TILL THE STORM PASSES BY

Dr. YK Chung
ICU TKOH

Ms. Yeung

- F/49 housewife
- NSND
- History of DM and thyrotoxicosis
- Previously FU in China and put on antithyroid drugs
- Defaulted FU for 5 years

History

- C/O right leg painful swelling for 4 days
- Started from right knee extending down to ankle
- No marine contact/ IVDU/ trauma/ laceration/ animal bite/ long-distance travel
- Not on OCP or HRT
- No recent surgery/ immobilization

Physical examination

- Temp 37 ºC
- GCS 15/15
- BP 150/70 mmHg
- Pulse 120-140 bpm, irregular
- SaO_2 95% (RA)

Physical examination

- Chest - ↓ bilateral breath sound and stony dullness on percussion (right side more severe)
- CVS/CNS/abdomen - normal
- Urine PT negative

Physical examination of right leg

- Overlying skin erythematous
- Tender and swollen
- No blister/bulla/crepitus/discoloration/gangrene/ anaesthesia
- Peripheral circulation normal, distal pulses palpable
- Bilateral ankle pitting edema

Investigations

- XR right lower limb: no fracture/ subcutaneous emphysema
- CXR cardiomegaly + bilateral pleural effusion (R>L)
- ECG AF 123 bpm

Investigations

- WCC 5.6 Hb 12 Plt 190
- Na 138 K 4 Urea 8 Cr 60
- Bili 51 ALP 167 ALT 18
- CK n
- pH 7.44 HCO3 27
- INR 1.3 APTT 28.5
- Amylase 15
- TNT not elevated

Management in medical ward

- IV ampicillin + cloxacillin
- Urgent doppler right leg → no DVT
- Amiodarone

Day 2

- Increased dyspnea
- Nausea, vomiting and abdominal pain

Day 2

- Afebrile
- SaO_2 95% ↑ 4L O_2 NC
- BP 140/80 mmHg
- Fast AF 130-150 bpm
- RR 30 bpm
- Abdomen exam repeated - NAD

Day 2

- CXR - ↑ bilateral pleural effusion and pulmonary congestion
- AXR - NAD
- Serial examination of right leg - no deterioration or NF changes

Blood tests

- WCC 14 Hb 14 Plt 159
- RFT n Na 136 K 3.7
- Bili 76 ALP 180 ALT 54
- Amylase 90
- CK 140
- Spot glucose 2.1
- TNT not raised
- Paracetamol/saliclate/ethanol level not elevated

Blood gas

- ABG
  - pH 7.14
  - pCO_2 3.2 kPa
  - pO_2 12.9 kPa
  - HCO3 9.6
  - BE -18
- Chloride 99
- AG = 29.4
- ΔAG = 17.4
- ΔHCO3 = 14.4
- Δratio = 1.2

Blood gas

- Exp pCO_2 = 1.5*HCO3+8±2
- Exp pCO_2 = 2.6-3.2 kPa (measured pCO_2 3.2kPa)
- Uncomplicated high anion gap metabolic acidosis

High AG acidosis?

- Denied toxic alcohol contact
- Serum osmo 288
- Calculated osmolarity
  = 2*(Na+K)+urea+glucose
  = 286
- Osmolar gap = 2 (<10)

High AG acidosis?

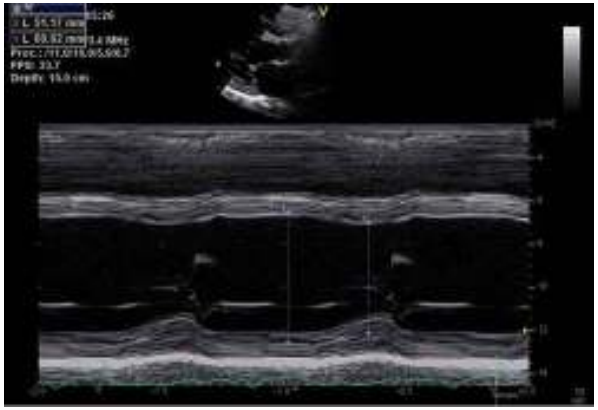
- X Toxic alcohol - normal OG
- X Uraemia - normal urea
- X Ketosis - ketone negative
- X Paraldehyde & ammonium chloride
- ✔Lactic acidosis - serum lactate 4 (0.5-2.2 mmol/L)

CT thorax + abdomen + right leg

- No PE
- No haemoperitoneum/pneumoperitoneum
- No IO/bowel ischemia
- No subcutaneous emphysema of right leg
- Bilateral pleural effusion

ECHO

- Globally impaired EF 30%
- No significant valvular lesion
- No RWMA
- No pericardial effusion



TRANSFERRED TO ICU…

Problems

- CHF with pulmonary congestion & pleural effusion
- Deteriorating LFT
- Persistent fast AF despite amiodarone
- DIC
- Lactic acidosis
- Right leg cellulitis

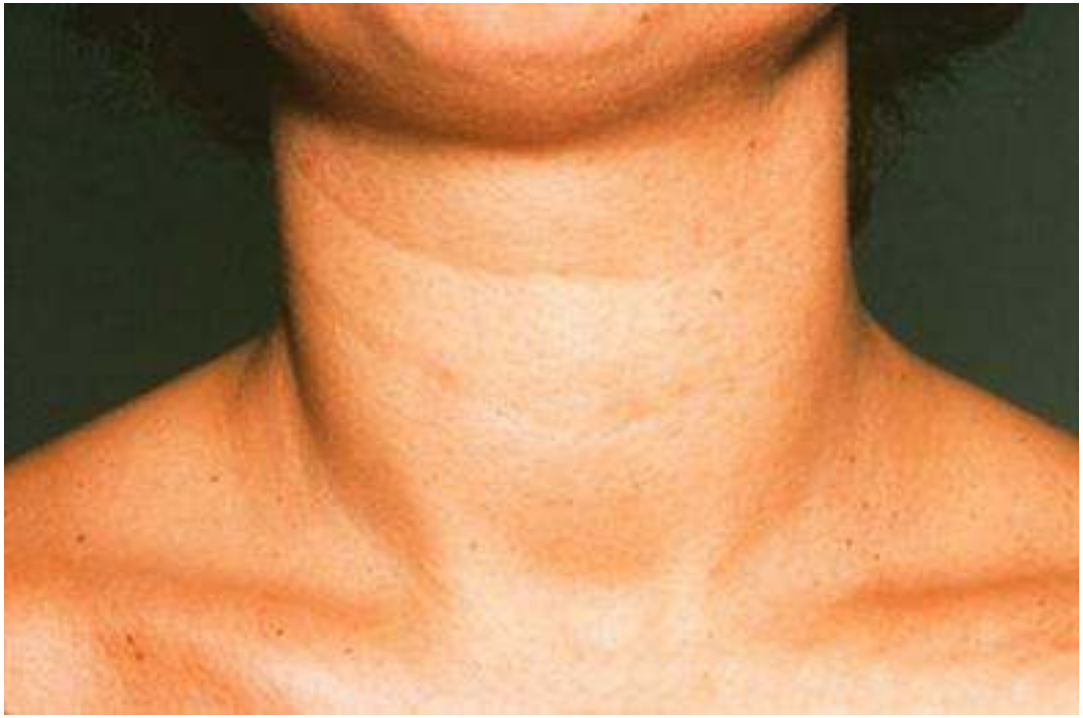
ONE MAN ONE DISEASE…HOW TO LINK THESE UP?


