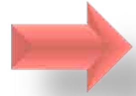
12th AME Italian Meeting Associazione Medici Endocrinologi
Italian Association of Clinical Endocrinologists
6th Joint Meeting with AACE American Association of Clinical Endocrinologists
Bari, 7-10 November 2013

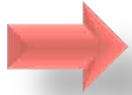
Bari,
7-10 novembre 2013

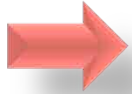
Meet the expert:

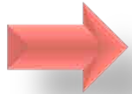
Crisi tireotossica

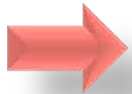
D.Barbaro


Cos'è la crisi tireotossica?


Cause e patogenesi


Clinica


Prevenzione


Terapia

…Finally, Waldestein et al in a 1960 pubblication required a temperature of 100 °F or greater and "marked tachycardia" in association with " accentuated signs and symptoms of thyrotoxicosis" to which Mazzaferri et al in 1969 added a fourth, optional criterion concerning evidence of dysfunction in one or more of the central nervous, cardiovascular, or gastrointestinal systems

$°C=(F-32)/1.8$

Henry B. Burch, Leonard Wartofsky
Life – threatening thyrotoxicosis thyroid storm
Endocrinology and metabolism clinics of North America 1993

Although hyperthermia, marked tachycardia and central nervous system dysfunction are dianostic criteria common to each of these reviews, numerous examles can be found in the literature in which one or more of these features was either a minor contributor or absent

Henry B. Burch, Leonard Wartofsky
Life – threatening thyrotoxicosis thyroid storm
Endocrinology and metabolism clinics of North America 1993

Therefore, the authors have constructed a diagnostic point scale for purpose of enabling a semiquantitative distinction between uncomplicated thyrotoxicosis, impending thyroid storm, and established thyrotoxic storm

Henry B. Burch, Leonard Wartofsky
Life – threatening thyrotoxicosis thyroid storm
Endocrinology and metabolism clinics of North America 1993

Table 1. KNOWN PRECIPITANTS OF THYROID STORM

Conditions Associated with a Rapid Rise in Thyroid Hormone Levels
Thyroid surgery
Withdrawal of antithyroid drug therapy
Radioiodine therapy
Vigorous thyroid palpation
Iodinated contrast dyes
Conditions Associated with an Acute or Subacute Nonthyroidal Illness
Nonthyroidal surgery
Infection
Cerebrovascular accident
Pulmonary thromboembolism
Parturition
Diabetic ketoacidosis
Emotional stress
Trauma

Henry B. Burch, Leonard Wartofsky
Life – threatening thyrotoxicosis thyroid storm
Endocrinology and metabolism clinics of North America 1993

TABLE 2. TRIGGERS OF THYROID STORM IN JAPANESE PATIENTS

Triggers	*Cases*	*Triggers*	*Cases*
Irregular use or discontinuation of antithyroid drugs	122	Pregnancy/delivery	5
Infection	87	Cerebrovascular disease	3
Diabetic ketoacidosis	12	Intense exercise	2
Severe emotional stress	12	Ischemic heart disease	1
Trauma	12	Adrenocortical insufficiency	1
Nonthyroid surgery	8	Administration of iodinated contrast medium	1
Radioiodine therapy	6	Extraction of teeth	1
		Others	31

Data are from the SURVEY-2 of TS with validation.
SURVEY-2, Second Nationwide Survey.

Haraldsdottir S et al
Case of sorafenib induced thyroid storm
J Clin Oncology. 2013

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Thyroid 2012

Donna 55 aa, ex fumatrice, affetta da M di Basedow dal 2004 in terapia fitoterapica ed omeopatica, per scelta personale.

