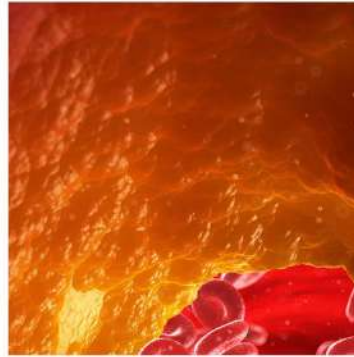
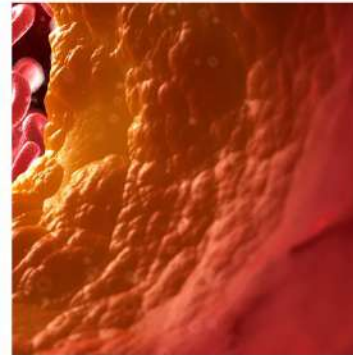
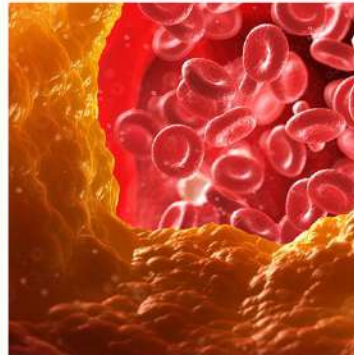


The 2019 EMEA Cardiometabolic Workshop



Saturday,
16 November 2019

Baku, Azerbaijan



Thyroid storm: Treatment and Cardiac complications

**Bernadette Biondi
Salman Razvi**

Learning objectives

- ✓ Recognize a thyroid storm
- ✓ Learn the initial treatment approach to patients with a thyroid storm
- ✓ Evaluate the cardiac complication of patients with over hyperthyroidism

History

- A young woman aged 35 years (height 165 cm, weight 65 kg) came to our ambulatory with dyspnea on exertion, tremor and tachycardia
- She was married with 2 children (aged 5 and 10)
- She had a family history of autoimmune thyroid disease and systemic autoimmune disease (vitiligo and celiac disease)
- She had no history of neck irradiation
- She complained about weight loss, weakness, tremor, palpitations, heat intolerance and anxiety
- She was a smoker

Physical examination and diagnosis

- Her physical examination showed an enlarged thyroid gland, systolic hypertension (blood pressure 170/80 mmHg), and an increased heart rate (128 beats/min)
- She had a small goiter. Thyroid sonography revealed a bilaterally enlarged thyroid gland. Scintigraphy and a 24-hour radioactive iodine showed a diffused increased tracer uptake
- The results of thyroid function tests showed a moderately severe hyperthyroidism, undetectable serum TSH and high levels of thyrotropin receptor antibodies
- She had mild ophthalmopathy

Treatment

- **We started therapy with methimazole (MMI) (20 mg/day) and propranolol (10 mg 3 times per day)**
- **She developed an allergic reaction**
- **This minor cutaneous reaction was managed with concurrent antihistamine therapy and MMI**
- **We proposed a definitive treatment with radioiodine or surgery which was refused by the patient**
- **MMI was prescribed again together with antihistamine therapy with an improvement of her allergy and hyperthyroidism**

Follow-up

- **After three months of medical treatment, she voluntarily decided to stop methimazole and beta-blocking drugs**
- **She came to our ambulatory (two months after the withdrawal of methimazole) with dyspnea and symptoms of hyperthyroidism**
- **Thyroid hormone levels had further increased**
- **We prescribed her propylthiouracil (PTU)**
- **However, after 10 days she stopped PTU because of nausea, vomiting and diarrhea**

Uncontrolled hyperthyroidism or thyroid storm?

