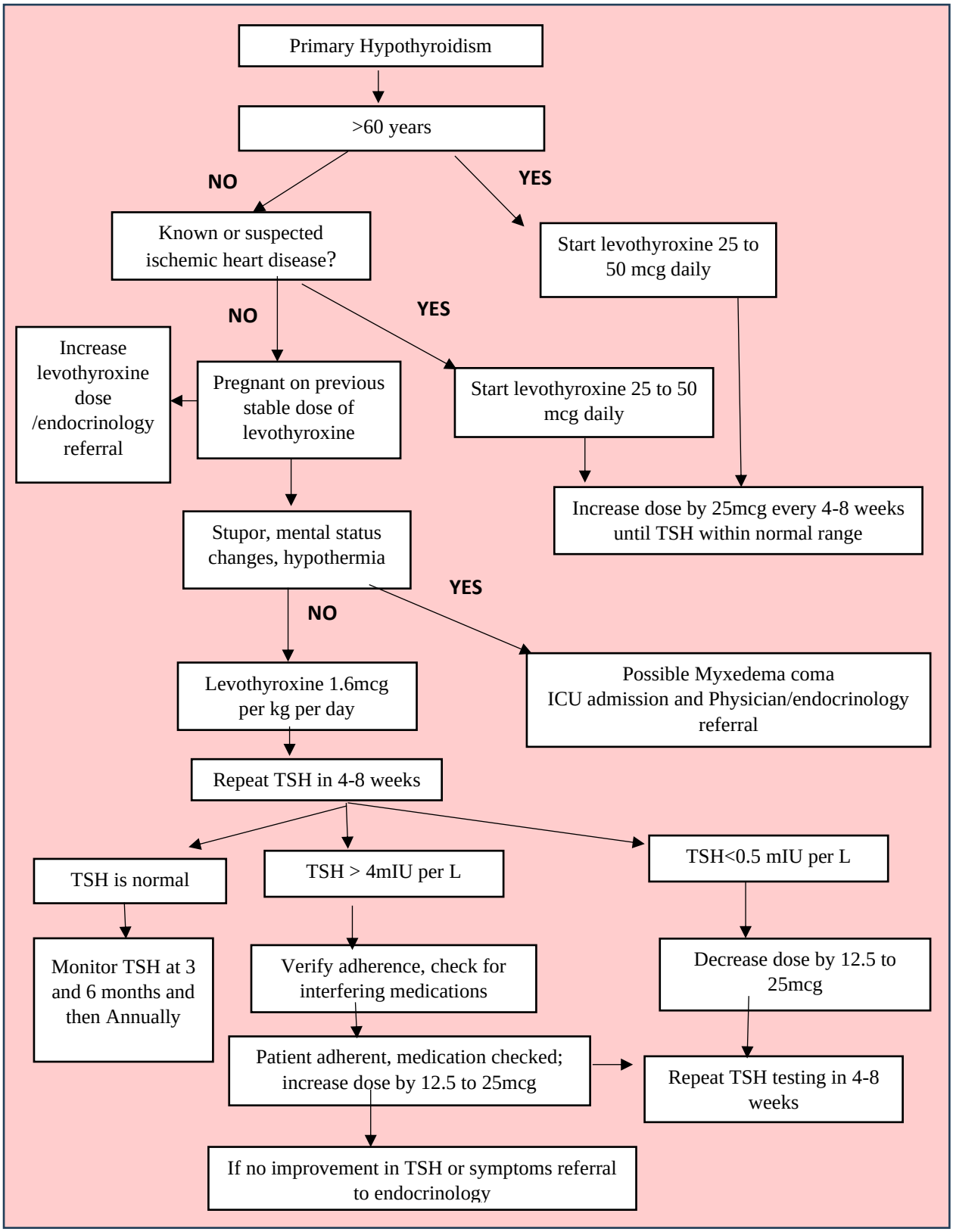
- Patients in whom it is difficult to render and maintain an euthyroid state.
- Pregnancy and women planning conception.
- Cardiac disease
- Presence of goiter, nodule, or other structural changes in the thyroid gland
- Presence of other endocrine diseases, such as adrenal and pituitary disorders
- Unusual constellation of thyroid function test results
- Unusual causes of hypothyroidism, e.g., drug-induced hypothyroidism

12.0 CLINICAL PATHWAYS

12.1 Algorithm for Evaluation for Suspected Hypothyroidism



12.2 Algorithm for Treatment of Primary Hypothyroidism



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