Glucocorticoids are used in the treatment of thyroid storm because:
(i) they have an inhibitory effect on peripheral conversion of T4 to T3. [The clinical relevance of this minor effect is unknown.]
(ii) they treat possible relative adrenal insufficiency. One study found inappropriately normal levels of cortisol in a subset of patients with thyroid storm. This study found improved control in those subjects treated with glucocorticoids.

Dosing of glucocorticoids in thyroid storm can be made with hydrocortisone 100 mg intravenously every 8 hours, with tapering as the signs of thyroid storm improve.

General

- The cardiovascular changes seen with thyrotoxicosis occur because of the different effects of thyroid hormone on the heart and on systemic vasculature.
- Thyroid hormone decreases systemic vascular resistance by a direct vasoactive action on smooth muscle and by endothelial release of nitric oxide or other endothelial-derived vasodilators.
- Iodine thyroid hormone on the heart is mediated partly by the genomic effects of T3 binding to specific nuclear receptors. In addition to these genomic effects of T3 in the heart, thyroid hormone also has nongenomic actions, directly altering the performance of sodium, potassium, and calcium channels.

Beta blockade

- In thyroid storm, propranolol is dosed at 60 to 80 mg every 4 hours, or 80 to 120 mg every 4 hours.
- The onset of action after oral dosing takes place within 1 hour. For a more rapid effect, propranolol can also be given intravenously at a rate of 0.1 to 0.2 mg over 10 minutes followed by 1 to 3 mg over 10 minutes, every few hours, depending on the clinical context.
- In addition to its effect on beta-adrenergic receptors, large doses (greater than 160 mg daily) decrease T3 levels by as much as 30%. This effect, mediated by the inhibition of 5′-deiodinase, is mediated slowly over 7 to 10 days.
- Esmolol can also be administered parenterally at a dose of 50 to 100 mg/kg/min. Relatively large doses of propranolol are required in the setting of thyrotoxicosis because of the faster metabolism of the drug and possibly because of a greater quantity of cardiac beta-adrenergic receptors.
- Longer-acting cardioselective beta-adrenergic receptor antagonists such as atenolol and metoprolol may be used also in conjunction with other agents, in the setting of thyroid storm.

Thionamides

- Several therapeutic agents used in the treatment of thyrotoxicosis are only considered when the first-line therapies of thionamides, iodide, beta-blockers, and glucocorticoids fail or cannot be used owing to toxicity.

(i) Iodide

- When iodide therapy cannot be used, another agent that can be used to inhibit thyroid hormone release is lithium. Lithium can also be used when thionamide therapy is contraindicated because of toxicity or allergy. Lithium has several effects on the thyroid gland, including directly decreasing thyroid hormone synthesis and secretion and thereby inhibiting thyroid hormone release, decreasing T3 and T4 levels, and inhibiting coupling of iodothyronine residues that form iodothyronines (T4 and T3).
- In thyroid storm, the dosing for lithium is 300 mg every 8 hours. To avoid lithium toxicity, lithium level should be monitored regularly (perhaps even daily) to maintain a concentration of about 0.6-1.0 mEq/L.

(ii) Reserpine & guanethidine

- Before beta-adrenergic receptor antagonists were used to counteract the peripheral effects of thyroid hormone, the antihypertensive agents, reserpine and guanethidine, were often used.
- Reserpine is an alkaloid that depletes catecholamines in sympathetic nerve terminals and the central nervous system.
- Guanethidine also inhibits the release of catecholamines.
- Side effects of these medications include hypotension and diarrhea. Guanethidine can also cause central nervous system depressant effects.
- These agents are indicated only in rare situations where beta-adrenergic receptor antagonists are contraindicated, and when there is no hypertension or evidence of central nervous system-mediated status changes.
- Dosing for guanethidine in thyroid storm is 30 to 40 mg orally every 6 hours, and for reserpine 2.5 to 5 mg intramuscularly every 4 hours.

(iii) Cholestyramine

- An anion exchange resin, has also been used in the treatment of thyrotoxicosis to deplete serum thyroxine from the enterohepatic circulation. In several trials, cholestyramine therapy, in combination with thionamides, caused a more rapid decline in thyroid hormone levels than standard therapy with thionamides alone. In these trials, cholestyramine was dosed at 4 g orally 4 times a day.
- The effects of cholestyramine is generally minimal and should not be administered at the exact same time as other medications because it may inhibit their absorption. On the other hand, cholestyramine is not expected to be associated with significant adverse effects.