- She was breathless at rest, fatigued and had fluid retention with peripheral oedema, pleural effusion, hepatic congestion and increased pulmonary arterial pressure
- The patient was hospitalized because of the onset of atrial fibrillation and the worsening of dyspnea
- We performed a Doppler Echocardiography and diagnosed her with “high-output heart failure”
- The Burch and Wartofsky’s scoring system was 50

Treatment during hospitalization

- We started treatment with beta-blockers, PTU, digoxin and diuretics which improved the congestive circulatory symptoms
- Hydrocortisone, sedation, oxygen and anticoagulation therapy were added
- The patient's condition progressively improved
- Prior to discharge, we ruled out the possibility of ischemic heart disease, autoimmune cardiomyopathy or valvular disease
- The patient was scheduled for thyroid surgery
- Lugol solution (10 drops 3 times daily for 10 days had been administered before surgery)

What is the most likely diagnosis in our patient?

- 1. Severe hyperthyroidism unresponsive to medical treatment?**
- 2. Persistent hyperthyroidism due to toxic adenoma?**
- 3. Autoimmune cardiovascular complications of hyperthyroidism?**
- 4. Thyroid storm induced by severe Graves' disease and caused by non-adherence to treatment?**

The 2015 European Thyroid Association Guidelines on Diagnosis and Treatment of Endogenous Subclinical Hyperthyroidism

Bernadette Biondi^a Luigi Bartalena^b David S. Cooper^c Laszlo Hegedüs^d
Peter Laurberg^e George J. Kahaly^f

Diagnosis of SHyper

Level I To establish the diagnosis of persistent SHyper	Level II To establish the aetiology of SHyper	Level III To establish the risks associated with SHyper and appropriate treatment
TSH (initial screening) FT ₄ , TT ₃ or FT ₃ (if serum TSH is low)	Thyroid ultrasonography ¹ Thyroid scan and possibly thyroid radioiodine uptake TSHR-Abs ²	CT, MRI ³ ECG ⁴ , Holter ECG ⁵ , Doppler echocardiography ⁶ BMD ⁷

¹ Ultrasonography can guide fine needle aspiration biopsy in cases of suspicious hypofunctioning thyroid nodules in nodular goitres. ² TSH-receptor antibodies (TSHR-Abs) can be useful to identify autoimmune SHyper. ³ Computed tomography (CT) or magnetic resonance imaging (MRI) should be used in selected patients to assess airway compression. ⁴ ECG should be considered in symptomatic patients. ⁵ Holter ECG is useful to assess atrial arrhythmias. ⁶ Doppler echocardiography is recommended in patients with AF, CHD or HF and/or underlying heart disease. ⁷ BMD should be evaluated in postmenopausal patients, in elderly patients and in patients with underlying bone risk factors.

Management of Graves Disease A Review

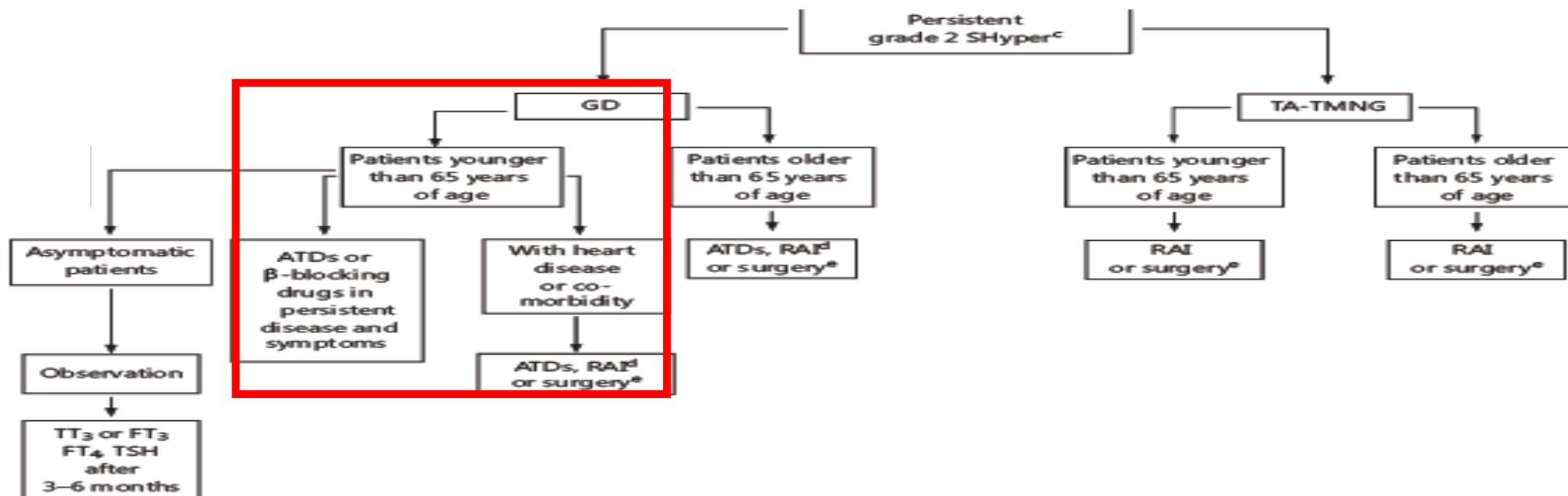
Table 2. Differential Diagnosis of Thyrotoxicosis

