

56 years old patient with palpitations and SOB

Olesya Krivospitskaya,
MD

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History of past illness:

- 56 years old male presented to ER with palpitations, , dyspnea, orthopnea, LE edema that was going on for 1 week.
- On the day of admission he felt extremely weak, SOB and his heart was racing, that made him come the hospital.
- The patient is active heroin user and is also on methadone treatment.

Past medical history:

- Past medical history:
 - COPD,
 - HTN,
 - hyperthyroidism (was on methimazole for the last two years, dose was increased two weeks before his presentation to the hospital, but the patient stopped medication about one week before ER visit, because he attributed his symptoms to methimazole side effects)
 - Peripheral vascular disease.
- Medications: albuterol, aspirin, budesonide-formoterol, enalapril, esomeprazole, folic acid, lasix, methimazole, spiriva.
- Family history: HTN (mother, sister), no history of diabetes or thyroid problems in his family.
- Social history: active heroine user and also on methadone, unemployed, smokes 1PPD for 40 years, no alcohol abuse.

Review of systems:

- Constitutional: No fevers. No weight loss. **Fatigue.**
- HEENT: No vision changes. No hoarseness. Neck: No neck swelling or pain.
- Cardiovascular: No chest pain. **Palpitations.**
- Respiratory: **Dyspnea. Orthopnea.**
- Gastrointestinal: No diarrhea. No constipation.
- Musculoskeletal: No muscle pain. **LE edema.**
- Skin: No rash. No skin changes. No hair loss.
- Neurologic: No tremor. No headache. No weakness.
- Psychiatric: No depression. No anxiety. Endo: No polyuria. No polydipsia.

Physical exam:

- Head: Normocephalic and atraumatic. Mouth/Throat: Oropharynx is clear and moist. No oropharyngeal exudate.
- Eyes: EOM are normal. Pupils are equal, round, and reactive to light. No scleral icterus.
- Neck: Normal range of motion. Neck supple. **JVD present.** No tracheal deviation present. No thyromegaly present.
- Cardiovascular: **Irregularly irregular rhythm**, normal heart sounds and intact distal pulses. No friction rub. No murmur heard.
- Pulmonary/Chest: **Bilateral crackles. Moderate respiratory distress.** No wheezes. No rales. No tenderness.
- Abdominal: Soft. Bowel sounds are normal. No distension and no mass. There is no tenderness. There is no rebound and no guarding. **Swollen abdominal wall.**
- Musculoskeletal: Normal range of motion. No edema and no tenderness. No cervical adenopathy.
- Neurological: She is alert and oriented to person, place, and time. No cranial nerve deficit. Normal muscle tone. Coordination normal. **Brisk reflexes in upper and lower extremities. LE edema 3+.**
- Skin: Skin is warm. Not diaphoretic. No erythema. No pallor. **Scar marks for heroin injections.**
- Psychiatric: normal mood and affect, behavior is normal. Judgment and thought content normal.
- Vitals: BP 106/75, **Pulse 146**, Temp 35.1 °C (95.2 °F) (Tympanic), Resp 15, Ht 175.3 cm (5' 9") , Wt 81.647 kg (180 lb), BMI 26.58 kg/m², SpO₂ 92%

Labs:

7.3 14.7 161
42.9

Thyroid labs:

TSH < 0.01, free T3 1073
(230-420), free T4 2.4
(0.9-1.7), TSI 5.1

Chest X-ray
showed bilateral
pulmonary edema

138	98	11
4.2	30	0.6

98

Ca 8.1

Mg 1.4

Phos 3.5

AST 27

ALT 23

Bilirubin total 2.9

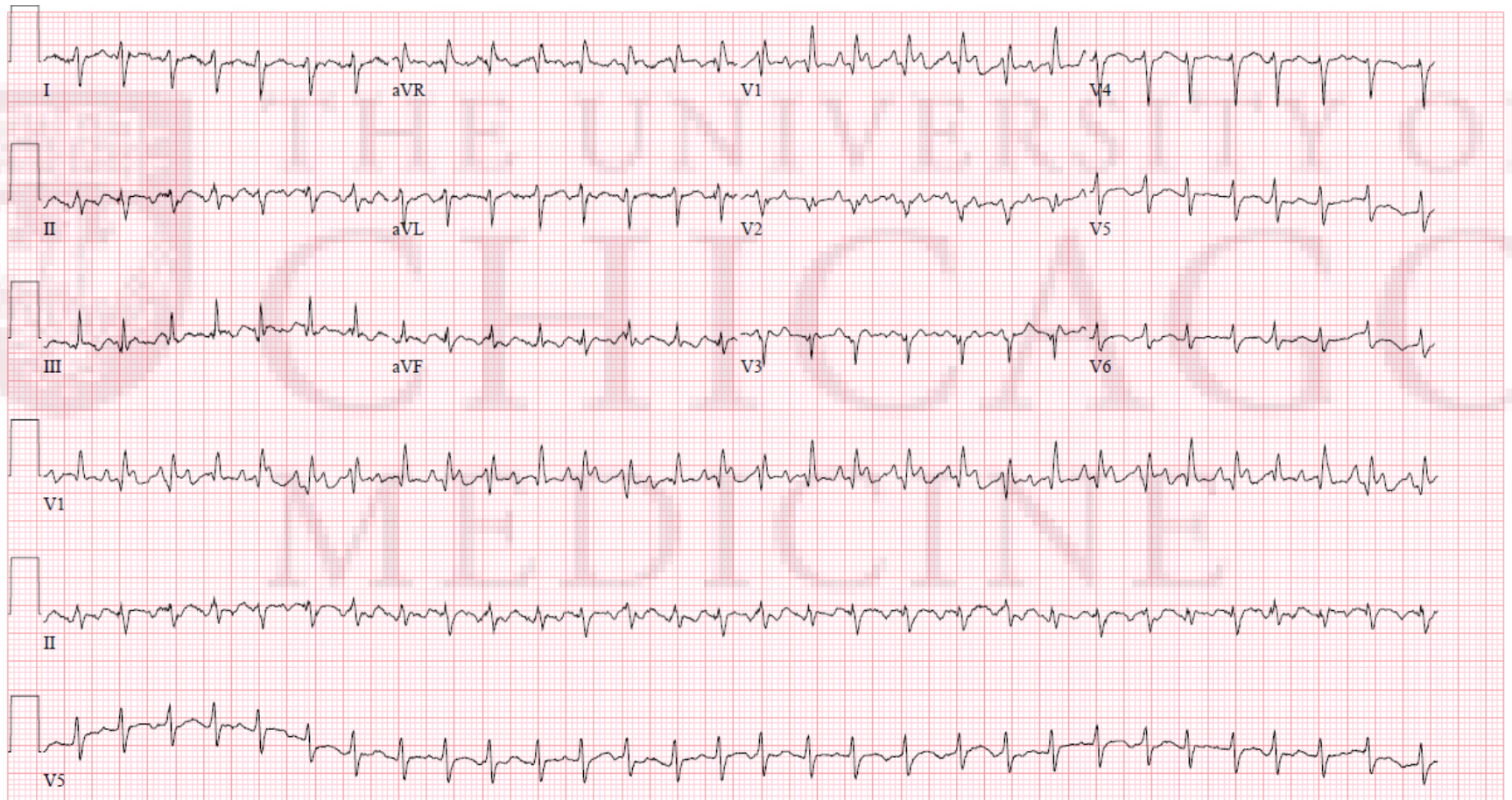
Bilirubin conjugated 1.9

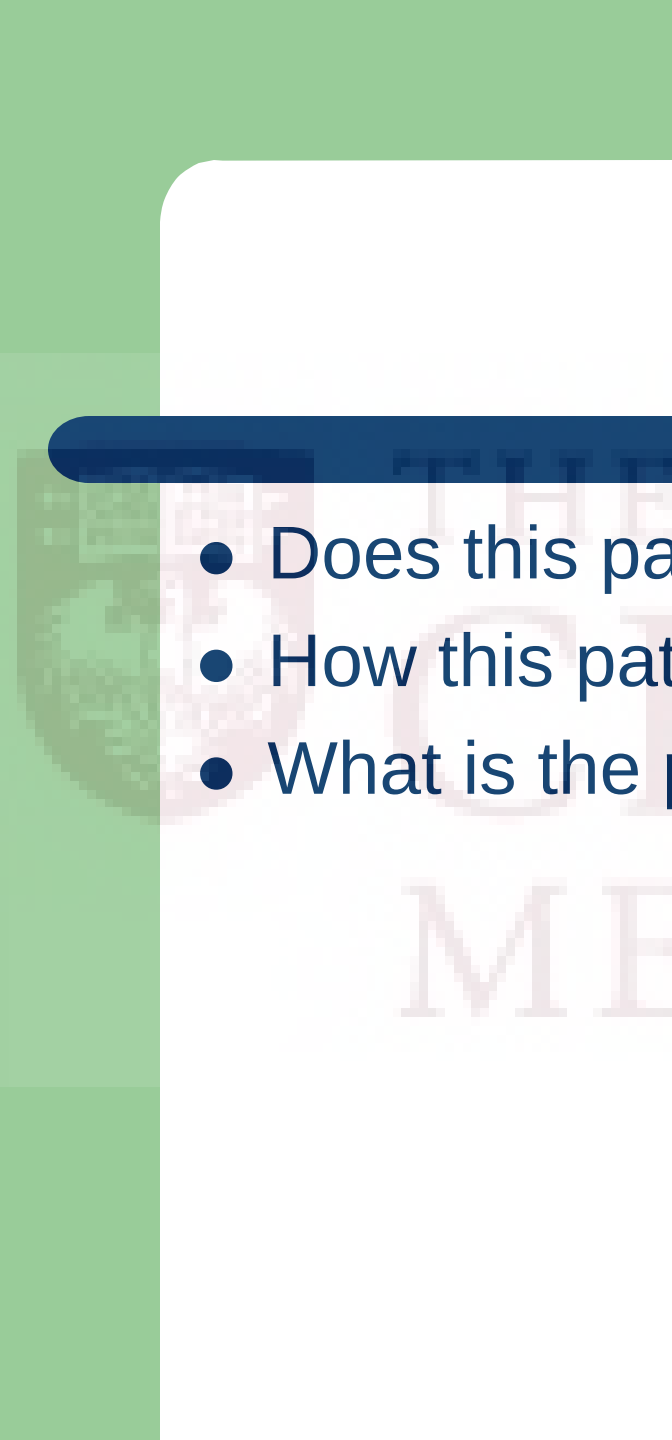
Bilirubin unconjugated 1.0

Alkaline phosphatase 162

BNP 2607

EKG



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- A solid green vertical bar on the left side of the slide, extending from the top to the bottom.
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- A dark blue horizontal bar with rounded ends, positioned above the list of questions.
- Does this patient has thyroid storm?
 - How this patient should be managed?
 - What is the prognosis and mortality rate?

Thyroid storm

- Rare, life-threatening condition characterized by severe clinical manifestations of thyrotoxicosis.
- Incidence of thyroid storm in hospitalized patients is 0.20 per 100,000 per year.
- Can develop in patients with long-standing untreated hyperthyroidism (Graves' disease, toxic multinodular goiter, solitary toxic adenoma), but often precipitated by an acute event such as thyroid or nonthyroidal surgery, trauma, infection, an acute iodine load, or parturition.
- Mortality rate is 10-30%.

Diagnostic criteria for thyroid storm

Diagnostic criteria for thyroid storm*

Thermoregulatory dysfunction		Cardiovascular dysfunction	
Temperature (°F °C)		Tachycardia	
99 to 99.9 37.2 to 37.7	5	99 to 109	5