THE PATIENTS KNOW MORE ABOUT THEIR DISEASES THAN ME. I MUST GET FASTER MODEM, HIGHER SPEED INTERNET ACCESS THAN THEM
©Mayrovic

History

- F/49
- History of DM and thyrotoxicosis
- Previously FU in China and put on antithyroid drugs
- Defaulted FU for 5 years

Physical exam



Physical exam

- Mild bilateral proptosis

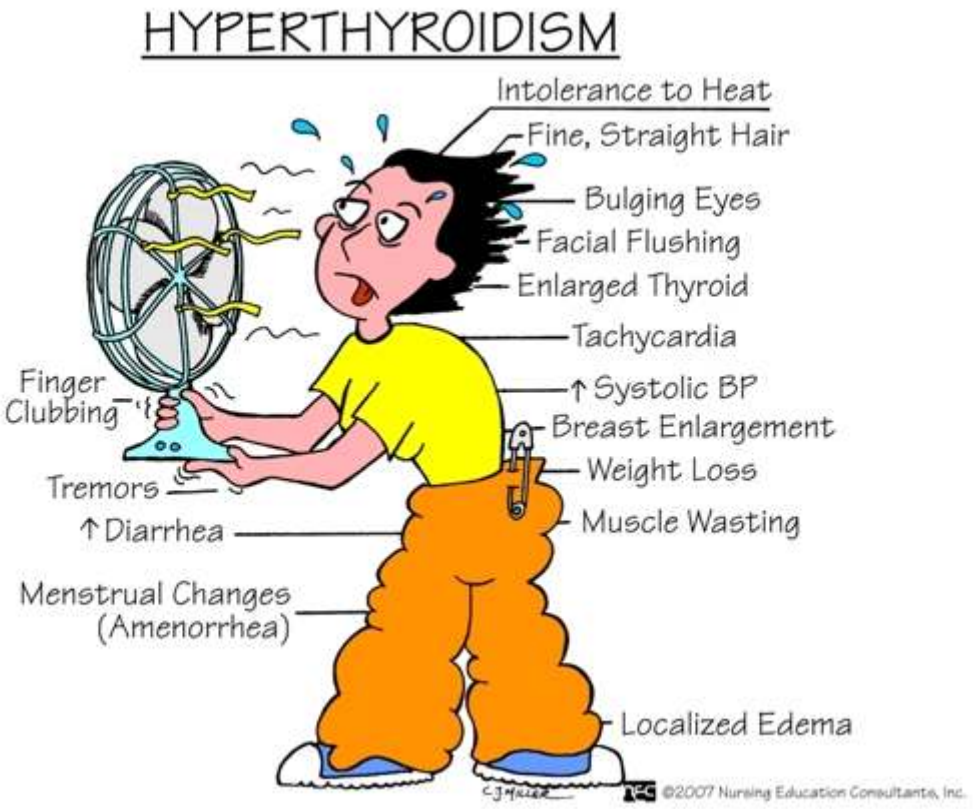
Further history….

- No palpitation/ weight loss/ ∆ appetite/ irritability/ tremor/ heat intolerance
- Diarrhea for 1 month

DDX

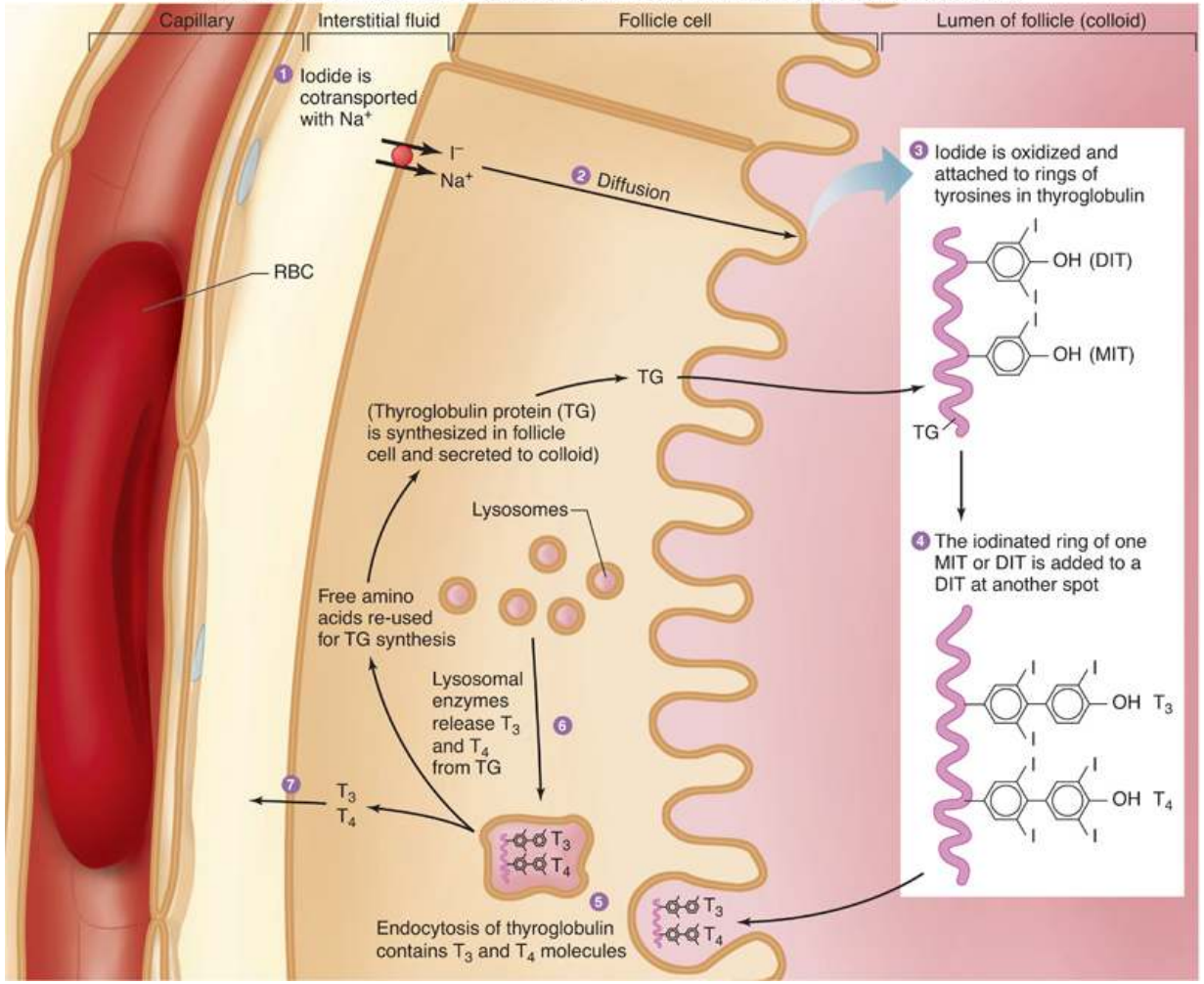
- Thyroid storm
- Sepsis with septic cardiomyopathy → septic workup
- Myocarditis/cardiomyopathy → blood & stool viral culture
- Drug toxicity → toxicology screening

