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Hypothyroidism and Myxedema Coma

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Introduction

Background

Hypothyroidism is a clinical syndrome in which the deficiency or absence of thyroid hormone slows bodily metabolic processes. Symptoms can manifest in all organ systems and range in severity based on the degree of hormone deficiency. The disease typically progresses over months to years but can occur quickly following cessation of thyroid replacement medication or surgical removal of the thyroid gland.

The term myxedema refers to the thickened, nonpitting edematous changes to the soft tissues of patients in a markedly hypothyroid state. Myxedema coma, a rare, life-threatening condition, occurs late in the progression of hypothyroidism. The condition is seen typically in elderly women and is often precipitated by infection, medication, environmental exposure, or other metabolic-related stresses. Because rapid confirmatory laboratory tests are often unavailable, the diagnosis may be made on clinical grounds with treatment started promptly.

Treatment of myxedema coma requires potentially toxic doses of thyroid hormone, and mortality rates exceeding 20% have been reported even with optimum therapy.

For more information, see Medscape's Hypothyroidism Resource Center.

Pathophysiology

Thyroid hormone is secreted in response to stimulation of the thyroid gland by thyroid-stimulating hormone (TSH) from the anterior pituitary gland. TSH is released through the action of thyrotropin-releasing hormone (TRH) from the hypothalamus.

Hypothyroidism can be caused by permanent loss or atrophy of functional thyroid tissue (primary hypothyroidism), insufficient stimulation of a normal thyroid gland by as a result of hypothalamic or pituitary disease (secondary hypothyroidism, often accompanied by compensatory thyroid gland enlargement), or a defect in the TSH molecule (control hypothyroidism).

Primary hypothyroidism accounts for approximately 90-95% of hypothyroidism, with a predominantly autoimmune-mediated etiology. TSH hypersecretion produces excessive thyroid tissue, resulting in goiter formation. Surgical and radiation ablation account for a large percentage of acquired cases of hypothyroidism. Congenital abnormalities, malignancies, and infiltrative disorders including amyloidosis and sarcoidosis can also lead to the disease. Iodine deficiency is rarely responsible for hypothyroidism in developed countries; however, it remains the primary cause worldwide.

Suprathyroidal disorders including hypopituitarism and hypothalamic lesions account for fewer than 10% of cases. Rarely, peripheral resistance to thyroid hormone may occur.

The congenital absence or deficiency of thyroid tissue may result in cretinism, a neurodevelopmental disorder characterized by lethargy, poor peripheral circulation, constipation, and goiter. Because infants are asymptomatic, neonatal screening is vital to prevent permanent sequelae.

Frequency

United States

Reports on screening surveys for thyroid disease show an incidence of 5.8% for subclinical thyroid abnormalities. However, those with overt signs and symptoms of hypothyroidism likely comprise less than 2% of women and 0.2% of men.

Myxedema coma occurs rarely, appearing in 0.1% of all cases of hypothyroidism.

International

Neonatal screening programs for congenital hypothyroidism show that in many areas around the world hypothyroidism appears in 1 of every 4000 newborns.^[1]

In developed countries, the incidence of subclinical hypothyroidism is approximately 8% in women and 3% in men. Endemic goiter usually occurs in environmentally iodine-deficient areas; throughout the world, goiter is estimated to affect 200 million people. Goiter is most common in mountainous areas of the Alps, Himalayas, and Andes, possibly due to low soil iodine content as a result of leaching away of minerals as glaciers melt.

Mortality/Morbidity

Mortality rate in myxedema coma has historically been as high as 80%. Some data suggest that aggressive management and early recognition have improved the mortality rate to 15-20%. However, a more recent observational study was unable to show significant differences in outcome based on replacement therapeutic methods, with a mortality rate remaining high at 40%.^[2]

Race

Anecdotal reports indicate the disease appears more often in white and Hispanic populations.

Sex

Incidence is greater in females than males (female-to-male ratio 5-10:1).

Age

The incidence of primary hypothyroidism increases progressively with age, typically at 40-50 years. After age 60 years, the prevalence of hypothyroidism may be as high as 8-10% in women.

Clinical

History

The symptoms characteristic of hypothyroidism are numerous yet often vague and subtle, especially in early stages of the disease.

