HYPERTHYROIDISM AND THYROID STORM

THYROID HORMONE AFFECTS ALL ORGAN SYSTEM AND IS RESPONSIBLE FOR INCREASING METABOLIC RATE, HEART RATE AND CONTRACTILITY AS WELL AS MUSCLE AND C.N.S. EXCITABILITY

T3 IS 3-4 TIMES MORE POTENT THAT T4

HYPERTHYROIDISM REFERS TO EXCESS CIRCULATING HORMONE RESULTING FROM HYPERFUNCTION OF THE THYROID GLAND

THYROTOXICOSIS REFERS TO EXCESS CIRCULATING THYROID HORMONE ORIGINATING FROM ANY CAUSE

THYROID STORM IS THE EXTREME MANIFESTATION OF THYROTOXICOSIS AND IS AN ACUTE, SEVERE, LIFE-THREATENING FORM OF THYROTOXICOSIS FOLLOWING THE PRESENCE OF ONE OR MORE PRECIPITANTS

CAUSES OF HYPERTHYROIDISM

- Divided into primary and secondary causes
  - Primary → due to excess production of thyroid hormones form the thyroid glands
  - Secondary → excess production of thyroid-releasing hormones or TSH in hypothalamus/pituitary
- Can also be due to non-thyroidal causes or drug-induced

Table 224-1 Causes of Hyperthyroidism: Primary and Secondary Hyperthyroidism	
Primary Hyperthyroidism	
Graves disease (toxic diffuse goiter) (**Figure 224-0.1**)	Most common of all hyperthyroidism (85% of all cases)
	Associated with diffuse goiter, ophthalmopathy, and local dermopathy
Toxic multinodular goiter	Second most common cause of hyperthyroidism
Toxic nodular (adenoma) goiter (**Figure 224-0.2**)	An enlarged thyroid gland that contains a small rounded mass or masses called nodules with overproduction of thyroid hormone
Secondary Hyperthyroidism	
Thyrotropin-secreting pituitary adenoma	Thyroid gland stimulated to produce hormones
Thyroiditis	Inflammation of the thyroid gland.
Hashimoto thyroiditis	Initially gland is overactive (hyperthyroidism state) but this is usually followed by a state of hypothyroidism
Subacute painful thyroiditis (de Quervain thyroiditis)	
Subacute painless thyroiditis	
Radiation thyroiditis	

Table 224-2 Other Causes of Hyperthyroidism	
Nonthyroidal Disease	
Ectopic thyroid tissue (struma ovarii)/teratoma	A rare form of mature teratoma that contains mostly thyroid tissue.
Metastatic thyroid cancer	Stimulates production of thyroid hormones.
Human chorionic gonadotropin	Secreting hydatidiform mole.
Drug-Induced	
Iodine	Iodine-induced thyrotoxicosis (called *Jod-Basedow disease*).
	After treatment of endemic goiter patients with iodine or stimulation of thyroid hormones from use of iodine-containing agents like radiographic contrast agents.
Amiodarone	Contains iodine. May cause either thyrotoxicosis or hypothyroidism.
α-Interferon	During treatment for other diseases, such as viral hepatitis and human immunodeficiency virus infection.
Interleukin-2	
Excessive thyroid hormone ingestion	—
Thyrotoxicosis factitia	Munchausen-like; thyroid hormone is taken by patient to fake illness.
Ingestion of meat containing beef thyroid tissue	Cow thyroid tissue contains thyroid hormones.

PATHOPHYSIOLOGY:

- The mechanisms underlying the shift from uncomplicated hyperthyroidism to thyroid storm ARE NOT CLEAR
- It is thought to involve ADRENERGIC HYPERACTIVITY EITHER DUE TO INCREASED HORMONE PRODUCTION OR INCREASED RECEPTOR SENSITIVITY → many of the signs and symptoms are related to adrenergic hyperactivity
- During thyroid storm, precipitants (infection, stress, AMI, trauma) → will multiply the effect of thyroid hormones by freeing thyroid hormones from their binding sites or increased receptor sensitivity

THYROID STORM PRECIPITATION:

Table 224-3 Precipitants of Thyroid Storm	
Systemic insult	Cardiovascular insult
Infection	Myocardial infarction
Trauma	Cerebrovascular accidents
General surgery	Pulmonary embolism
Hyperosmolar coma	Obstetrics-related
Endocrinal insult	Parturition
Diabetic ketoacidosis	Eclampsia
Drug- or hormone-related	Unknown etiology in up to 25% of cases
Withdrawal of thyroid medication	
Iodine administration	
Thyroid gland palpation	
Ingestion of thyroid hormone	

CLINICAL FEATURES OF THYROID STORM:

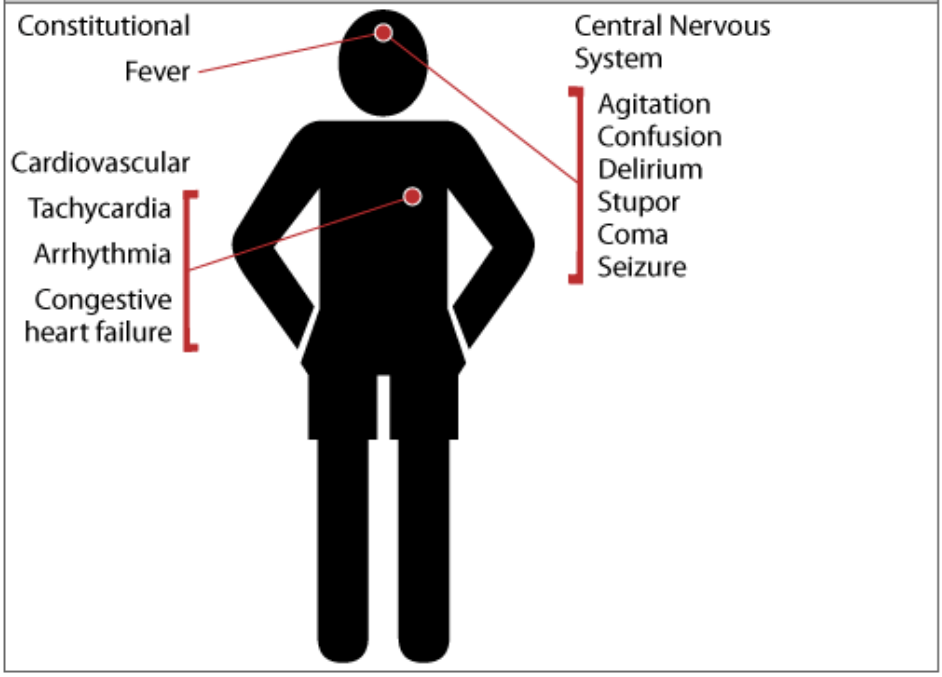
- HISTORY:
  - Patient may only complain of constitutional symptoms → weakness, fatigue, heat intolerance, diaphoresis, fever, weight loss, anxiety and emotional lability can all occur
  - Determine compliance with treatment as well as increased doses of thyroid hormone or anti-thyroidhormone
- PHYSICAL EXAMINATION:
  - Patients often appear toxic and agitated

Table 224-4 Symptoms and Signs of Thyrotoxicosis

Affected System	Symptoms	Signs
Constitutional	Lethargy	Diaphoresis
	Weakness	Fever
	Heat intolerance	Weight loss
Neuropsychiatric	Emotional lability	Fine tremor
	Anxiety	Muscle wasting
	Confusion	Hyperreflexia
	Coma	Periodic paralysis
	Psychosis	
Ophthalmologic	Diplopia	Lid lag
	Eye irritation	Dry eyes
		Exophthalmos
		Ophthalmoplegia
		Conjunctival infection
Endocrine: thyroid gland (**Figure 224-1**)	Neck fullness	Thyroid enlargement
	Tenderness	Bruit
Cardiorespiratory	Dyspnea	Widened pulse pressure
	Palpitations	Systolic hypertension
	Chest pain	Sinus tachycardia
		Atrial fibrillation or flutter
		Congestive heart failure
GI	Diarrhea	Hyperactive bowel sound
Endocrine: thyroid gland (**Figure 224-1**)	Neck fullness	Thyroid enlargement
	Tenderness	Bruit
Cardiorespiratory	Dyspnea	Widened pulse pressure
	Palpitations	Systolic hypertension
	Chest pain	Sinus tachycardia
		Atrial fibrillation or flutter
		Congestive heart failure
GI	Diarrhea	Hyperactive bowel sound
Reproductive	Oligomenorrhea	Gynecomastia
	Decreased libido	Telangiectasia
Gynecologic	Menorrhagia	Sparse pubic hair
	Irregularity	
Hematologic	Pale skin	Anemia
		Leukocytosis
Dermatologic	Hair loss	Pretibial myxedema
		Warm, moist skin
		Palmar erythema
		Onycholysis

- Thyroid storm will have symptoms of thyrotoxicosis as well

Table 224-5 Presenting Signs and Symptoms of Thyroid Storm



- Fever is quite high
- Direct inotropic and chrontropic effects of thyroid hormone cause decreased SVR, increased blood volume, increased contractility and increased cardiac output
- AF occurs in 10-35%

- THYROID STORM IS A CLINICAL DIAGNOSIS FOR PATIENTS WITH PRE-EXISTING HYPERTHYROIDISM → fever and tachycardia are cardinal features