100 to 100.9 37.8 to 38.2	10	110 to 119	10
101 to 101.9 38.3 to 38.8	15	120 to 129	15
102 to 102.9 38.9 to 39.4	20	130 to 139	20
103 to 103.9 39.4 to 39.9	25	≥140	25
≥104.0 >40.0	30	Atrial fibrillation	10
Central nervous system effects		Heart failure	
Mild	10	Mild	5
Agitation		Pedal edema	
Moderate	20	Moderate	10
Delirium		Bibasilar rales	
Psychosis		Severe	15
Extreme lethargy		Pulmonary edema	
Severe	30	Precipitant history	
Seizure		Negative	0
Coma		Positive	10
Gastrointestinal-hepatic dysfunction			
Moderate	10		
Diarrhea			
Nausea/vomiting			
Abdominal pain			
Severe	20		
Unexplained jaundice			

* A score of 45 or more is highly suggestive of thyroid storm; a score of 25 to 44 supports the diagnosis; and a score below 25 makes thyroid storm unlikely. Adapted from: Burch HB, Wartofsky L. Life-threatening thyrotoxicosis. Thyroid storm. *Endocrinol Metab Clin North Am* 1993; 22:263.

Our patient's score was 50

Management of thyroid storm:

- All principles of management are outlined on the basis of case studies and clinical experience.
- Major principles:
 - A beta-blocker to control the symptoms and signs induced by increased adrenergic tone,
 - A thionamide to block new hormone synthesis,
 - An iodine solution to block the release of thyroid hormone,
 - An iodinated radiocontrast agent (if available) to inhibit the peripheral conversion of T4 to T3,
 - Glucocorticoids to reduce T4-to-T3 conversion, promote vasomotor stability, and possibly treat an associated relative adrenal insufficiency.