- Lethargy
- Generalized weakness
- Brittle or thinning hair
- Menstrual irregularity
- Menorrhagia
- Forgetfulness
- Fullness in throat
- Deep, husky voice secondary to mucopolysaccharide infiltration of the vocal cords
- Cold intolerance

- Weight gain
- Muscle/joint pain or weakness
- Inability to concentrate
- Headaches
- Constipation
- Emotional lability
- Depression
- Blurred vision
- Dry hair

Physical

- Pseudomyotonic reflexes - Prolonged relaxation phase, usually at least twice as long as the contraction phase
- Hypothermia (especially in myxedema coma)
- Skin changes - Dry, cool, coarse, and thickened with a yellowish appearance
- Subcutaneous tissues - Nonpitting, waxy, dry edema, secondary to accumulation of polysaccharides
- Loss of axillary and pubic hair
- Pallor
- Loss of outer one third of eyebrows
- Abdominal distention
- Goiter
- Unsteady gait/ataxia
- Pericardial effusion
- Dull facial expression
- Coarsening or huskiness of voice
- Periorbital edema
- Bradycardia, narrow pulse pressure
- Macroglossia
- Thyroidectomy scar - In patients with altered mental status, suggests myxedema coma as a potential cause

Causes

The most common etiology of hypothyroidism worldwide is iodine deficiency as associated with endemic goiter. Conversely, a study among Chinese patients also demonstrated a significant increase in overt hypothyroidism in those with an *excessive* intake of iodine.^[3] Within the United States and developed nations, the major causes of hypothyroidism are autoimmune destruction of the thyroid gland (eg, Hashimoto thyroiditis) and iatrogenic

secondary to the treatment of Graves disease (surgical or radioactive iodine ablation of the thyroid gland). Primary hypothyroidism (dysfunction of the thyroid gland) accounts for up to 90-95% of cases. Secondary hypothyroidism (dysfunction of the pituitary or hypothalamus) accounts for most of the remainder of cases. ED management rarely requires distinguishing between primary and secondary origins.

- Primary causes include autoimmune, idiopathic, postoperative, and congenital etiologies; radiation; radioiodine therapy; iodine deficiency; metabolic disorders; and medications (eg, lithium, amiodarone, phenytoin, carbamazepine, iodides). Furthermore, those with underlying autoimmune thyroiditis are susceptible to disease progression while taking these medications.
- Secondary causes include pituitary and hypothalamic disorders such as trauma, neoplasm, irradiation, and infiltrative diseases including sarcoidosis or amyloidosis.
- In a patient with underlying hypothyroidism, inciting factors responsible for developing myxedema coma are numerous and include infection, trauma, cold exposure, or medications such as sedatives and anesthetics.

Differential Diagnoses

Congestive Heart Failure and Pulmonary Edema
Depression and Suicide
Encephalopathy, Hepatic
Hypothermia
Shock, Septic

Other Problems to Be Considered

Nephrotic syndrome
Chronic nephritis
Euthyroid sick syndrome
Primary amyloidosis
Dementia

Workup

Laboratory Studies

The following measurements and studies are indicated in hypothyroidism:

- Electrolytes
 - Hyponatremia is common secondary to extracellular volume expansion produced by elevated antidiuretic hormone.
 - Blood glucose level ranges from normal to low secondary to decreased gluconeogenesis and reduced insulin clearance.
 - Creatine phosphokinase (CPK), aspartate aminotransferase (AST) or serum glutamic oxaloacetic transaminase (SGOT), and lactate dehydrogenase (LDH) levels may be elevated in myxedema coma due to increased muscle membrane permeability. Creatine kinase (CK)-myocardial band (MB) levels are typically normal.
- ABG: Hypoventilation commonly results in hypercapnia and hypoxia in patients with myxedema coma.
- Urinalysis: Evaluate for source of infection.
- Secondary studies
 - Thyroid function studies may not be immediately available to assist in clinical decision making in the ED.

- Thyroid-stimulating hormone (TSH) is elevated in primary hypothyroidism, but it may be normal or low in secondary causes of hypothyroidism.
- Free thyroxine (T4) levels are low.
- Triiodothyronine (T3) resin uptake is decreased.
- Free T4 index (T3 resin uptake x total serum T4) is low.
- Critically ill patients may develop euthyroid sick syndrome, which must not be confused with a primary thyroid abnormality. These patients have low to normal TSH and T4 levels with low T3 levels.