Table 224-6 Differential Diagnosis for Thyroid Storm
Infection and sepsis
Sympathomimetic ingestion (e.g., cocaine, amphetamine, ketamine drug use)
Heat exhaustion
Heat stroke
Delirium tremens
Malignant hyperthermia
Malignant neuroleptic syndrome
Hypothalamic stroke
Pheochromocytoma
Medication withdrawal (e.g., cocaine, opioids, etc.)
Psychosis
Organophosphate poisoning

- BURCH AND WARTOFSKY HAVE DELINEATED A POINT SYSTEM ASSESSING DEGREES OF DYSFUNCTION IN FOUR SYSTEM AND THIS ASSISTS IN DETERMINING LIKELIHOOD OF THYROID STORM (see table overleaf)

Table 224-7 Burch and Wartofsky's Diagnostic Parameters and Scoring Points for Thyroid Storm	
Diagnostic Parameters	**Scoring Points**
1. Thermoregulatory dysfunction	
Temperature °C (°F)	
37.2–37.7 (99–99.9)	5
37.7–38.3 (100–100.9)	10
38.3–38.8 (101–101.9)	15
38.9–39.4 (102–102.9)	20
39.4–39.9 (103–103.9)	25
≥40 (≥104.0)	30
2. Central nervous system effects	
Absent	0
Mild (agitation)	10
Moderate (delirium, psychosis, extreme lethargy)	20
Severe (seizures, coma)	30
3. GI-hepatic dysfunction	
Absent	0
Moderate (diarrhea, nausea/vomiting, abdominal pain)	10
Severe (unexplained jaundice)	20
4. Cardiovascular dysfunction	
Tachycardia (beats/min)	
90–109	5
110–119	10
120–129	15
≥140	25
5. Congestive heart failure	
Absent	0
Mild (pedal edema)	5
Moderate (bibasilar rales)	10
Severe (pulmonary edema)	15
6. Atrial fibrillation	
Absent	0
Present	10

Scoring system:

Score of ≥45: Highly suggestive of thyroid storm.

Score of 25–44: Suggestive of impending storm.

Score of <25: Unlikely to represent thyroid storm.

LABORATORY EVALUATION:

- TSH → low in primary hyperthyroidism due to negative feedback of high T4/T3. But a low TSH can occur in chronic liver or kidney disease or the effect of drugs such as glucocorticoids. TSH is increased in secondary hyperthyroidism due to overproduction in the pituitary
- Free T3/Free T4 → not necessarily acutely elevated when the transition to thyroid storm occurs
- Thyroid antibody titres → if Grave's disease is suspected, thyroid antibody titres (thyroid peroxidase, thyroglobulin or TSH antibodies) all tested
- Miscellaneous → BSL (↑d due to catecholamine surge), deranged LFTs
- ECG → AF (10-35%), sinus tachycardia in 40%

TREATMENT FOR THYROID STORM:

Table 224-8 Treatment for Thyroid Storm
1. Supportive care
General: oxygen, cardiac monitoring.
Fever: external cooling; acetaminophen, 325–650 milligrams PO/PR every 4–6 h (aspirin is contraindicated because it may increase free T_4).
Dehydration: IV fluids, IV 5% dextrose in water may be used to replace glycogen depletion if hypoglycemic.
Nutrition: glucose, multivitamins, thiamine, including folate (deficient secondary to hypermetabolism).
Cardiac decompensation (atrial fibrillation, congestive heart failure): rate control and inotropic agent, diuretics, sympatholytics as required.
2. Inhibition of thyroid hormone release with thionamides
PTU, a loading dose of 600–1000 milligrams given PO and followed by 200–250 milligrams every 4 h. Total daily dose should be given: 1200–1500 milligrams/d. Drug can be given via nasogastric tube or PR. (PTU is the preferred thionamide as it also blocks peripheral conversion of T_4 to T_3.)
or
Methimazole, 40 milligrams given PO as loading dose and followed by 25 milligrams every 4 h. Total daily dose should be given: 120 milligrams/d. If given PR, 40 milligrams should be crushed in aqueous solution.
3. Inhibition of new thyroid hormone production (at least 1 h after step 2)
Lugol solution, 8–10 drops PO every 6–8 h.
or
Potassium iodide (SSKI), five drops PO every 6 hours.
or
IV iopanoic acid (Telepaque®), 1 gram every 8 h for first 24 h, then 500 milligrams twice a day.
or
Ipodate (Oragrafin®), 0.5–3 grams/d PO (especially useful with thyroiditis or thyroid hormone overdose).
or
Lithium carbonate (if allergic to iodine or agranulocytosis occurs with thionamides), 300 milligrams PO every 6 h (1200 milligrams/d) and subsequently to maintain serum lithium at 1 mEq/L.
4. β-adrenergic receptor blockade
Propranolol, IV in slow 1- to 2-milligram boluses, which may be repeated every 10 to 15 min until the desired effect is achieved. For less toxic patient, PO dose of 20 to 120 milligrams per dose or 160 to 320 milligrams/d in divided doses (contraindicated in bronchospastic disease and congestive heart failure). Treat congestive heart failure before starting propranolol (e.g., starting dobutamine).
or
Esmolol, 500 micrograms/kg IV bolus, then 50–200 micrograms/kg/min maintenance (selective β-adrenergic blocker).
or
Reserpine, 2.5–5.0 milligrams IM every 4–6 h, preceded by 1-milligram test dose while monitoring blood pressure (use if β-blocker contraindicated and congestive heart failure, hypotension, and cardiac shock not present, see the Alternative Treatments section).
or
Guanethidine, 30–40 milligrams PO every 6 h (use if β-blocker contraindicated and congestive heart failure, hypotension, and cardiac shock not present, see the Alternative Treatments section).
5. Preventing peripheral conversion of T_4 to T_3
Hydrocortisone, 100 milligrams IV initially, then 100 milligrams three times/d until stable (also for adrenal replacement due to hypermetabolism).
or
Dexamethasone, 2 milligrams IV every 6 h.
6. Treat precipitating event
All triggers of thyroid storm should be searched and treated accordingly (infection, myocardial infarct, diabetic ketoacidosis, etc.).
7. Definitive therapy
Radioactive iodine ablation therapy or surgery may be necessary.