β-blockers

- Should be used with extreme caution if the patient has heart failure or other contraindications to beta-blockade.
- Propranolol is frequently selected for initial therapy because it can be given intravenously, but this should only be done in a setting where hemodynamics can be monitored. Usually the dose is 60 to 80 mg orally every four to six hours.
- An alternative regimen is esmolol, loading dose of 250 to 500 mcg/kg is given, followed by an infusion at 50 to 100 mcg/kg per minute.
- In patients with reactive airways disease, cardioselective beta-blockers such as metoprolol or atenolol could be considered.

β-blockers

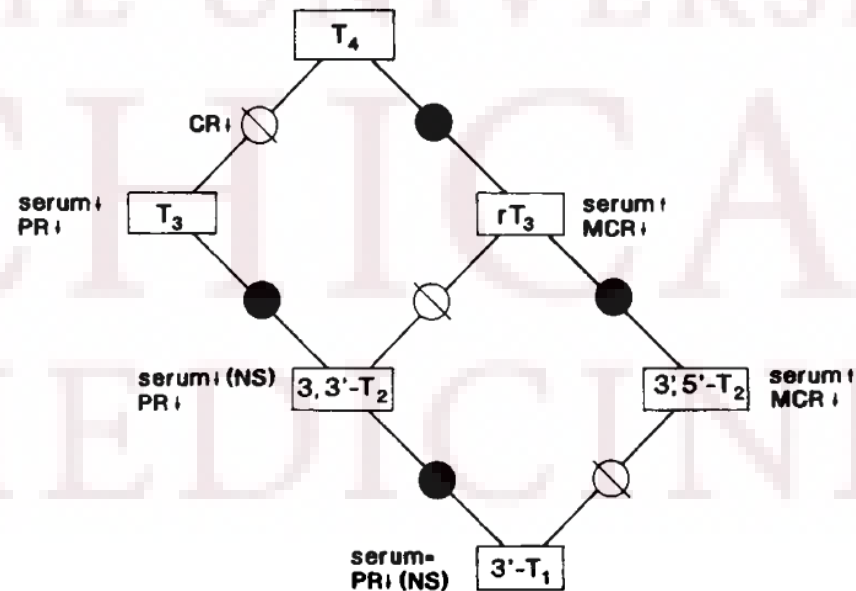


FIG. 1. Effect of propranolol on extrathyroidal kinetics of iodothyronines. MCR, metabolic clearance rate; open circles, 5'-deiodination; black circles, 5-deiodination).

β-blockers

TABLE 3. CLINICAL RESPONSE TO β-BLOCKERS IN HYPERTHYROIDISM IS INDEPENDENT OF DECREASE OF PLASMA T₃

<i>Drug</i>	<i>β₁ selectivity</i>	<i>ISA^a</i>	<i>MSA</i>	<i>Decrease of T₃</i>	<i>Clinical response</i>	<i>Reference</i>
Propranolol	—	—	+	+	+	1-4
Alprenolol	—	+	+	+	+	37,38
Metopropol	+	—	±	±	+	4,35,37
Acebutolol	+	±	±	—	+	26,40
Oxprenolol	—	+	±	—	+	26,40
Practolol	+	+	—	—	+	33
Atenolol	+	—	—	—	+	25,26,37, ^b 39
Sotalol	—	—	—	—	+	24,37,41
Timolol	—	—	—	—	+	44
Nadolol	—	—	—	—	+	27,36,42 ^b