Diagnosis	Clinical Findings	Laboratory Results	Imaging Findings	Other Features
Graves disease	Diffuse goiter, orbitopathy	Increased FT ₄ and T ₃ , low TSH, positive TSH-receptor antibody	Elevated 24-h RAI uptake (often >30%-50%), diffuse uptake on scan, increased vascularity on Doppler-flow ultrasound	Typically seen in younger age groups and women
Toxic multinodular goiter	Multinodular goiter	Increased FT ₄ , T ₃ , or both	Multiple hyperfunctioning nodules on imaging	More common in older persons, women, and in areas of relative iodine deficiency
Solitary toxic nodule	Large (>3 cm) solitary thyroid nodule	Increased FT ₄ , T ₃ , or both	Solitary hyperfunctioning nodule with suppression of the paranodular tissue and contralateral lobe	More common in older persons, women, and in areas of relative iodine deficiency
Painless thyroiditis	Mild hyperthyroidism and small nonpainful goiter; self-limited condition (usually <2-3 mo)	Variable elevation of FT ₄ (often 1.6-2.0 × ULN), increased T ₃ (often 1.0-1.5 × ULN), usually positive anti-TPO antibodies	Absent to very low (0%-5%) 24-h RAI uptake, normal or decreased vascularity on Doppler-flow ultrasound	Has a predilection for the postpartum period and is also associated with lithium use; may recur over years
Subacute de Quervain thyroiditis	Painful enlarged thyroid that often occurs after an upper respiratory tract infection	Variable elevation of FT ₄ (often 1.6-2.0 × ULN), increased T ₃ (often 1.0-1.5 × ULN), very high ESR (typically >50 mm/h)	Absent to very low (0%-5%) 24-h RAI uptake	Usually not associated with permanent sequelae
Drug-induced thyroiditis	Mildly enlarged thyroid	Variable elevation of FT ₄ (often 1.6-2.0 × ULN), increased T ₃ (often 1.0-1.5 × ULN)	Absent to very low (0%-5%) 24-h RAI uptake	Associated with use of amiodarone, lithium, interferon-α, sorafenib and other multikinase inhibitors
Iodine-induced hyperthyroidism	Hyperthyroidism in days to months after iodine exposure in patients with preexisting thyroid disease, typically a multinodular goiter	Variable elevation of FT ₄ (often 1.6-2.0 × ULN), increased T ₃ (often 1.0-1.5 × ULN)	Absent to very low (0%-5%) 24-h RAI uptake	Associated with iodine exposure usually in the form of amiodarone or iodinated contrast agents
Ingestion of thyroid hormone	Thyrotoxic symptoms and signs without an enlarged thyroid	Elevated T ₄ and T ₃ in patients ingesting T ₄ ; elevated T ₃ with low FT ₄ in patients ingesting T ₃	Absent to very low (0%-5%) 24-h RAI uptake	May be intentional or inadvertent
Struma ovarii	Thyrotoxic symptoms and signs without an enlarged thyroid	Elevated FT ₄ and T ₃	Increased RAI uptake over the pelvis	May rarely be malignant
Molar pregnancy and choriocarcinoma	Thyrotoxic signs and symptoms with an enlarged thyroid	Elevated FT ₄ (often 1.6-2.0 × ULN) and T ₃ (often 1.6-2.0 × ULN)	Elevated 24-h RAI uptake (>30%-50%)	Caused by high levels of hCG, which has thyroid-stimulating action when present in high serum concentrations