Thyroid storm



Iodine Uptake

- Iodide (I-) actively transported into the follicular cells by an Na+/I- symport in the basal membrane
- This pump concentrates iodine in the colloid at a level up to 250x > plasma level - ***iodide trapping***
- The pump activated by **thyroid stimulating hormone (TSH)**



Transport

- T½ of T3 - 1 day
- T½ of T4 - 6 days
- 99% TH are protein bound, mainly by TBG
- Remainder by pre-albumin or albumin

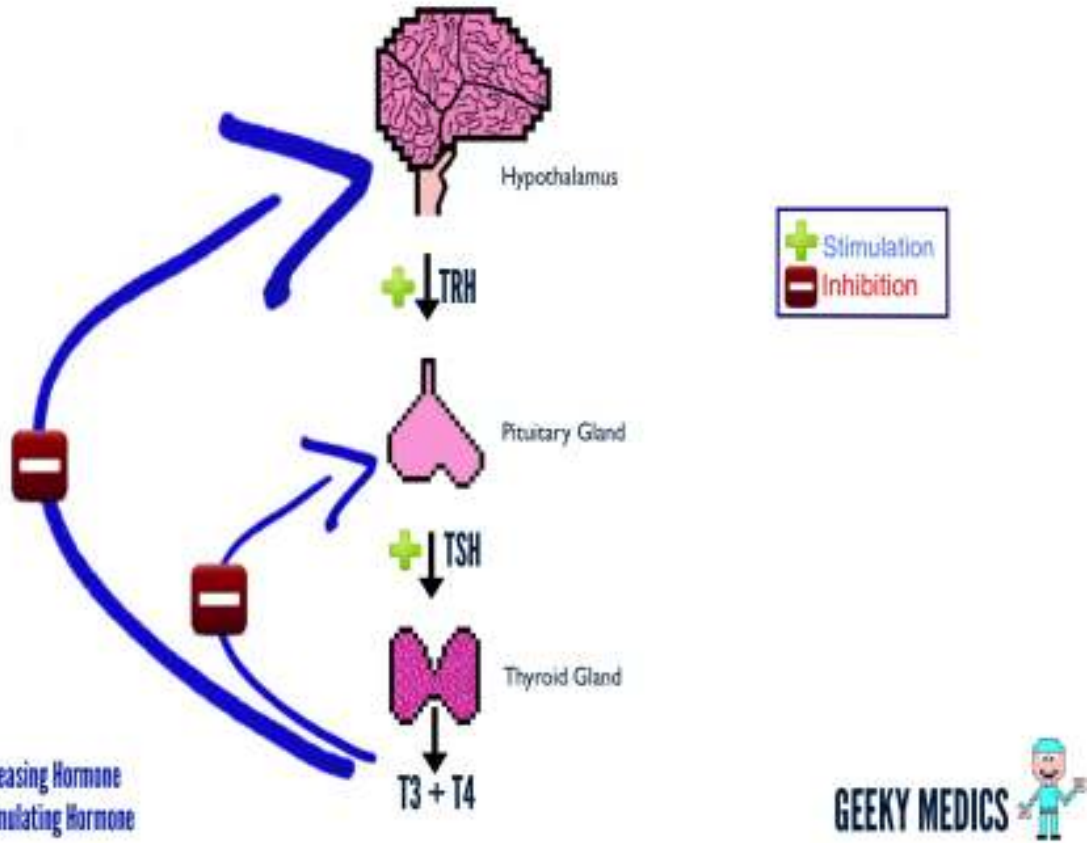
Degradation

- Only free T3 and free T4 enter cells to exert actions
- T3 (50%) deiodinated from T4 in peripheral tissues, esp. liver and kidneys

Deiodination

- 3 types of deiodinase
- Type I - primary source of T3
- In liver, kidney and thyroid tissues
- Inhibited by PTU, beta-blockers, iodide and steroid
- Forms the basis for drug treatment of thyrotoxicosis

Hypothalamic - Pituitary - Thyroid Axis



Thyroid storm

- Syndrome of decompensated hyperthyroidism
- ≠ compensated thyrotoxicosis of severe illness
- Though management are similar for these 2 entities
- Typically occurs in patients with undiagnosed or under-treated hyperthyroidism

Matthew D.Management of Hypothyroidism and Hyperthyroidism in the Intensive Care Unit. *Critical Care Clinics* Vol 17, Issue 1 (January 2001)
Takashi Akamizu. Diagnostic Criteria, Clinical Features, and Incidence of Thyroid StormBased on Nationwide Surveys. *THYROID* Volume 22, Number 7, 2012

Thyroid storm

- Always evoked by a precipitating event
- Mortality 10-30%
- Commonest cause of death - MOF, CHF

Matthew D.Management of Hypothyroidism and Hyperthyroidism in the Intensive Care Unit. *Critical Care Clinics* Vol 17, Issue 1 (January 2001)
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Pathogenesis

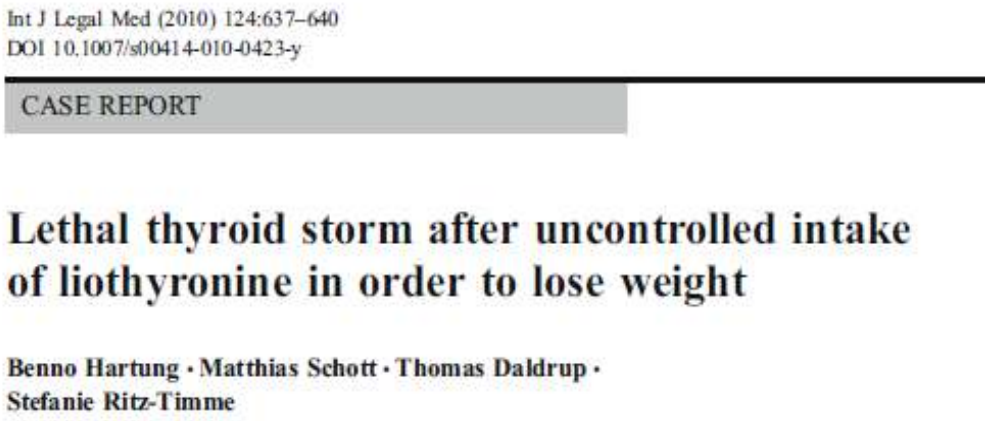
- Unknown mechanism
- ?Exaggerated response to TH in target cells
- ?Increase tissue T3 level
- ?Exaggerated response to sympathetic stimulation

Causes of hyperthyroidism

- Graves' disease (GD)
- Toxic adenoma or multinodular goitre
- Thyroiditis

Causes of hyperthyroidism

- Exogenous iodine/thyroxine
  - Excessive thyroxine intake (weight reduction pills)
  - Iodine-containing drugs (amiodarone, radiocontrast)
  - Post-RAI



Int J Legal Med (2010) 124:637–640
DOI 10.1007/s00414-010-0423-y

CASE REPORT

Lethal thyroid storm after uncontrolled intake of liothyronine in order to lose weight

Benno Hartung · Matthias Schott · Thomas Daldrup · Stefanie Ritz-Timme

Causes of hyperthyroidism (rare)

- Hypersecretory thyroid carcinoma
- TSH-secreting pituitary adenoma
- HCG-secreting tumour
- Hydatidiform mole
- Interferon alpha/ IL-2

Precipitating event

- Infection
- Discontinuation of antithyroid drugs
- Iodine, exogenous thyroxine
- Surgery or trauma
- Medical illness, e.g. myocardial infarction, thromboembolism
- Pregnancy
- Salicylate - ↑ free TH

Clinical presentation

- Hyperthermia
- Sinus tachycardia or supraventricular arrhythmias
- CHF
- CNS (agitation, seizure, confusion or coma)
- GI (vomiting, diarrhea, ileus or impaired LFT)
- Typical GD s/s - goitre, ophthalmopathy, tremor, hyperreflexia

Beware of atypical features in eldery!