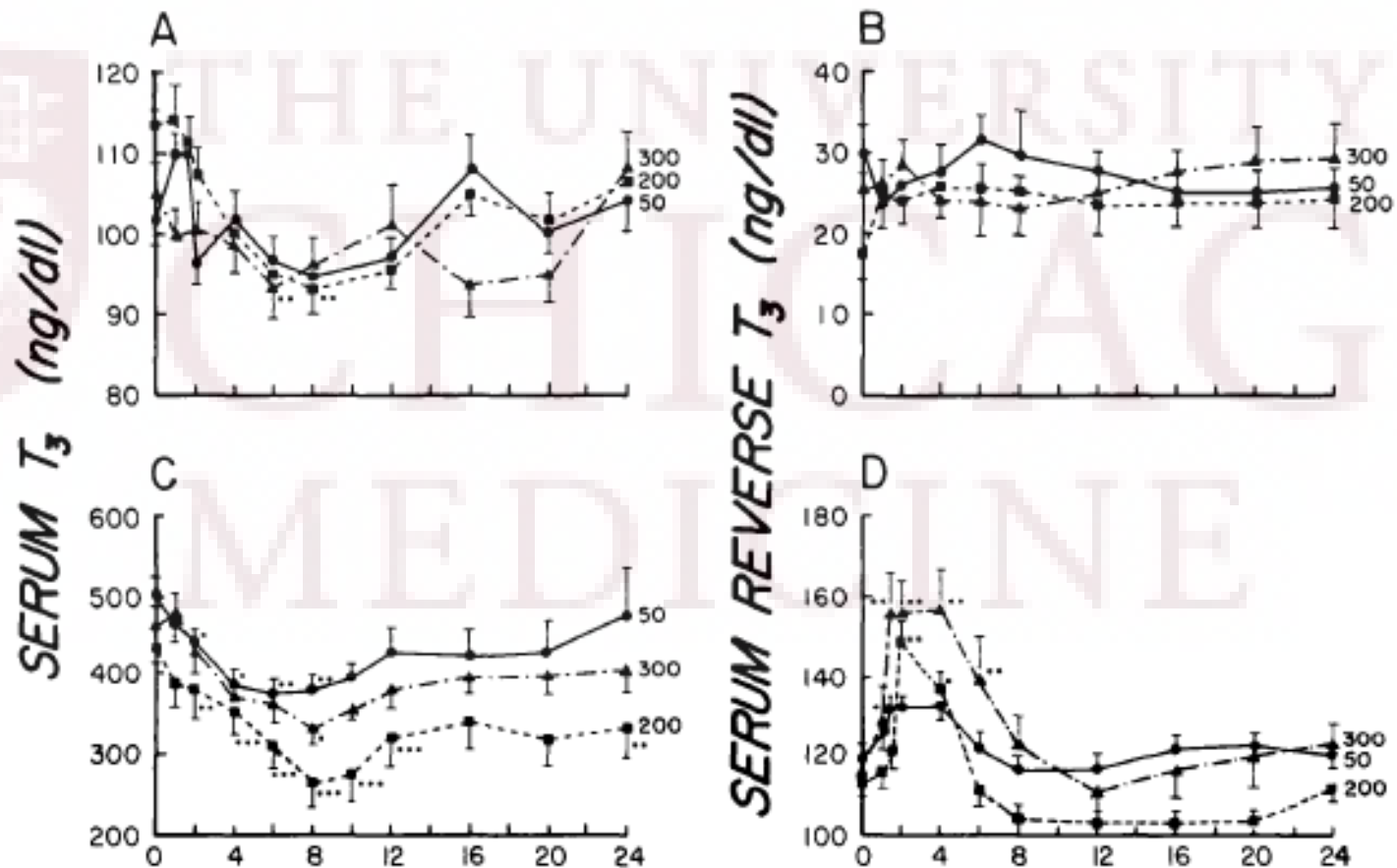
^aISA, intrinsic sympathicomimetic activity; MSA, membrane-stabilizing activity.

^bA decrease of plasma T₃ was observed in studies 37 and 42.

Thionamides

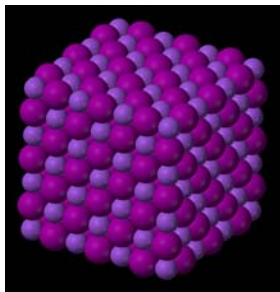
- Block de novo thyroid hormone synthesis within 1 to 2 hrs after administration, however they have no effect on the release of preformed hormone from the thyroid gland.
- PTU is preferred over methimazole: PTU blocks T4 to T3 conversion, there is some evidence that over the first few hours after administration, PTU more rapidly reduces serum T3 concentrations than methimazole. However methimazole is less hepatotoxic, therefore all patients should be transitioned to methimazole before the discharge.

Thionamides



Iodine

- Blocks the release of T4 and T3 from the gland within hours.
- The Wolff–Chaikoff effect can be used as a treatment principle: autoregulatory phenomenon that inhibits organification (oxidation of iodide) in the thyroid gland, the formation of thyroid hormones inside the thyroid follicle, and the release of thyroid hormones into the bloodstream.
- The administration of iodine should be delayed for at least one hour after thionamide administration to prevent the iodine from being used as substrate for new hormone synthesis.
- Oral doses are Lugol's solution, 10 drops (20 drops/mL, 8 mg iodine/drop) three times daily, or SSKI, five drops (20 drops/mL, 38 mg iodide/drop) every six hours.



Glucocorticoids

- Reduce T4 to T3 conversion, and may have a direct effect on the underlying autoimmune process if the thyroid storm is due to Graves' disease, and treat potentially associated limited adrenal reserve.
- Typical dose: hydrocortisone 100 mg intravenously every 8 hrs.