(iv) Plasmapheresis

- When clinical deterioration occurs in thyroid storm, despite the use of all of these medications, removal of thyroid hormone from circulation can be a therapeutic consideration. Plasma exchanges, which can deplete thyroid hormone, result in decreased serum thyroid hormone levels, but the efficacy of this treatment is limited.
- Plasma exchange has been found to be effective in rapidly reducing thyroid hormone levels in thyroid storm.

- Supportive care is an important part of the multisystem therapeutic approach to thyroid storm.
- Because fever is very common with severe thyrotoxicosis, antipyretics should be used; paracetamol is the preferable choice. Systolic fever should be avoided in thyrotoxicosis because systolic fever can decrease thyroid protein synthesis, increase in free thyroid hormone levels, and intrathyroidal radioactive iodine in thyrotoxicosis. Thus, fever-free and dehydration are also common in severe thyrotoxicosis. The fluid losses could result from the combination of fever, diaphoresis, vomiting, and diarrhea.
- Intravenous fluids with dextrose (isotonic saline with 5% or 10% dextrose) should be given to replenish glycan stores.
- Patients should also receive multivitamins, particularly thiamine, to prevent Wernicke's encephalopathy, which could result from the administration of intravenous fluids with dextrose in the presence of thiamine deficiency.
- Treating the precipitant, which in thyroid storm is particularly common precipitant is thought to be infection. If a precipitating factor were not readily apparent, a vigorous search for an infectious source would be warranted in the factible thyrotropic patient; this would be done with blood, urine, and sputum cultures, and a chest radiograph. Generally, however, empiric antibiotics are not recommended without an identified source of infection.

Mechanism of action

- In the setting of thyroid storm, iodine therapy complements the effects of thionamide therapy. Thionamide therapy decreases the synthesis of new thyroid hormone; iodide therapy blocks the release of stored hormone, and decreases iodide transport and oxidation in follicular cells.
- Small increments in available iodide cause increased formation of thyroid hormone; however, large amounts of exogenous iodine actually inhibit hormone formation. This decrease in organification due to increasing doses of inorganic iodine is known as the Wolff-Chaikoff effect. However, despite maintenance of high doses of iodide, the thyroid gland eventually escapes this inhibition as the iodide transport system adapts to the higher concentration of iodide by modulating the activity of the sodium-iodide symporter.
- Although iodine is effective at rapidly reducing serum thyroid hormone levels, usually within 7 to 14 days, most patients escape the inhibition and return to hyperthyroidism within 2 to 3 weeks, if no other treatment is given. Therefore, the use of iodide to treat thyrotoxicosis is of limited use, and is thus used only in severe thyrotoxicosis or thyroid storm in patients with thyrotoxic storm.

Problems with use of iodine

- In the acute setting, if iodine therapy is given before thionamide therapy, new hormone synthesis can be stimulated.
- When planning definitive therapy for thyrotoxicosis after the acute phase of thyroid storm, use of exogenous iodine at any time can predispose a patient to increased surgical risk because of iodine stores, and can be theapse of radioiodine ablation until an adequate clearance of the iodine load is achieved.

Iodine

- Oral formulations of inorganic iodine include Lugol's solution and saturated solution of potassium iodide. The dosing for these preparations in thyroid storm is 0.2 to 2 g daily, with four to five drops of Lugol's solution (assuming 20 drops/mL, 8 mg iodide/cap) every 6 to 8 hours and five drops of saturation solution of potassium iodide (with 20 drops/mL, 38 mg iodide) every 6 hours.
- The iodinated contrast agents, iopanoic acid and iodide, may have multiple effects on thyroid hormone in the periphery and within the thyroid gland. These iodinated contrast agents competitively inhibit Types 1 and 2-5 monodeiodinase in the liver, brain, and thyroid, blocking conversion of T4 to T3, resulting in a rapid decrease in T3 and an increase in reverse T3. These iodinated contrast agents have also been found to inhibit binding of T3 to and cellular receptors. In thyroid storm, iodide (308 mg iodide/500 mg capsules) is dosed at 1 to 3 g daily, usually, iopanoic acid is dosed at 50 to 100 mg every 8 hours for the first 24 hours, followed by 500 mg twice daily.