Imaging Studies

- Chest radiography
 - An enlarged cardiac silhouette in a chest radiograph may suggest pericardial effusion. A chest radiograph depicting a pericardial effusion is shown in the image below.

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Pericardial effusion. Note the "water-bottle" appearance of the cardiac silhouette.

- However, chest radiography is reported to have a 30% false-negative rate in detecting hypothyroid pericardial effusions.
- Chest radiography can help detect pulmonary infections often associated with myxedema coma.
- Acute abdominal series: An ileus may be associated with hypothyroidism, and it may be present in myxedema coma.
- Head CT scan (noncontrast)
 - In patients with altered mental status, the scan may be helpful in ruling out other etiologies such as intracerebral hemorrhage.
 - The scan may be helpful in ruling out other etiologies of altered mental status, such as intracerebral

hemorrhage.

- Echocardiography: Perform this study if pericardial effusion is suspected.

Other Tests

- Electrocardiogram
 - Bradycardia, low voltage, prolonged PR interval, T-wave abnormalities, and electrical alternans (suggestive of effusion) may be present.
- Core temperature
 - Patients with myxedema coma have a temperature below 37°C (98.6°F) in 15% of cases.
 - Fifteen percent of those patients have a temperature below 29.5°C (85°F).

Treatment

Prehospital Care

Stabilize acute life-threatening conditions in patients with hypothyroidism, and initiate supportive therapy.

Emergency Department Care

Patients with myxedema coma may present in extremis; implement initial resuscitative measures, including intravenous (IV) access, cardiac monitoring, and oxygen therapy, as indicated. Mechanical ventilation is indicated for patients with diminished respiratory drive or obtundation.

- Evaluate for life-threatening causes of altered mental status (eg, bedside glucose, pulse oximetry).
- If myxedema coma is suspected on clinical impression, start IV thyroid hormone treatment.
- Confirmatory tests often are not available to an ED physician.
- With a diagnosis of myxedema coma, initiate hormonal therapy.
- Myxedema coma may lead to profound hemodynamic instability and airway compromise. Emergency physicians should anticipate a potentially difficult airway in patients with myxedema coma.^[4]
- Investigate immediately for inciting events such as infection.
- Treat respiratory failure with appropriate ventilatory support.
 - The condition often requires mechanical ventilation.
 - Treat underlying pulmonary infection.
- Hypotension may respond to crystalloid infusion.
 - Occasionally, vasopressive agents are required.
 - In refractory cases, hypotension may resolve with thyroid hormone replacement.
- Treat hypothermia.
 - Most patients with myxedema coma respond to passive rewarming measures such as blankets and removal of cold or wet clothing; aggressive rewarming may lead to peripheral vasodilatation and hypotension. However, hemodynamically unstable patients with profound hypothermia require active rewarming measures.
 - Treat hyponatremia initially with water restriction; however, if sodium levels are less than 120 mEq/L or any seizures occur, hypertonic saline is indicated.

- Avoid medications such as sedatives, narcotics, and anesthetics. Metabolism of these agents may be slowed significantly, causing prolonged effects.

Consultations

- For patients with myxedema coma, consult a critical care intensivist regarding admission to an ICU and optimization treatment.
- An endocrinologist should be consulted to help confirm the diagnosis and assist in patient management after admission.

Medication

Initiate thyroid hormone replacement as the mainstay therapy for patients with myxedema coma. Patients may remain refractory to other treatment and supportive therapies until thyroid hormone replacement takes effect. Infusing thyroid hormone in the euthyroid patient is unlikely to result in significant morbidity except in patients with ischemic heart disease. Hormonal therapy should be instituted early in patients with a high clinical suspicion of myxedema coma prior to laboratory confirmation.

Monitor the patient's heart during hormone treatment, decreasing or discontinuing the dosage with any evidence of ischemia or dysrhythmia.

The magnitude of hypothyroidism dictates dose and route. Mild cases may be treated with gradual oral replacement, but patients with myxedema coma usually require large doses of IV replacement. General guidelines suggest administration of intravenous levothyroxine at a dose of 500-800 mcg. Alternatively, intravenous liothyronine can be given at a dose of 25 mcg.

Administer antibiotics if infection is suspected to be a precipitating event.

Physicians often recommend glucocorticoid replacement therapy because adrenal insufficiency may be concomitant (especially in patients with secondary hypothyroidism).

Thyroid products

These agents are used for the replacement of thyroid hormone.