Table 5.—Review of the Literature

Author	Year	Iodides	Thioureas	Steroids or Corticotropin	Reserpine	Guaneth- idine	No. of Cases	No. of Deaths	Percent Died
Bayley ¹	1934	+					51	51 †	100
Ransom and Bayley ²	1934	+					37	37 †	100
Maddock et al ³	1937	+					88	88 †	100
Bansi ⁴	1939	+					32	25	78
MacArthur et al ⁵	1947	+					36	24	67
Rives and Shepard ¹³	1951	+	+				25	10	40
Waldstein et al ⁶	1959	+	+	+	+		21	6	28
This series	1969	+	+	+	+	+	22	4	18(7 ‡)

* Modified from S. S. Waldstein.⁶

† Only deaths reported.

‡ Last ten years.

Other therapies

- Plasmapheresis
- Definitive therapy with radioactive iodine or thyroidectomy is recommended

Plasmapheresis (2 case reports)

Table 1. Follow-Up of Thyroid Hormone Assay Values at Diagnosis, Before and After Pneumonectomy, and After Treatment (With Both Medication and Plasmapheresis)

Days Before (-) or After (+) Surgical Intervention	TSH (mU/L)	FT4 (pmol/L)	FT3 (pmol/L)	TSH Antibody (mU/mL)	Therapy
Normal values	0.47–4.7	9.7–23.4	4.3–8.1	<1	
-65 days	<0.002				Temazepam, thiamazole 20 mg, propranolol
-56 days	<0.02	66.7	28.5	71	Propranolol 3 × 40 mg/d, thiamazole 3 × 20 mg/d, iodide 3 × 10 gtts/d
-6 days	<0.01	34.8	4.3		Propranolol 3 × 40 mg/d, thiamazole 3 × 20 mg/d
+4 days	<0.02	38.2	12.8		Propranolol 3 × 40 mg/d, thiamazole 3 × 20 mg/d, PTU 4 × 200 mg/d, mechanical cooling
+10 days	<0.02	53.6	12.8	11	Propranolol 3 × 40 mg/d PTU 4 × 200 mg/d, potassium perchlorate 2 × 500 mg/d, mechanical cooling
+17 days	<0.02	20.6	9.8	6.6	PTU 4 × 200 mg/d, potassium perchlorate 2 × 500 mg/d, propranolol 3 × 40 mg/d, plasmapheresis since 4 days
+30 days	<0.02	23.8	13.8		Thiamazole 4 × 10 mg/d, propranolol 3 × 40 mg/d, elthyron 50 µg/day
+39 days (leaving ICU)	<0.02	11.5		13	Propranolol 40 mg/d, thiamazole 2 × 10 mg/d
+48 days	<0.02	19.4	7.5		
+147 days	<0.01	21.3			

ICU = intensive care unit; PTU = propylthiouracil; TSH = thyroid-stimulating hormone.