→ LYCOPUS VIRGINICUS 5 CH
3-4 granuli una volta al giorno
→ Calcium fluoratum D12 Schüssler DHU
2 cp da sciogliere sotto la lingua
prima dei 3 pasti

– OLIGOLITO IODUM (Pegaso)
1 fl sublinguale 3 volte la settimana (LUN-MER-VEN)

– THYROIDINUM 30 CH granuli
5 granuli 3 volte la settimana (MART-GIOV-SAB)

Giunge in PS per cardiopalmo, dispnea e comparsa di febbre che il curante ha trattato con Acidoacetilsalicilico 500 mg/due cp die

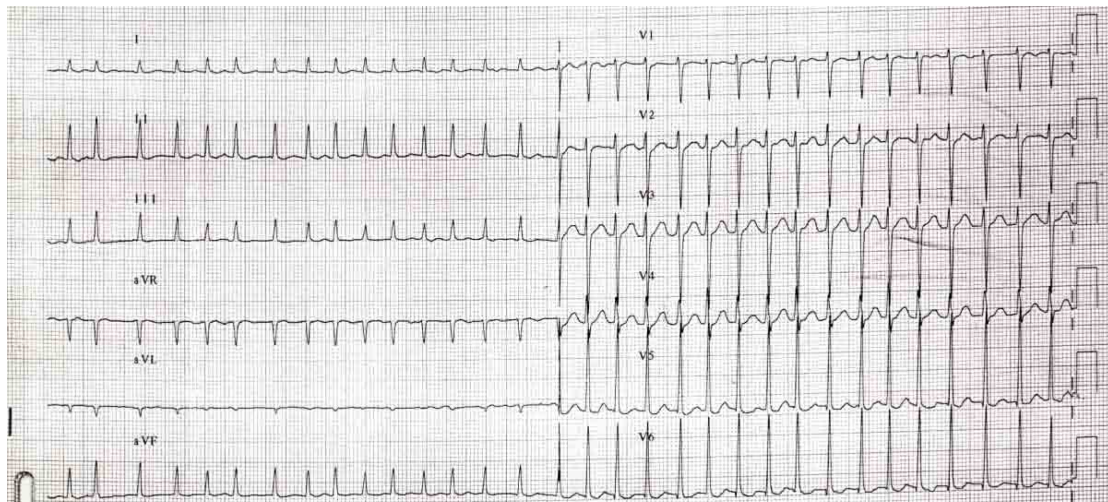
J Clin Invest. 1972 May; 51(5): 1125–1134. PMCID: PMC292242
doi: 10.1172/JCI106905

Salicylate-induced increases in free triiodothyronine in human serum

Evidence of inhibition of triiodothyronine binding to thyroxine-binding globulin and thyroxine-binding prealbumin

P. R. Larsen

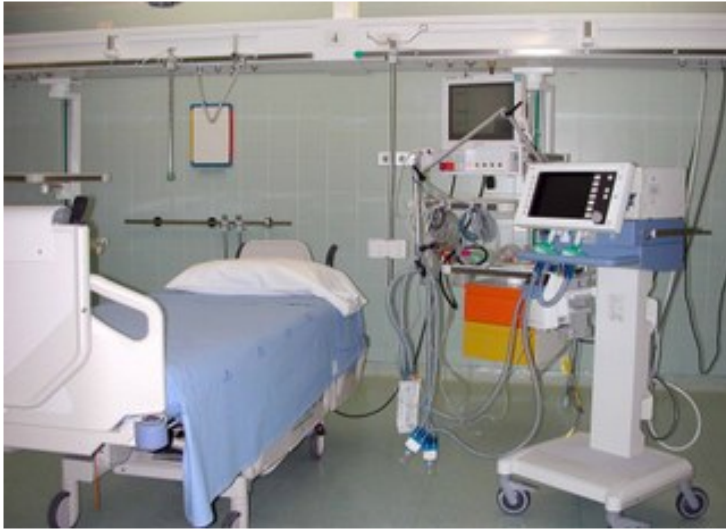
EO: FA ad elevata risposta ventricolare (fc 190b/min), PA 150/80, SpO_2 94% in aria; T° 37,9; tremori generalizzati, torace ed addome n.d.p.



Ore 12,12: trattata in OBI: Diltiazem 6 fiale (300 mg) in 500 mL a 21 mL/h; furosemide 60 mg e.v.