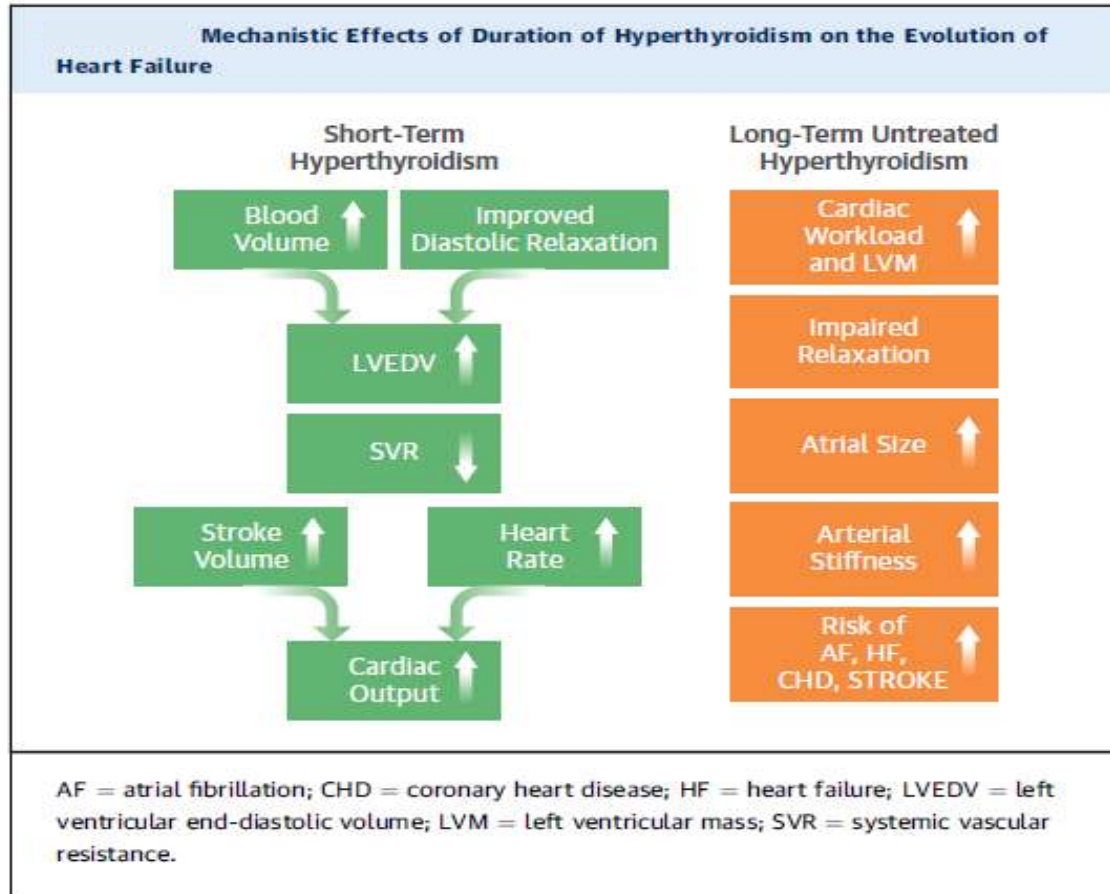
Abbreviations: ESR, erythrocyte sedimentation rate; FT₄, free thyroxine; hCG, human chorionic gonadotropin; RAI, radioactive iodine; T₃, triiodothyronine; T₄, thyroxine; TPO, thyroid peroxidase; TSH, thyrotropin (thyroid-stimulating hormone); ULN, upper limit of normal.