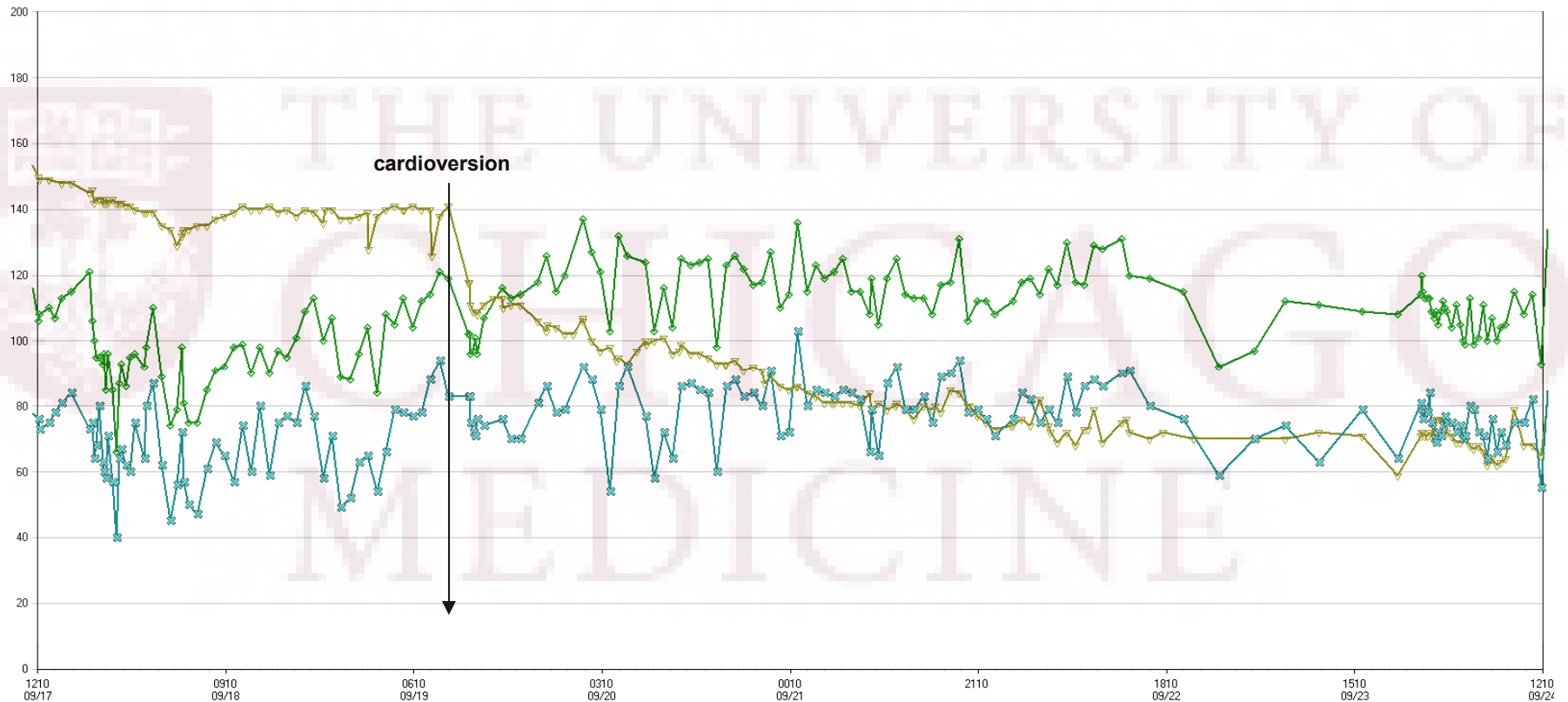
Plasmapheresis (2 case reports)

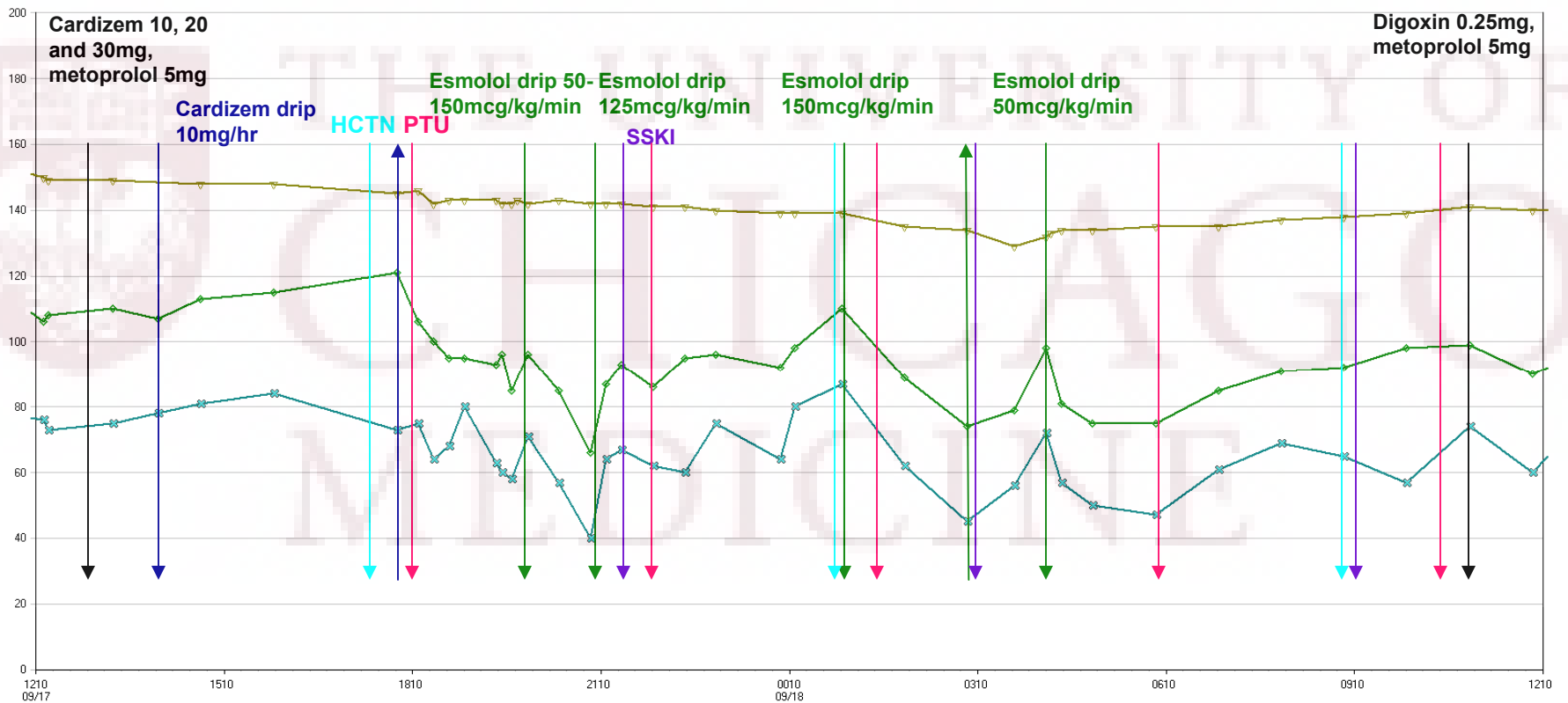
Table 1
Thyroid Hormone Status Throughout Hospital Course of Study Patient^a