Coma and Thyroid Storm in Apathetic Thyrotoxicosis

MICHEL W. GHOBRIAL, MD, and EDWARD B. RUBY, MD, Philadelphia, Pa

ABSTRACT: We report the case of an 87-year-old woman with coma who was found to be in thyrotoxic crisis. The patient had a recent history of decreased mentation and apathy, and laboratory findings were found to be consistent with hyperthyroidism. After a stormy course, the clinical condition recovered to baseline, with return of laboratory values to normal following antithyroid therapy. We provide the details of this rarely documented presentation of apathetic hyperthyroidism with thyroid storm and coma and review the characteristics of similar cases in the literature.

Laboratory investigations

- Low levels of TSH and high levels of free T3 and free T4
- GD/toxic nodules have higher proportion T3 (T3/T4 ratio > 20)
- Thyroiditis/iodine exposure have higher proportion T4 (T3/T4 ratio < 15)

Laboratory investigations

- Diagnosis of TS is not judged by the extent of TFT elevation
- No cutoff value for TS
- Thyroid profile similar to overt uncomplicated thyrotoxicosis
- Sometimes even not elevated
- TFT results not always available in emergency condition

Imaging

- USG
  - Easily available & non-invasive
  - Size and vascularity of thyroid gland
  - GD: enlarged gland with enhanced Doppler flow
  - Thyroiditis or exogenous cause: small gland with diminished flow
  - Expertise required

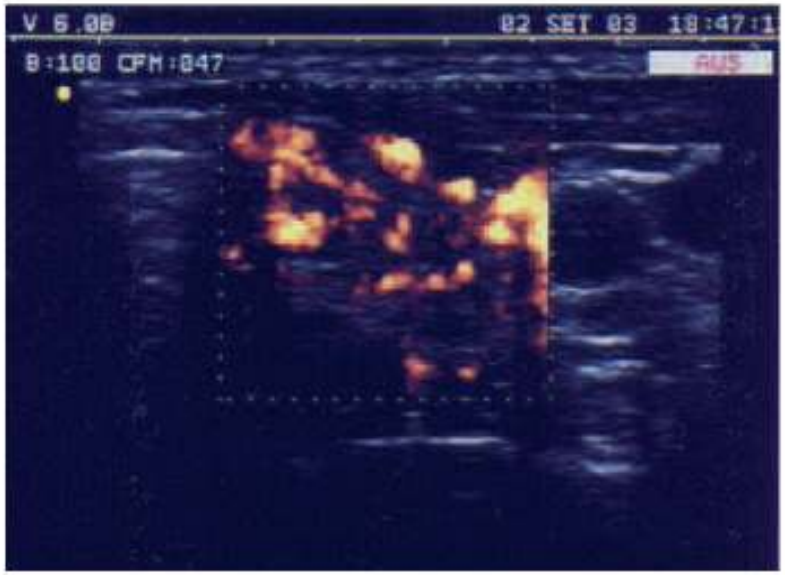


Figure 1. Graves' disease: the transverse sonogram of the left lobe shows diffusely enlarged, heterogeneous and hypoechoic parenchyma (like the near neck muscles); the power-Doppler study demonstrates a typical hypervascular pattern referred to as the *"thyroid inferno"*.

ANY DIAGNOSTIC CRITERIA FOR THYROID STORM?

Table I. Burch and Wartofsky's scoring system

Parameters	Scoring system
Thermoregulatory dysfunction	
Oral temperature (°F)	
99-99.9	5
100-100.9	10
101-101.9	15
102-102.9	20
103-103.9	25
104	30
Cardiovascular dysfunction	
Tachycardia	
90-109	5
110-119	10
120-129	15
130-139	20
>140	25
Congestive heart failure	
Absent	0
Mild (*pedal edema*)	5
Moderate (*bibasal rales*)	10
Severe (*pulmonary oedema*)	15
Atrial fibrillation	
Absent	0
Present	10
Central nervous system symptoms	
Absent	0
Mild agitation	10
Moderate (*Delirium, psychosis, extreme lethargy*)	20
Severe (*Seizure, coma*)	30
Gastrointestinal /hepatic dysfunction	
Absent	0
Moderate (*Diarrhea, nausea, vomiting, abdominal pain*)	10
Severe (*Unexplained jaundice*)	20
Precipitating event	
Absent	0
Present	10

Burch & Wartofsky's scoring system

≥45 suggestive of TS

25 - 44 suggestive of "impending" TS

< 25 unlikely TS

Burch HB, Wartofsky L. *Endocrinol Metab Clin NorthAmer 1993*; 22: 263-277

Critics on BWS

- Can’t distinguish TS from severe compensated thyrotoxicosis
- Non-specific
- Complicated
- Not evidence based
- Not formally validated

A Migneco.Management of thyrotoxic crisis.*European Review for Medical and Pharmacological Sciences.* 2005; 9: 69-74

THYROID
Volume 22, Number 7, 2012
© Mary Ann Liebert, Inc.
DOI: 10.1089/thy.2011.0334

ORIGINAL STUDIES, REVIEWS, AND SCHOLARLY DIALOG
THYROID FUNCTION AND DYSFUNCTION

Diagnostic Criteria, Clinical Features, and Incidence of Thyroid Storm Based on Nationwide Surveys

Takashi Akamizu,[1] Tetsurou Satoh,[2] Osamu Isozaki,[3] Atsushi Suzuki,[4] Shu Wakino,[5] Tadao Iburi,[6] Kumiko Tsuboi,[7] Tsuyoshi Monden,[8] Tsuyoshi Kouki,[9] Hajime Otani,[10] Satoshi Teramukai,[11] Ritei Uehara,[12] Yosikazu Nakamura,[12] Masaki Nagai,[13] and Masatomo Mori,[2] for the Japan Thyroid Association

- New criteria proposed by Japan Thyroid Association in 2012
- Based on analysis of literatures, followed by survey of thyrotoxic cases in Japan
- Different from BWC in 2 ways:
  - Requirement of laboratory evidence of thyrotoxicosis as a prerequisite
  - Not a scoring system

Symptoms

1. CNS
2. Fever (≥38ºC)
3. Tachycardia (≥130bpm)
4. CHF
5. GI and hepatic

Diagnostic criteria for “Definite” TS

- Meet the prerequisite and either:
  - (i) At least one CNS symptom plus one other symptom
  - (ii) Three or more symptoms other than CNS

Diagnostic criteria for “Suspected” TS

- A prerequisite plus two manifestations other than CNS symptom

- If prerequisite cannot be met, but the patient has history of thyroid disease, presents with exophthalmos and goiter, and meets (i) or (ii) from the criteria for definite cases, still a suspected case