The 2015 European Thyroid Association Guidelines on Diagnosis and Treatment of Endogenous Subclinical Hyperthyroidism

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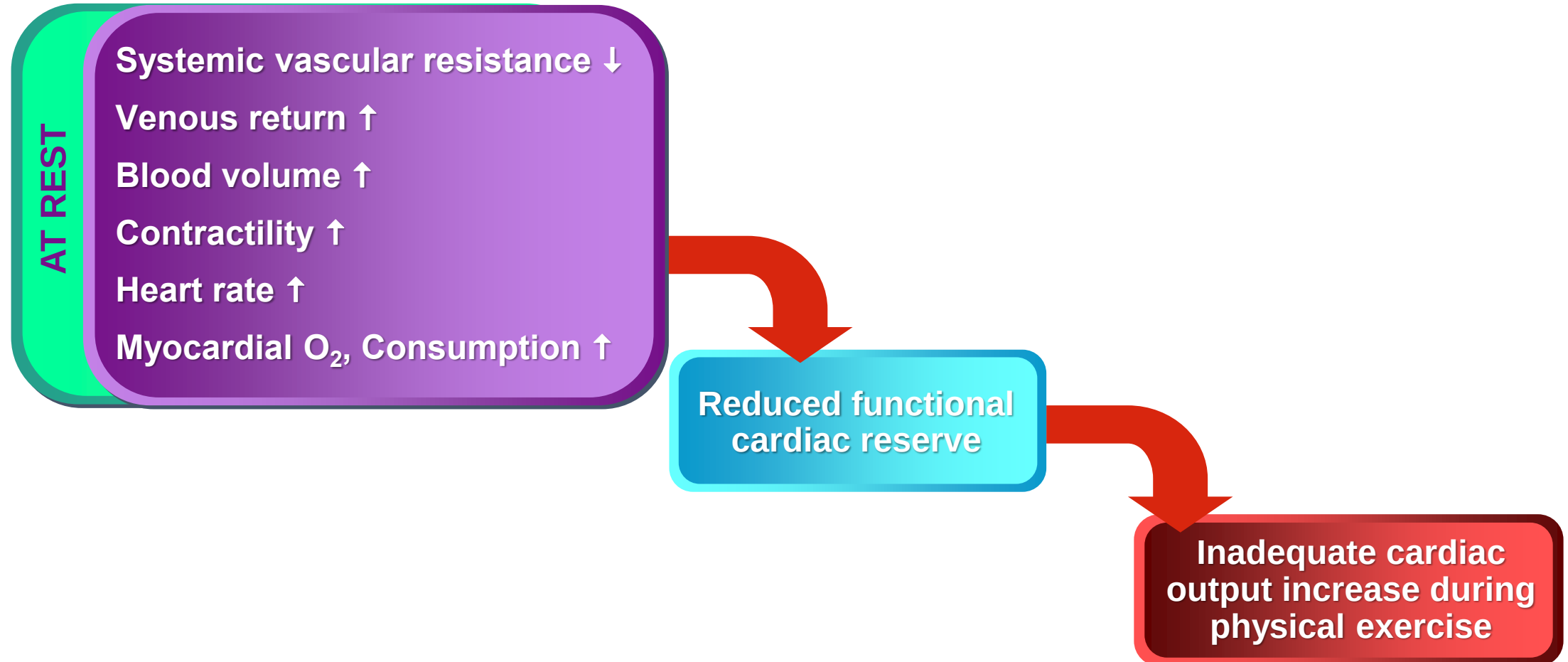


CARDIOVASCULAR RISK OF UNTREATED HYPERTHYROIDISM



- Risk of Atrial Fibrillation and Stroke
- Risk of Heart Failure
- Coronary Heart Disease Events
- Cardiovascular Mortality

REDUCED CARDIOVASCULAR RESPONSE TO PHYSICAL EXERCISE IN HYPERTHYROIDISM



REVIEW

MECHANISMS IN ENDOCRINOLOGY

Heart failure and thyroid dysfunction

Bernadette Biondi

*Department of Clinical and Molecular Endocrinology and Oncology, University of Naples Federico II, Via S. Pansini 5, 80131 Naples, Italy**(Correspondence should be addressed to B Biondi; Email: bebiondi@unina.it)***‘High-output’ HF in hyperthyroidism.**

Congestive circulation may occur with increased cardiac output in the absence of underlying heart disease due to the effects of:

Persistent tachycardia

Increased cardiac preload

Reduced systemic vascular resistance

Elevated ventricular filling pressure

Increased pulmonary arterial pressure

AUTOIMMUNE CARDIOVASCULAR INVOLVEMENT IN GRAVES' DISEASE

- **Cardiomyopathy**
- **Peripartum Cardiomyopathy**
- **Cardiac valve involvement**
- **Pulmonary hypertension**

THYROID STORM

- The thyrotoxic crisis (or thyroid storm) is a life threatening exacerbation of the hyperthyroid state characterized by decompensation of one or more organs
- It usually complicates GD, but sometimes can occur in association with toxic nodular goiter
- It accounts for <1-2% of the hospital admissions for thyrotoxicosis
- The mortality of this condition is high, ranging from 20-30%

POINT SCALE FOR THE DIAGNOSIS OF THYROID STORM^a

<i>Criteria</i>	<i>Points</i>	<i>Criteria</i>	<i>Points</i>
Thermoregulatory dysfunction		Gastrointestinal–hepatic dysfunction	
Temperature (°F) ^b		Manifestation	
99.0–99.9	5	Absent	0
100.0–100.9	10	Moderate (diarrhea, abdominal pain, nausea/vomiting)	10
101.0–101.9	15	Severe (jaundice)	20
102.0–102.9	20		
103.0–103.9	25		
≥104.0	30		
Cardiovascular		Central nervous system disturbance	
Tachycardia (beats per minute)		Manifestation	
100–109	5	Absent	0
110–119	10	Mild (agitation)	10
120–129	15	Moderate (delirium, psychosis, extreme lethargy)	20
130–139	20	Severe (seizure, coma)	30
≥140	25		
Atrial fibrillation			
Absent	0		
Present	10		
Congestive heart failure		Precipitant history	
Absent	0	Status	
Mild	5	Positive	0
Moderate	10	Negative	10
Severe	20		
<i>Scores totaled</i>			
>45	Thyroid storm		
	Impending storm		
<25	Storm unlikely		

^aSource: Burch and Wartofsky (26). Printed with permission.

^bCelsius 37.2–37.7 (5), 37.8–38.3 (10), 38.3–38.8 (15), 38.9–39.4 (20), 39.4–39.9 (25), ≥40 (30 points).

THYROID STORM: DRUGS AND DOSES

Drug	Dosing	Comment
Propylthiouracil ^a	500–1000 mg load, then 250 mg every 4 hours	Blocks new hormone synthesis
Methimazole	60–80 mg/d	Blocks T ₄ -to-T ₃ conversion Blocks new hormone synthesis
Propranolol	60–80 mg every 4 hours	Consider invasive monitoring in congestive heart failure patients Blocks T ₄ -to-T ₃ conversion in high doses Alternate drug: esmolol infusion
Iodine (saturated solution of potassium iodide)	5 drops (0.25 mL or 250 mg) orally every 6 hours	Do not start until 1 hour after antithyroid drugs
Hydrocortisone	300 mg intravenous load, then 100 mg every 8 hours	Blocks new hormone synthesis Blocks thyroid hormone release Alternative drug: Lugol’s solution May block T ₄ -to-T ₃ conversion
		Prophylaxis against relative adrenal insufficiency Alternative drug: dexamethasone

^aMay be given intravenously.

What is the most likely diagnosis in our patient?

- X** Severe hyperthyroidism unresponsive to medical treatment ?
- X** Persistent hyperthyroidism due to toxic adenoma ?
- X** Autoimmune cardiovascular complications of hyperthyroidism?
- ✓** **Thyroid storm induced by severe GD and caused by non-adherence to treatment ?**



- **Thyroid storm complicated by cardiopulmonary failure can be the initial presentation of undiagnosed or untreated thyrotoxicosis**
- **Quick recognition and treatment is critical for the patient's survival**
- **Cardiopulmonary failure is the most common cause of death in thyroid storm**
- **This diagnosis should be considered by emergency medical physicians to decrease the morbidity and mortality associated with thyroid storm**