Ore 16,15: ricovero in Sub-Intensiva per FA ad elevata risposta Ventricolare in Ipertiroidismo

Ore 19,15	CONSULENZA CARDIOLOGICA (dott.ssa [illegible])
	Pz in shock (PAS 90), all'ingresso FA ad elevata risposta
	(→ infusione di Diltiazem), PA non contattabile
	Al mio arrivo FC 52 bpm
→	Durante esecuzione di ecocardiogramma paziente in ACC
	(ecocardiogramma eseguito evidenzia cavità vsx non dilatata
	FE 20%-25%, cavità dx dilatata, dilatazione biatriale, non
	versamento pericardico) si contatta la ICR



Esame	Valore		Unità	Valori di riferimento
S-Glucosio	177	H	mg/dL	70 - 110
S-Acido urico	5.02		mg/dl	2.40 - 6.00
S-Urea	84	H	mg/dl	20 - 50
S-Creatinina	1.85	H	mg/dL	0.50 - 0.90
S-Trigliceridi	56		mg/dl	Valore desiderabile <150
S-Colesterolo totale	67	L	mg/dl	120 - 200
S-Bilirubina totale	7.55	H	mg/dl	0.30 - 1.20
S-Bilirubina diretta	4.66	H	mg/dL	< 0.30
S-Bilirubina indiretta	2.89	H	mg/dL	0.20 - 0.90
S-Creatinchinasi (CK)	41		U/L	20 - 140
S-Lattico deidrogenasi (LDH)	449	H	U/L	125 - 220
S-Aspartato aminotransferasi (AST)	869	H	U/L	5 - 35
S-Alanina aminotransferasi (ALT)	1 314	H	U/L	5 - 35
S-Gamma glutamiltransferasi (GGT)	38	H	U/L	5 - 35
S-Fosfatasi alcalina (ALP)	71		U/L	35 - 104
S-Colinesterasi	3 936	L	U/L	5 100 - 15 500
S-Amilasi totale	196	H	U/L	20 - 100

Esami al ricovero: TSH <0.001

fT4 >60 pg/ml (7-18)

fT3 >40 pg/mL (2.4-4.7)

E' una CT?

Diagnostic criteria for thyroid storm*

Thermoregulatory dysfunction	
Temperature (°F | °C)	
99 to 99.9 | 37.2 to 37.7	5
100 to 100.9 | 37.8 to 38.2	10
101 to 101.9 | 38.3 to 38.8	15
102 to 102.9 | 38.9 to 39.4	20
103 to 103.9 | 39.4 to 39.9	25
≥104.0 | >40.0	30
Central nervous system effects	
Mild	10
Agitation	
Moderate	20
Delirium	
Psychosis	
Extreme lethargy	
Severe	30
Seizure	
Coma	
Gastrointestinal-hepatic dysfunction	
Moderate	10
Diarrhea	
Nausea/vomiting	
Abdominal pain	
Severe	20
Unexplained jaundice	

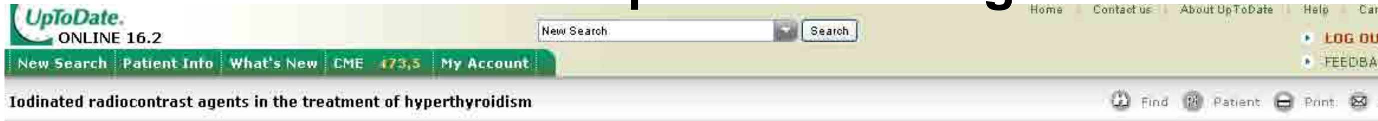
Cardiovascular dysfunction	
Tachycardia	
99 to 109	5
110 to 119	10
120 to 129	15
130 to 139	20
≥140	25
Atrial fibrillation	10
Heart failure	
Mild	5
Pedal edema	
Moderate	10
Bibasilar rales	
Severe	15
Pulmonary edema	
Precipitant history	
Negative	0
Positive	10

* 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.

UpToDate

Dopo 24 ore di trattamento tireostatico (PTU 200X5)+MP (80mg) si aggiunge alla terapia

Acido Iopanoico 500mgx2



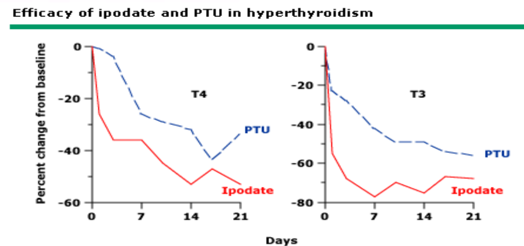
Iodinated radiocontrast agents in the treatment of hyperthyroidism

Author	Section Editor	Deputy Editor
Douglas S Ross, MD	David S Cooper, MD	Kathryn A Martin, MD

Last literature review version 16.2: maggio 2008 | **This topic last updated:** ottobre 30, 2006 **(More)**

INTRODUCTION — Ipodate and iopanoic acid, two oral iodine-containing drugs marketed as oral cholecystographic agents, have been used in the treatment of hyperthyroidism. These drugs are the most potent inhibitors of 5'-monodeiodinase, thereby impairing the extrathyroidal conversion of thyroxine (T4) to the more potent triiodothyronine (T3). The release of iodine in pharmacologic quantities from these agents has the additional benefits of blocking thyroid hormone release and interfering with its synthesis in some patients. (See "Iodine in the treatment of hyperthyroidism").