Limitations of the Japanese criteria

- Prerequisite needs lab. data which is not always available
- TH may be normal in some TS cases
- Study confined in Japan ?generalizability

ATA/AACE Guidelines

HYPERTHYROIDISM AND OTHER CAUSES OF THYROTOXICOSIS: MANAGEMENT GUIDELINES OF THE AMERICAN THYROID ASSOCIATION AND AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS

AMERICAN THYROID ASSOCIATION
FOUNDED 1923

Rebecca S. Bahn (Chair), MD[1,]; Henry B. Burch, MD[2]; David S. Cooper, MD[3]; Jeffrey R. Garber, MD, FACP, FACE[4]; M. Carol Greenlee,MD [5]; Irwin Klein, MD[6]; Peter Laurberg, MD[7]; I. Ross McDougall, MD[8]; Victor M. Montori, MD[1]; Scott A. Rivkees, MD[9]; Douglas S. Ross, MD[10]; Julie Ann Sosa, MD[11]; Marius N. Stan, MD[1]*

TABLE 5. POINT SCALE FOR THE DIAGNOSIS OF THYROID STORM

Criteria	*Points*	*Criteria*	*Points*
Thermoregulatory dysfunction		**Gastrointestinal-hepatic dysfunction**	
Temperature (°F)		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		

Scores totaled	
>45	Thyroid storm
25–44	Impending storm
<25	Storm unlikely

Source: Burch and Wartofsky, 1993 (21). Printed with permission.

Parameters	Score
Fever	0
Tachycardia ~ 130	15
Pulmonary edema	15
AF	10
Precipitating event	10
Jaundice	20
CNS	0
	70

- Prerequisite not confirmed….has history of thyroid disease, presents with exophthalmos and goiter, …..3 systems of involvement (GI + tachycardia + CHF)

- A suspected TS case

IS DIAGNOSTIC CRITERIA REALLY IMPORTANT IN MANAGEMENT?

Principles of thyroid storm management

- Stop synthesis of new hormone
- Stop release of stored thyroid hormone
- Prevent conversion of T4 to T3
- Control adrenergic symptoms
- Supportive care

Beta-blockers

- Block T4 conversion to T3
- Block beta adrenergic response
- Pay extreme caution in heart failure cases
- Can induce hypotension or even cardiac arrest in severe heart failure cases
- Used under close hemodynamic monitoring

ATA/AACE Guidelines.*ENDOCRINE PRACTICE* Vol 17 No. 3 May/June 2011

Propranolol

- Oral/NG
- 60-80 mg every 4 hours
- Onset 1 hour, half life 4-6 hours
- IV propranolol (0.5-1 mg over 10 minutes, then 1-2 mg over 10 minutes, repeated every few hours)
- Non-selective blocker → C/I in asthma

Esmolol

- Short acting
- Half life 9 minutes
- Loading iv 250-500 mcg/kg followed by infusion of 50-100 mcg/kg/min

Thionamides

Imidazole	Thiouracil
Carbimazole – a/v in UK & Commonwealth Methimazole - a metabolite of CMZ	Propylthiouracil
Inhibit new TH synthesis	Inhibit new TH synthesis + inhibit peripheral T4 to T3 conversion
Longer half life	Shorter half life
Once daily dose	3-4 times per day
20-25mg Q6h (more frequent dose in TS due to poor GI absorption)	200-300mg Q6h
Oral or rectal route No IV preparation	Oral or rectal route No IV preparation

Thionamides

- Block TH synthesis within 1-2 hours
- Cannot block release of pre-formed thyroid hormone
- PTU preferred in TS due to additional benefit in blocking peripheral conversion of T4 to T3
- CMZ less hepatotoxic than PTU
- Common mild S/E - bad taste, pruritus, urticaria, fever and joint pain

Thionamides

- IV thionamide use has been reported in small case series
- Dissolve oral tablets in normal saline
- Potential risk of contamination and embolism

Agranulocytosis

- 0.4%
- Slightly higher incidence in PTU
- G-CSF can be considered in drug induced agranulocytosis

Hepatotoxicity

- 0.2%
- PTU - allergic hepatitis with hepatocellular injury
- CMZ - cholestasis

Vasculitis

- More common with PTU
- ANCA related
  - ARF
  - Arthritis
  - Skin ulcer
  - Rash
  - Haemoptysis

Iodine

- Block new hormone synthesis
- Block the release of pre-stored hormone (where thionamides unable to do so)

WHY IODINE CAN INHIBIT THYROID HORMONE SYNTHESIS?

Wolff-Chaikoff effect

- A normal physiological phenomenon to protect human from wide variety of iodine intake and to maintain euthyroidism
- Sudden increase in serum iodine (>1 μmol/L) inhibits oxidation of iodide inside follicles
- Inhibit TH synthesis

Escape phenomenon

- Within 2-4 weeks of continued exposure to excess iodide, iodide organification and TH synthesis resume in a normal fashion
- Results from decreased trapping of iodide and restoration of intrathyroidal iodide pool to normal level
- ?Adaptation of the iodide transport system

Jod-Basedow effect

- “Jod” = iodine (German)

- Development of hyperthyroidism following administration of iodine independent of intrathyroidal iodine autoregulation

- Typically occurs in people, who live in iodine deficient areas (with underlying autonomous thyroid gland), when given small increase in iodine intake, resulting in increase TH synthesis independent of normal regulatory mechanism

Formulation

- Lugol's solution & potassium iodide (SSKI)
- 0.2-2 g daily
- 4-8 drops Lugol's (8 mg iodine/drop) every 6-8 hours
- Esophagitis & duodenitis
- 5 drops of potassium iodide (38mg iodine/drop) every 6 hours
- Rectal route possible
- IV in case reports
- Oral radiocontrast - ipodate and iopanoic acid not available in many countries ?HK (0.5-1 g once daily)

When to start iodine?

- Start iodine 1 hour after antithyroid drugs
- Prevent stimulation of new thyroid hormone synthesis by iodine

ATA/AACE Guidelines.*ENDOCRINE PRACTICE* Vol 17 No.3 May/June 2011

Steroid

- Inhibits peripheral conversion of T4 to T3
- Treat relative adrenal insufficiency
- Direct effect on autoimmune process in GD
- Hydrocortisone 100 mg Q8h iv

Lithium

- Used when thionamide contraindicated
- Decrease TH synthesis and secretion
- 300 mg every 8 hours oral
- Maintain serum level of Li at 1.0 mEq/L

Potassium perchlorate

- Perchlorate anion (ClO_4^-) is a competitive inhibitor of iodide transport
- Fell out of favor due to its side effects - aplastic anemia & nephrotic syndrome
- Resurgence of interest - effective treatment in type 1 amiodarone-induced thyrotoxicosis (AIT)
- < 1 g daily; limited treatment course to 4 weeks

Antiadrenergic agents

- Reserpine & guanethidine
- Depletes catecholamine stores in sympathetic nerve terminals
- Inhibits release of catecholamines
- Side effects - hypotension, diarrhea, CNS depression
- Consider when beta-blockade contraindicated

Cholestyramines

- Anion exchange resin
- Decrease reabsorption of thyroid hormone from enterohepatic circulation
- Especially useful in iatrogenic hyperthyroidism