Day	TSH (mIU/L)	Free T ₄ (ng/dL)	T ₃ (ng/dL)	Symptoms	Treatment
<i>Reference range</i>	<i>0.45-4.5</i>	<i>0.7-1.7</i>	<i>58-159</i>		
0	2.33	0.9	126	Sore throat	Stopped methimazole
13	<0.03	3.1	376	Tachycardia	Started on propranolol
18	<0.03	2.6	232	Lethargy, fever	Intravenously administered corticosteroids
19	<0.03	2.6	267	Delirium	Plasmapheresis day 1
20	<0.03	2.2	220	Asymptomatic	Plasmapheresis day 2
21	0.07	1.8	239	Asymptomatic	Plasmapheresis day 3
23	<0.03	2.2	167	Asymptomatic	Postplasmapheresis total thyroidectomy
24	<0.03	1.8	48	Asymptomatic	Postthyroidectomy day 1

^a T₃ = triiodothyronine; T₄ = thyroxine; TSH = thyroid-stimulating hormone.

Back to our case





PTU reduced to Q6H,
PTU reduced to Q8H,
SSKI was discontinued, HCTN reduced to 50mg Q8H
PTU discontinued, methimazole 10mg BID started
HCTN discontinued
Methimazole decreased to 5mg BID
Methimazole decreased to 2.5mg BID

	Ref. Range	9/17/20 12 20:32	9/19/20 12 03:37	9/20/20 12 03:51	9/21/20 12 03:44	9/22/20 12 03:57	9/23/20 12 04:55	9/24/20 12 03:44	9/25/20 12 03:40	9/26/20 12 03:47	9/27/20 12 03:43	9/28/20 12 05:29
T3, Free	Latest Range: 230-420 pg/dL	1073 (H)	285	230	184 (L)	171 (L)	149 (L)	152 (L)	152 (L)	157 (L)	189 (L)	182 (L)
T4, Free	Latest Range: 0.9-1.7 ng/dL	2.40 (H)	1.90 (H)	1.65	1.29	1.00	0.78 (L)	0.64 (L)	0.59 (L)	0.55 (L)	0.55 (L)	0.56 (L)
TSH	Latest Range: 0.30-4.00 mcU/mL	<0.01 (L)	<0.01 (L)	<0.01 (L)	<0.01 (L)	<0.01 (L)	<0.01 (L)	0.04 (L)	0.01 (L)	<0.01 (L)	<0.01 (L)	<0.01 (L)

Take home points

- Thyroid storm is a rare, life-threatening condition characterized by severe clinical manifestations of thyrotoxicosis. It is often underdiagnosed.
- Mortality is high.
- Early recognition and aggressive treatment are important.

References

- **Life-threatening thyrotoxicosis. Thyroid storm.** Burch HB, Wartofsky L. Endocrinol Metab Clin North Am. 1993 Jun;22(2):263-77.
- **Propranolol and thyroid hormone metabolism.** Wiersinga WM. Thyroid. 1991 Summer;1(3):273-7.
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- **Thyroid storm. A review of 22 episodes with special emphasis on the use of guanethidine.** Mazzaferri EL, Skillman TG. Arch Intern Med. 1969 Dec;124(6):684-90.
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- **Successful treatment of thyroid storm with plasmapheresis in a patient with methimazole-induced agranulocytosis.** Vyas AA, Vyas P, Fillipon NL, Vijayakrishnan R, Trivedi N. Endocr Pract. 2010 Jul-Aug;16(4):673-6.