Efficacy of ipodate and PTU in hyperthyroidism



Percent change from baseline in serum concentrations of T4 (left panel) and T3 (right panel) in patients with hyperthyroidism who were treated with ipodate (1 g/day) or propylthiouracil (200 mg TID). Ipodate produced more rapid correction of the hyperthyroidism. *Data from Wu, SY, Shyh, TP, Chopra, IJ, et al, J Clin Endocrinol Metab 1982; 54:630.*

Esami al ricovero:	**Esami dopo 30 ore da Acido iopanoico**
TSH <0.001	**TSH<0.001**
fT4 >60 pg/ml (7-18)	**fT4 30.1 pg/ml (7-18)**
fT3 >40 pg/mL (2.4-4.7)	**fT3 3.6 pg/mL (2.4-4.7)**

THYROID
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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

Definition

Thyrotoxic storm or crisis is a life-threatening condition requiring emergency treatment. The condition, which is often triggered by severe physical or mental stress, arises in thyrotoxic patients. These patients manifest multiple organ failure as a result of the breakdown of compensatory mechanisms.

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Mortalità

11.0 % in TS1

9.5 % in TS2

MOF	25%
HF	21%
UNKNOWN	23%
OTHER (respiratory failure, DIC, GI perforation, Sespsi)	

Possibilità di sequele 10 -15 %

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Symptoms (Note 1)

1. Central nervous system (CNS) manifestations (Note 2)
2. Fever (38°C or higher)
3. Tachycardia (130 beats/min or faster) (Note 3)
4. Congestive heart failure (CHF) (Note 4)
5. Gastrointestinal (GI) and hepatic manifestations (Note 5)

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Diagnostic criteria for "definite"

Patients who meet the prerequisite for thyrotoxicosis and either of the following criteria are regarded as definite cases (Note 6):

(i) At least one CNS manifestation plus one or more of the other symptoms just listed;
(ii) Three or more of the manifestations just listed other than CNS manifestations

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Diagnostic criteria for suspected cases

Patients who meet either of the following criteria are regarded as suspected cases:

(i) A prerequisite for diagnosis is diagnosis of thyrotoxicosis plus two of the manifestations just listed, excluding CNS manifestations;
(ii) In cases where it cannot be confirmed whether the patient meets the prerequisite for diagnosis, it is known that the patient has a history of thyroid disease, presents with exophthalmos and goiter, and meets (i) or (ii) from the criteria for definite cases (Note 6).

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TABLE 1. CHARACTERISTICS OF PATIENTS REPORTED IN THE LITERATURE WITH THYROID STORM, IN PATIENTS WITH THYROTOXICOSIS WITHOUT TS, AND IN JAPANESE PATIENTS WITH THYROID STORM

			TS reported, with validation, in the SURVEY-2 of Japanese patients	
	TS reported in the literature	*Tox-NoTS patients*	*TS1*	*TS2*
Number	106	133	282	74
Age (years old)	42.1 ± 14.9 (7–73)	43.2 ± 15.5 (14–80)	44.7 ± 16.7 (6–87)	44.6 ± 14.6 (20-80)
Male:female	30:76	34:99	74:204	15:59
Basic thyroid diseases				
Graves' disease	95.2%	97.7%	98.9%	97.30%
Others	4.8%	2.3%	1.1%	2.70%
Free T4 (ng/dL)	6.76 ± 3.17	6.35 ± 5.13	6.38 ± 3.40	6.18 ± 2.56
Free T3 (pg/mL)	15.9 ± 7.9	16.5 ± 8.2	19.70 ± 12.70	17.81 ± 8.78
Fever ≥38°C	55.7%	3.0%	41.5%	41.9%
Pulse rate				
≥120/min	82.1%	24.0%	84.0%	75.7%
≥130/min	67.9%	7.5%	76.2%	60.8%
CNS symptoms[a]	64.2%	Not frequent	84.4%	2.7%
GI/hepatic symptoms[b]	51.9%	Not frequent	69.5%	63.5%
CHF[c]	38.7%	Not frequent	39.4%	37.8%
NYHA classification IV	20.1%	Rare	24.1%	9.5%
Killip classification ≥III	20.1%	Rare	22.7%	17.6%
Precipitating factors	76.4%	Not applicable	71.3%	64.9%
Mortality rate	17.0%	Very low	11.0%	9.5%