Note: Replacement therapy: dialysis and plasmapheresis are last resorts for patients who do not respond to treatments 1–5.

- The order of therapy is very important (especially with use of thionamide prior to iodine therapy)

- GENERAL TREATMENT AIMS:
  - SUPPORTIVE CARE
  - INHIBITION OF THYROID HORMONE RELEASE
  - INHIBITION OF NEW HORMONE PRODUCTION
  - PERIPHERAL β-ADRENERGIC BLOCKADE
  - PREVENTING PERIPHERAL CONVERSION OF T4 TO T3
- SUPPORTIVE CARE:
  - Fluid losses should be replaced → high losses due to fever, diaphoresis, vomiting and diarrhoea → glucose-containing to replenish glycogen stores
  - CHOLESTYRAMINE → inhibits thyroid hormone reabsorption through interruption of enterohepatic re-circulation of thyroid hormone
  - Rate control/inotropes for cardiac decompensation
- INHIBITION OF THYROID HORMONE RELEASE:
  - THIONAMIDE (PROPYLTHIOURACIL, PTU) → or methimazole. Decreases synthesis or new hormone, but also has immunosuppressive effects. PTU also inhibits conversion of T4 to T3
    - Dose of PTU is 600-1000microg loading then 200-250q4h → orally, NG, or PR
- INHIBITION OF NEW HORMONE PRODUCTION:
  - IODINE → lugol solution to stop new production but thionamide bust be instituted first.
    - Iodide therapy blocks release of prestored hormone and decreased iodide transport
    - Do not give to those with amiodarone-induced thyrotoxicosis or iodine-overload induced thyrotoxicosis → alternative is lithium or potassium perchlorate
      - Amiodarone is 37% iodine by weight, which amounts to 10-20 times the normal dietary requirement of iodine → thyrotoxic (causing hypo or hyperthyroidism) in 20-30% patients
    - Iodine dose is 8-10 drops initially
- PREVENTING PERIPHERAL CONVERSION OF T4 TO T3:
  - Conversion of T4 to T3 is responsible for 85% of T3 present in the circulation
  - Blocked by PTU and propranolol to some degree but GLUCOCORTICOIDS ARE ESSENTIAL
  - Glucocorticoid use in thyroid storm improve survival outcome, probably due to possibility of relative adrenal insufficiency
- BETA-ADRENERGIC RECEPTOR BLOCKADE:
  - PROPRANOLOL → give in 1-2mg IV boluss, which may be repeated every 10-15 minutes until desired effect. Oral doses 20-120mg per dose up to 360mg daily
  - Alternatives to β-blockade may be necessary if severe asthmatic include GUANETHEDINE/RESERPINE as they do not block beta receptors.
    - Reserpine is an alkaloid agent depletes catecholamines stores
    - Guanethedine inhibits release of catecholamines

- ALL THYROID STORM PATIENTS REQUIRE ADMISSION TO THE INTENSIVE CARE UNIT
    - HYPERTHYROID PATIENTS WITH MINMAL SYMPTOMS CAN ONLY BE DISCHARGED FOR FOLLOW-UP WITH ENDOCRINOLOGIST OR PRIMARY CARE PHYSICIAN

Table 224-10 Common Adverse Side Effects from Antithyroid Drugs