Liothyronine (Triostat, Cytomel)

Synthetic form of natural thyroid hormone (T3) converted from thyroxine (T4); short duration of activity allows quick dose adjustments in event of overdose.

Dosing

Adult

25-50 mcg slow IV infusion initially, followed by 65-100 mcg/d divided tid/qid

Pediatric

Not established

Interactions

Increases effects of anticoagulants; activity of some beta-blockers may decrease when patient converted to euthyroid state

Contraindications

Documented hypersensitivity; uncorrected adrenal insufficiency

Precautions**Pregnancy**

A - Fetal risk not revealed in controlled studies in humans

Precautions

Decrease dosage in patients with known or suspected cardiovascular disease; periodically monitor thyroid status

Levothyroxine (Synthroid, Levothroid, Levoxyl)

Also known as T4; many physicians prefer the more gradual onset of action of this form of thyroid hormone.

Dosing**Adult**

400-500 mcg via slow IV infusion, followed by 50-100 mcg/d

Pediatric

4-10 mcg/kg/d IV divided tid/qid

Interactions

Cholestyramine may decrease absorption; estrogens may decrease response in patients with nonfunctioning thyroid glands; increases effect of anticoagulants; activity of some beta-blockers may decrease when hypothyroid patient converted to euthyroid state

Contraindications

Documented hypersensitivity; uncorrected adrenal insufficiency

Precautions**Pregnancy**

A - Fetal risk not revealed in controlled studies in humans

Precautions

Caution in angina pectoris or cardiovascular disease; monitor thyroid status periodically

Corticosteroids

These agents are used for prevention and/or treatment of adrenal insufficiency.

Hydrocortisone (Solu-Cortef)

DOC due to mineralocorticoid activity and glucocorticoid effects.

Dosing**Adult**

100 mg IV tid

Pediatric

0.5-1 mg/kg IV tid

Interactions

Estrogens may decrease clearance; may increase digitalis toxicity secondary to hypokalemia

Contraindications

Documented hypersensitivity; viral, fungal, or tubercular skin infections

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Caution in hyperthyroidism, osteoporosis, peptic ulcer, cirrhosis, nonspecific ulcerative colitis, diabetes, and myasthenia gravis

Follow-up

Further Inpatient Care

- Admit patients with myxedema coma to ICU.
- Provide supportive ventilatory and hemodynamic management.
- Treat precipitating events (eg, infection).
- Continue rewarming as required.
- Confirm diagnosis with laboratory testing.
- Continue thyroid hormone replacement, and convert to oral therapy when tolerated.
- Clinical improvement should be apparent within 24-36 hours of initiating thyroid hormone replacement.

Complications

- Treatment-induced congestive heart failure in patients with coronary artery disease
- Myxedema coma
- Increased susceptibility to infection
- Megacolon
- Organic psychosis with paranoia
- Adrenal crisis with vigorous treatment of hypothyroidism
- Hypersensitivity to opiates
- Pericardial effusion and cardiac tamponade^[5]

Prognosis

- The prognosis of hypothyroidism is good with early treatment. However, once the disease has progressed

to myxedema coma, the mortality rate may exceed 20% in the treated population.

- Relapses occur if treatment is discontinued.

Patient Education

- Importance of medication compliance
- Need for lifelong treatment
- Watch for signs of infection
- Watch for signs of thyrotoxicity
- For excellent patient education resources, visit eMedicine's Endocrine System Center. Also, see eMedicine's patient education articles Thyroid Problems and Myxedema Coma.

Miscellaneous

Medicolegal Pitfalls

- Failure to consider the diagnosis in the setting of altered mental status
 - Myxedema coma is rare and associated with significant signs and symptoms that may overshadow the underlying diagnosis.
 - Always consider myxedema coma in patients with altered mental status and in those who have been on thyroid medication or had thyroid surgery.
- Hypothyroid patients, especially those with myxedema coma, often are hypothermic. A normal or elevated temperature can reflect underlying infection.
- Failure to further evaluate and treat additional etiologies of altered mental status

Special Concerns

- Patients with hyperammonemia and altered level of consciousness may easily be misdiagnosed as having hepatic encephalopathy. Both may have a similar presentation of obtundation/coma, ascites, liver malfunction, and anemia.^[6]

Multimedia



Media file 1: Pericardial effusion. Note the "water-bottle" appearance of the cardiac silhouette.