Systeme International (SI) units for free T4 to picomoles per liter (conversion factor, 12.87); for free T3 to picomoles per liter (0.0154).
[a]CNS symptoms with agitation, restlessness, delirium, mental aberration/pshychosis, somnolence/lethargy, convulsion or coma.
[b]GI/hepatic symptoms with abdominal pain, diarrhea, nausea/vomiting, or jaundice with liver dysfunction.
[c]CHF with pedal edema, bibasilar rales, or pulmonary edema.
TS, thyroid storm; Tox-NoTS, thyrotoxicosis without TS; CNS, central nervous system; GI, gastrointestinal; CHF, congestive heart failure; NYHA, New York Heart Association; T4, thyroxine; T3, triiodothyroine.

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Mortalità significativamente aumentata se bilirubina totale > 3.0 mg/dl

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TABLE 9. FINAL CRITERIA FOR THE DIAGNOSIS OF THYROID STORM

Grade of TS	*Combinations of features*	*Requirements for diagnosis*
TS1	First combination	Thyrotoxicosis and at least one CNS manifestation and fever or tachycardia, or CHF or GI/hepatic manifestations
TS1	Alternate combination	Thyrotoxicosis and at least three combinations of fever, or tachycardia, or CHF, or GI/hepatic manifestations
TS2	First combination	Thyrotoxicosis and a combination of two of the following: fever or tachycardia or CHF or GI/hepatic manifestations
TS2	Alternate Combination	Patients who meet the diagnostic criteria for TS1 except that serum FT3 or FT4 values are not available but whose data before or after the episode suggest that they are thyrotoxic at the time of TS.

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E’ possibile una prevenzione?

Pazienti ipertiroidei misconosciuti	No
Pazienti ipertiroidei noti (trattamento adeguato)	Sì
Pazienti ipertiroidei con quadro severo	Sì

- Terapia pronta con dosaggi importanti e globale, in caso di severa comorbidità terapia tipo “CT”

Table 3. Medical Treatment of Thyroid Storm.

	Oral Dose	Rectal Dose	Intravenous Dose
Therapy against new thyroid hormone production			
Propylthiouracil	Loading dose of 500-1000 mg followed by 250 mg every 4 hours	400-600 mg every 6 hours	
Methimazole	60-120 mg per day in 4-6 doses	20-40 mg every 8-6 hours	10-30 mg every 8-6 hours
Therapy against thyroid hormone release			
SSKI	5 drops every 6 hours	250-500 mg every 6 hours	
Lugol's solution	8 drops every 6 hours	80 drops per day/5-10 drops every 8-6 hours	
Sodium iodide			0.5 g every 12 hours
Lithium	300 mg every 8-6 hours		
Blocking the peripheral effects of thyroid hormone			
Propranolol	60-120 mg every 4-6 hours		
Esmolol			50-100 mcg/kg/min
Hydrocortisone			300 mg loading dose IV then 100 mg every 8 hours
Enhancing thyroid hormone clearance			
Cholestyramine	1-4 g twice a day		

Abbreviations: IV intravenous; SSKI, saturated solution of potassium iodine.

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Thyroid storm: an update review
J intensive Care Med 2013

Therapeutic Plasma Exchange

In refractory cases of thyrotoxic crisis in which clinical deterioration occurs despite the use of conventional therapies or a toxicity emerges (such as leukopenia due to PTU), alternative measures aimed at clearing thyroid hormone from th circulation should be instituted

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Surgical Management

These include those patients who clinically deteriorate or do not improve within 24 to 48 hours despite intensive medical treatment, develop side effects from the treatment (ie thionamide-induced agranulocytosis or severe thrombocytopenia), or need expedient resolution of their hyperthyroidism due to severe underlying cardiac or pulmonary comorbidities

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