Plasmapheresis

- Removal of protein bound hormone, catecholamines, cytokines and antibodies
- Rapid improvement in clinical condition
- Considered early in desperate cases (MOF) or when traditional treatment fails
- Combined use with antithyroid drugs

Therapeutic Apheresis and Dialysis 2011;15(6):522-531

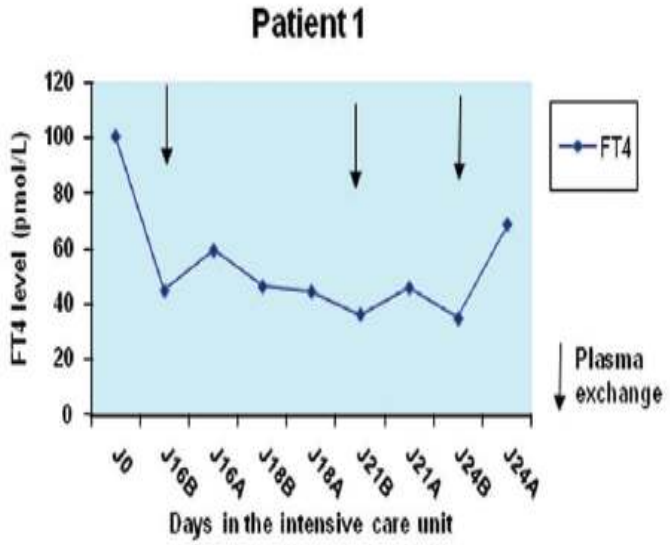
Plasmaphresis

- Grade IIc recommendation in American Society for Apheresis (ASFA)
- Indications
  - **Cardiothyrotoxicosis** – rapid improvement
  - **Neurological** – slow response due to blood brain barrier
  - **Severe myopathy**
  - **Rapid clinical deterioration**
  - **Contraindications or failure to conventional treatment**
  - **As a preparation before emergency surgery**

Guidelines on the use of therapeutic apheresis in clinical practice.J Clin Apher 2010;25:83-177

Plasmaphresis

- TH tends to rise again after TPE
- Mobilization effect from extravascular compartment
- Daily TPE until clinical improvement
- 40-50 ml/kg replacement per session
- Check fT3 and fT4 before and after each session



Guidelines on the use of therapeutic apheresis in clinical practice.J Clin Apher 2010;25:83-177

Supportive treatment

- ABC
- Antipyretics
  - X salicylates (displace TH from TBG)
- External cooling
- Fluid and electrolyte (avoid fluid overload in CHF)
- Diuretics for CHF
- Nutrition
- Treat underlying precipitating cause

BACK TO OUR PATIENT …

Day 2

- Consult endocrinologist
- Thyroid USG - diffusely enlarged thyroid glands with increased blood flow
- TFT pending

Treatment

- PTU 200mg Q6h oral
- Hydrocortisone 100mg Q8h iv
- Esmolol (start @ 50 mcg/kg/min infusion)
- Lugol's solution 6 drops Q6h oral (1 hour after)
- Supportive treatment

Day 3

- fT4 63.6 (12-22)
- fT3 21.3 (3.9-6.7)
- TSH <0.01
- Anti-thyroglobulin antibody negative
- Anti-thyroid microsomal antibody positive (1:6400)

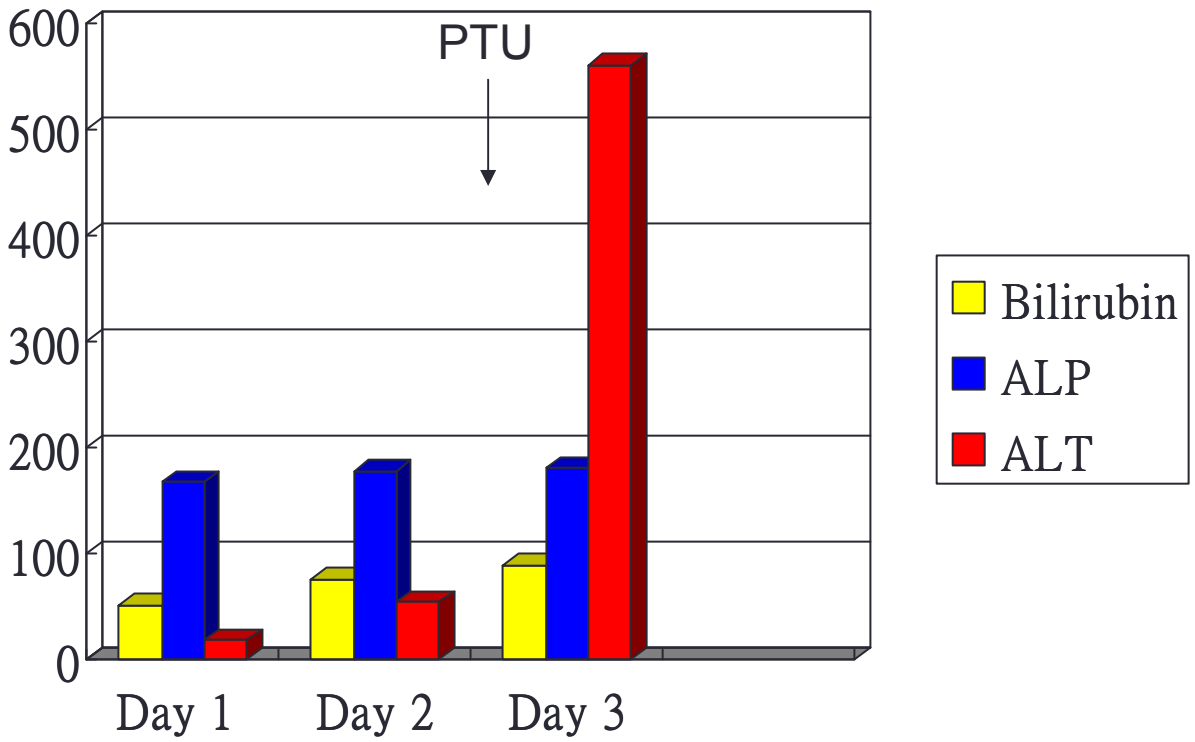
Day 3

- Right leg cellulitis resolved
- Septic workup negative
- Toxicology screen negative
- Stool culture negative

Day 3

- CHF improved
- Persistent fast AF 120-140 bpm (esmolol ↑ 90 mcg/kg/min)

Another problem arises….