References

1. [Guideline] Screening for congenital hypothyroidism: US Preventive Services Task Force reaffirmation recommendation. *Ann Fam Med*. Mar-Apr 2008;6(2):166. [[Medline](#)].
2. Beynon J, Akhtar S, Kearney T. Predictors of outcome in myxoedema coma. *Crit Care*. 2008;12(1):111. [[Medline](#)].
3. [Best Evidence] Teng W, Shan Z, Teng X, Guan H, et. al. Effect of iodine intake on thyroid diseases in China. *N Eng J Med*. Jun 2006;354(26):2783-2793. [[Medline](#)].
4. Lee CH, Wira CR. Severe angioedema in myxedema coma: a difficult airway in a rare endocrine emergency. *Am J Emerg Med*. Oct 2009;27(8):1021.e1-2. [[Medline](#)].
5. Sanda S, Newfield RS. A child with pericardial effusion and cardiac tamponade due to previously unrecognized hypothyroidism. *J Natl Med Assoc*. Dec 2007;99(12):1411-3. [[Medline](#)].
6. Ragland G. Hypothyroidism and myxedema coma. In: Tintinalli JE, Krome RL, et al, eds. *Emergency Medicine: A Comprehensive Study Guide*. 4th ed. New York, NY: McGraw-Hill; 1996:964-67.
7. Flynn RW, MacDonald TM, Morris AD. The thyroid epidemiology, audit, and research study: thyroid dysfunction in the general population. *J Clin Endocrinol Metab*. Aug 2004;89(8):3879-84. [[Medline](#)].
8. Franklyn JA. The management of hyperthyroidism. *N Engl J Med*. Jun 16 1994;330(24):1731-8. [[Medline](#)].
9. Hehrmann R. [Coma in myxedema--a rare complication of hypothyroidism. Possible iatrogenic factors should be taken into account]. *Fortschr Med*. Dec 10 1996;114(34):474-8. [[Medline](#)].
10. Kinuya S, Michigishi T, Tonami N, et al. Reversible cerebral hypoperfusion observed with Tc-99m HMPAO SPECT in reversible dementia caused by hypothyroidism. *Clin Nucl Med*. Sep 1999;24(9):666-8. [[Medline](#)].
11. Menendez CE, Rivlin RS. Thyrotoxic crisis and myxedema coma. *Med Clin North Am*. Nov 1973;(6):1463-

70. [\[Medline\]](#).
12. Rimar D, Kruzel-Davila E, Dori G, Baron E, Bitterman H. Hyperammonemic coma--barking up the wrong tree. *J Gen Intern Med.* Apr 2007;22(4):549-52. [\[Medline\]](#).
13. Roberts CG, Ladenson PW. Hypothyroidism. *Lancet.* Mar 6 2004;363(9411):793-803. [\[Medline\]](#).
14. Smith SA. Commonly asked questions about thyroid function. *Mayo Clin Proc.* Jun 1995;70(6):573-7. [\[Medline\]](#).
15. Ragland E, Urbanic RC, Harwood-Nuss AL, et al, eds. *Thyroid Emergencies.* 1996. Philadelphia, Pa: Lippincott-Raven Pub; 736-41.
16. Tunbridge WM, Evered DC, Hall R, et al. The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinol (Oxf).* Dec 1977;7(6):481-93. [\[Medline\]](#).
17. Vanderpump MP, Tunbridge WM, French JM, et al. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. *Clin Endocrinol (Oxf).* Jul 1995;43(1):55-68. [\[Medline\]](#).
18. Wang C, Crapo LM. The epidemiology of thyroid disease and implications for screening. *Endocrinol Metab Clin North Amer.* 1997;26(1):189-218. [\[Medline\]](#).
19. Wartofsky L, Ingbar SH. Diseases of the thyroid. In: Wilson JD, Braunwald E, et al, eds. *Harrison's Principles of Internal Medicine.* 1991:1692-1712.
20. Wogan JM. Endocrine disorders. In: Rosen P, Barkin RM, et al, eds. *Emergency Medicine: Concepts and Clinical Practice.* 1992:2242-59.
21. Yamamoto T, Fukuyama J, Fujiyoshi A. Factors associated with mortality of myxedema coma: report of eight cases and literature survey. *Thyroid.* Dec 1999;9(12):1167-74. [\[Medline\]](#).

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