Day 3

- Confused speech E4V4M6
- CT brain normal
- NH3 90 (11-51)

Day 3

- USG abdomen normal
- Viral hepatitis serology negative
- Anti-mitochondrial (AMA)/ anti-smooth muscle antibody (ASMA) negative

Impaired liver function in hyperthyroidism

- Common 45-90%
- Usually mild and asymptomatic
- ↑ ALP most common - bone resorption
- Followed by ↑ AST and bilirubin

Clinical and Experimental Gastroenterology 2013:6 9 -17

Causes of liver injury in hyperthyroidism

- Thyrotoxic hepatitis
  - Thyrotoxicosis induce hypermetabolism
  - Inducing relative ischemia in liver (ischemic hepatitis)
  - Further exacerbated by right heart failure
  - Resolve when euthyroidism achieved

Causes of liver injury in hyperthyroidism

- Antithyroid drugs
  - Metabolized mainly in liver
  - CMZ → cholestasis
  - PTU → hepatocellular injury

Causes of liver injury in hyperthyroidism

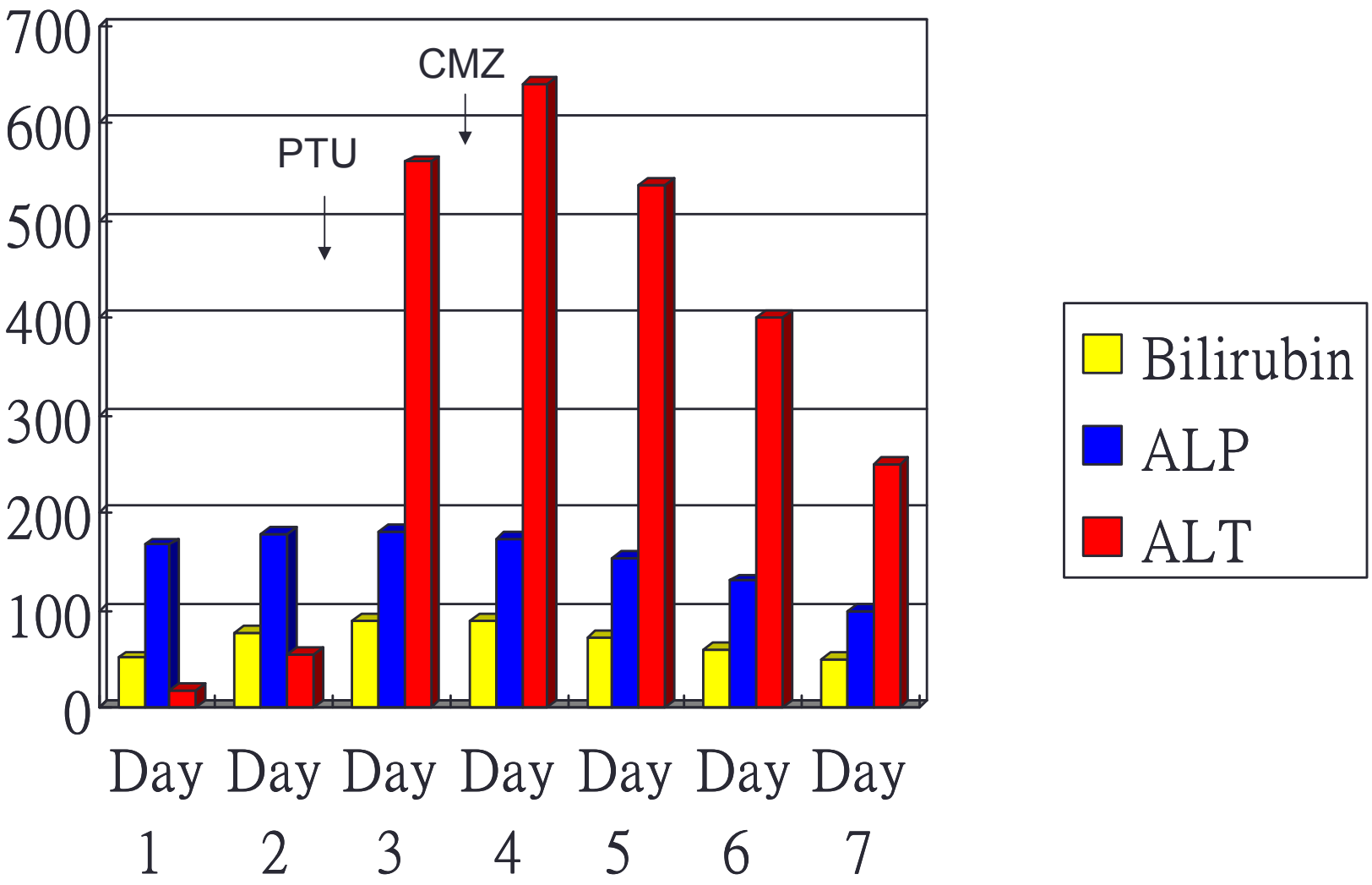
- PTU
  - More hepatotoxic than CMZ
  - Hepatotoxicity occurs within first 3 months after use
  - Induce liver injury by immunological mechanism
  - Usually benign prognosis
  - Mild asymptomatic case → observe
  - Severe symptomatic → withdrawal

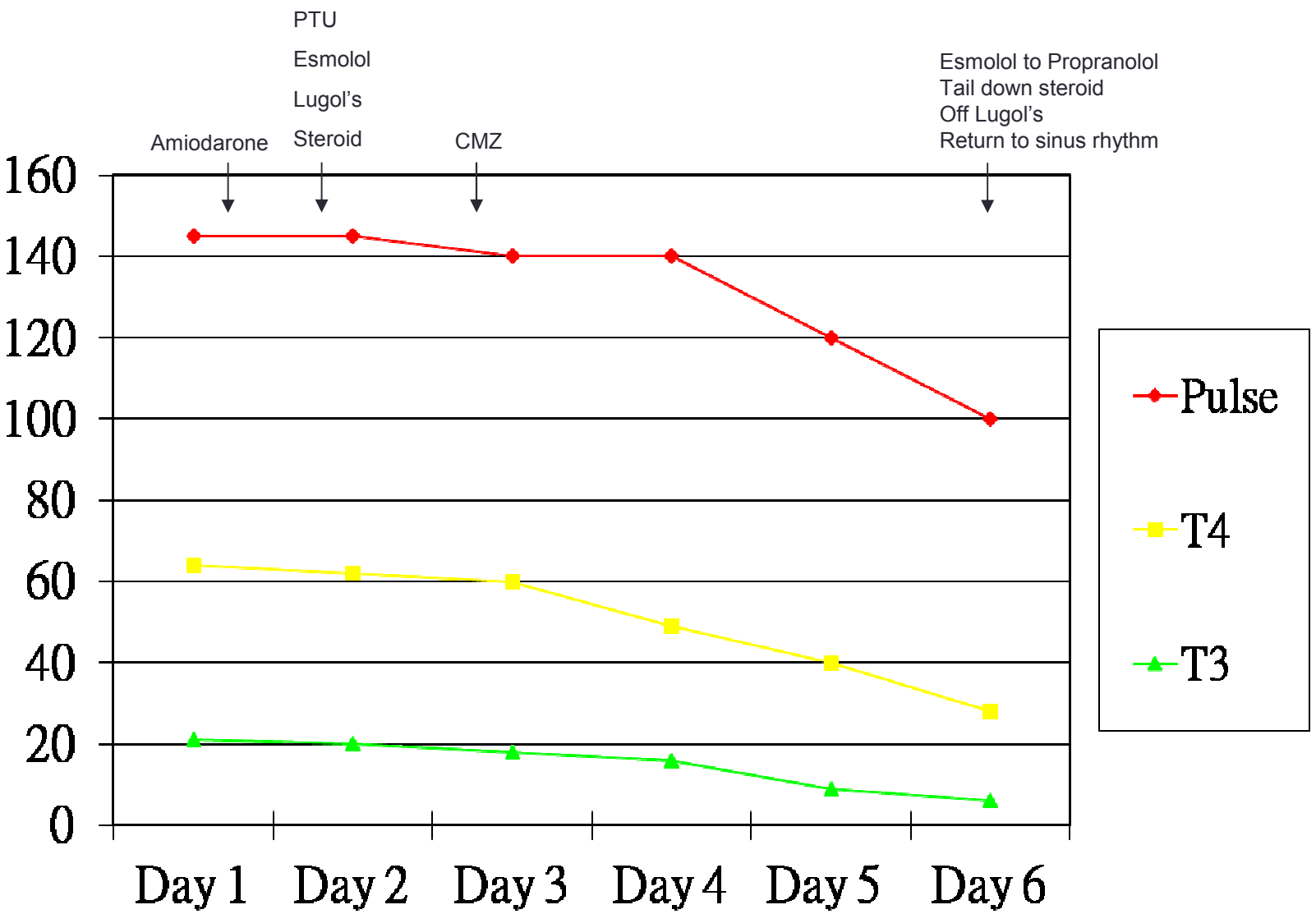
Causes of liver injury in hyperthyroidism

- Autoimmune hepatitis
  - Associated with GD
  - Sometimes triggered by PTU by unknown mechanism
  - Requires immunosuppressive therapy in severe case

Day 3

- Impaired LFT multifactorial
- Thyroid storm
- PTU related
- PTU is metabolized by liver in greater proportion than CMZ
- Switched to CMZ 20mg TDS oral


700
600
500
400
300
200
100
0
CMZ
PTU
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Bilirubin
ALP
ALT


PTU
Esmolol
Lugol's
Steroid
Amiodarone
CMZ
Esmolol to Propranolol
Tail down steroid
Off Lugol's
Return to sinus rhythm
160
140
120
100
80
60
40
20
0
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Pulse
T4
T3

Progress

- Discharged to ward on day 7
- Home on day 10

On discharge

- LFT
  - Bilirubin 45
  - ALP 117
  - ALT 56
- fT4 14.7 (12-22)
- fT3 4 (3.9-6.7)

Beta-blocker use in this case

- Use of esmolol uncomplicated despite poor EF
- Effect in controlling tachycardia not obvious until T4/T3 under control
- Initial ineffectiveness in heart rate control might be due to ↑ no. of β receptors in heart
- Useful in stopping peripheral conversion
- Damped down peripheral adrenergic action

SYA Ngo et al.*Resuscitation*:2007;73:485-490

Other anti-arrhythmics in TS

- CCB should be avoided due to risk of severe hypotension unless beta-blocker contraindicated
- Digoxin usually ineffective in TS

SYA Ngo et al.*Resuscitation*:2007;73:485-490

Amiodarone and thyroid function

- Associated with thyroid dysfunction
- Also long half life (100 days) and adhere to adipose tissue due to lipophilia
- Most patients remain euthyroid (>90%) when treated with amiodarone
- Risk of developing amiodarone-induced hypo- or hyperthyroidism depends on underlying thyroid status and dietary iodine intake

Amiodarone and thyroid function

- Direct effect
  - Inhibits 5'-monodeiodination of T4 and therefore ↓ T3 production
  - Blocks T3 binding to nuclear receptors
  - Destructive thyroiditis

Amiodarone and thyroid function

- Indirect effect (high iodine content)
  - Each amiodarone molecule has 2 iodine atoms
  - 100mg amiodarone releases 3mg iodine into circulation (average diet contains 0.3mg iodine per day!!!)
  - Provides abundant iodine substrate for TH synthesis
  - In normal people, iodine transport and TH synthesis inhibited when iodine concentration reaches high level (Wolff-Chaikoff effect)

Amiodarone and thyroid function

- Indirect effect
  - In those who have autoimmune thyroid disease “fail to escape” from Wolff-Chaikoff effect → results into hypothyroidism in Hashimoto’s thyroiditis
  - Patients with nodular goitre which fails to autoregulate, such a high iodine substrate results in excessive TH synthesis and thus thyrotoxicosis (Jod-Basedow)
  - People from iodine deficient areas more prone to develop hyperthyroidism; while those from iodine sufficient areas more prone to have hypothyroidism

Type 1 amiodarone-induced thyrotoxicosis (AIT)

- Common in individuals with nodular goitre, latent autoimmunity or those coming from iodine deficient countries
- Pathogenesis - Jod-Basedow effect
- Treatment - potassium perchlorate & thionamides

Type 2 AIT

- Destructive thyroiditis → inflammation
- Occurs in those without underlying thyroid disease
- More common than type 1 AIT
- Treatment - steroid
- Mixed type AIT - both type 1 & 2 mechanisms

Differentiate type 1 and type 2 AIT

- Thyroid ultrasonography
  - Absent hypervascularity in type 2 AIT; type 1 AIT show increased vascularity
- Thyroidal 131I uptake
  - Very low (3%) in type 2 AIT; normal, or even increased in type 1 AIT
- MIBI (99mTc) scintigraphy
  - Hyperfunctioning tissue in type 1 AIT; no uptake in type 2 AIT
- IL-6 or C-reactive protein
  - Elevated in type 2 AIT, non-specific
- TSH receptor autoantibody
  - Type 1 AIT/ GD

Amiodarone in thyroid storm

- Immediate effect
  - Control heart rate
  - Inhibit TH synthesis at high dose (Wolff-Chaikoff effect)
- Later effect
  - Type 1 AIT (Jod-Basedow)
  - Type 2 AIT
  - Takes weeks or months to develop

IF PATIENT REQUESTS RAI DURING FU, WHAT SHOULD WE ADVISE HER?

RAI (I-131)

- Make sure no contraindications: pregnancy, lactation, severe ophthalmopathy or very large goitre
- Avoid pregnancy for at least 12 months after RAI
- Pregnancy test before RAI
- Avoid close contact with children or pregnant women for 2 to 4 weeks depending on the dose and type of RAI used

RAI (I-131)

- Delayed for several weeks or months following treatment of iodine

- Iodine can impair uptake and efficacy of RAI therapy

Hyperemesis gravidarum

- Serum TSH low and FT4 high
- Result of crossreactivity between hCG and TSH at the thyroid receptor
- Supportive therapy - antiemetics, hydration, electrolyte replacement and nutrition
- Spontaneous recovery occurs by 18 wga
- Anti-thyroid medications indicated only if persistence of thyrotoxicosis beyond 18 to 20 wga

Management of hyperthyroidism in pregnancy

- Thionamide is the mainstay treatment
- PTU is used more frequently than methimazole
- Methimazole may be teratogenic
- Reported anomalies - cutis aplasia, choanal atresia, gastrointestinal, and facial abnormalities

Anti-thyroid drugs in pregnancy

- All anti-thyroid drugs can cross placenta
- Cause fetal hypothyroidism
- Lowest possible dose should be used
- To achieve a maternal FT4 slightly more than normal level

Novel therapy

CLINICAL REPORT

Thyroid arterial embolization for the treatment of hyperthyroidism in a patient with thyrotoxic crisis

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Manuscript submitted 26th September, 2008
Manuscript accepted 18th December, 2008

Clin Invest Med 2009; 32 (1): E78-E83.

Thyroid artery embolization

- Zhao et al reported treatment of 41 patients with hyperthyroidism using thyroid arterial embolization
- 38 patients who had been followed up for 1-3 years
- 27 became euthyroid (71.1%), 4 improved (10.5%) with reduced dosage of antithyroid drugs for maintenance and 7 recurred (18.4%)

Zhao W et al. *J Clin Immunol* 2008;28:456-63

THANK YOU & GOOD LUCK IN EXAM!