On Call (!) - Endocrine Emergencies

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Objective

- Clinical Pearls in the Diagnosis and Management of common Endocrine (non-DM) Emergencies

Case Scenario (1)

You received a call from A & E to review a patient who was just admitted. The case was a 29 year old Chinese lady who presented with fever of 39 degrees and confusion of 1 day duration. She was previously well and has no significant past medical history of note.

On examination, she was a slim lady of medium build.

Temperature 39 deg, HR 130 bpm (regular), BP 80/40 mmHg, SpO_2 88% RA

Confused, not oriented to time, person or place

JVP 4cm

Moderate diffuse goitre with "bulgy" eyes

H: S1S2 no murmurs

L: Bilateral basal crepitations

A: Soft, non tender

Bilateral pedal edema

Investigations

FBC normal except raised TW 12K

Renal panel unremarkable

Liver panel AST, ALT, ALP all 2x ULN, Alb 30

FT4: 70 (8.8-14.4pmol/L) TSH <0.015 (0.65-3.70mU/L), FT3 40 (3.2-5.3pmol/L)

CE normal, ECG: Sinus tachycardia

CXR: Pulmonary congestion

Thyroid storm

- Definition
  - ***Life-threatening condition caused by the exaggeration of clinical manifestations of thyrotoxicosis***
- SGH 2006-2011: 28 out of 2660 cases of patients adm for thyrotoxicosis (1.05%)
- Mortality in SGH series 25%
- Clinical diagnosis: Burch Wartosky's score is a guide, but NOT definition

Swee DS, Chng CL, Lim A. Clinical Characteristics and Outcome of Thyroid Storm: A Case Series and Review of Neuropsychiatric Derangements in Thyrotoxicosis. Endocr Pract 2015;21(2):182-189

Uncomplicated Thyrotoxicosis Vs Storm

Clinical Feature	Uncomplicated Thyrotoxicosis	Thyroid Storm
Thermoregulatory	Heat intolerance, diaphoresis	Hyperpyrexia, large insensible fluid losses
Nervous system	Hyperkinesis, nervousness	Confusion, seizure, coma
Cardiovascular	Tachycardia (90–120 bpm)	Accelerated tachycardia (>130 bpm), atrial dysrhythmia, heart failure
Gastrointestinal	Hyperdefecation	Nausea, vomiting, diarrhea
Hepatic	Mild transaminase elevation	Hepatic dysfunction, jaundice
Psychiatric	Agitation, emotional lability	Psychosis
Precipitant history	Absent	Present
Death	Rare	Frequent (10%–20%)

BURCH And WARTOFSKY'S
Diagnostic Criteria For Thyroid Storm

Thermoregulatory Dysfunction	
TEMPERATURE	**Score**
37.2 - 37.7 C (99 - 99.9 F)	5
37.8 - 38.2 C (100 - 100.9 F)	10
38.3 - 38.8 C (101 - 101.9 F)	15
38.9 - 39.3 C (102 - 102.9)	20
39.4 - 39.9 C (103 - 103.9 F)	25
> 40 C (> 104.0 F)	30

Central Nervous System Effects		
MANIFESTATION		**Score**
ABSENT		0
MILD	(AGITATION)	10
MODERATE	DELIRIUM	20
	PSYCHOSIS	
	EXTREME LETHARGY	
SEVERE	SEIZURE COMA	30

INTERPRETATION	SCORE
HIGHLY SUGGESTIVE OF STORM	> 45
SUGGESTIVE OF IMPENDING STORM	25 - 44
UNLIKELY TO REPRESENT STORM	< 25

ALL ABOUT INTERNAL MEDICINE (AAIM)
http://allaboutim.webs.com

Gastrointestinal Hepatic Dysfunction		
MANIFESTATION		**Score**
ABSENT		0
MODERATE	DIARRHEA	10
	NAUSEA / VOMITING	
	ABDOMINAL PAIN	
SEVERE	UNEXPLAINED JAUNDICE	20

Cardiovascular Dysfunction		
TACHYCARDIA		
99 - 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 EDEMA	15
ATRIAL FIBRILLATION		
ABSENT		0
PRESENT		10
PRECIPITANT HISTORY		
NEGATIVE		0
POSITIVE		10

Caveats of BWPS

Atypical Manifestations

- Apathetic thyroid storm
- Psychosis, coma
- Status epilepticus
- Nonembolic cerebral infarction
- Abdominal pain and fever in young women
- Small bowel obstruction
- Acute renal failure resulting from rhabdomyolysis

Qns 1

What is the most likely etiology of thyrotoxicosis in this patient?

A. Graves' disease
B. Toxic multinodular goitre
C. Toxic thyroid adenoma
D. Subacute thyroiditis

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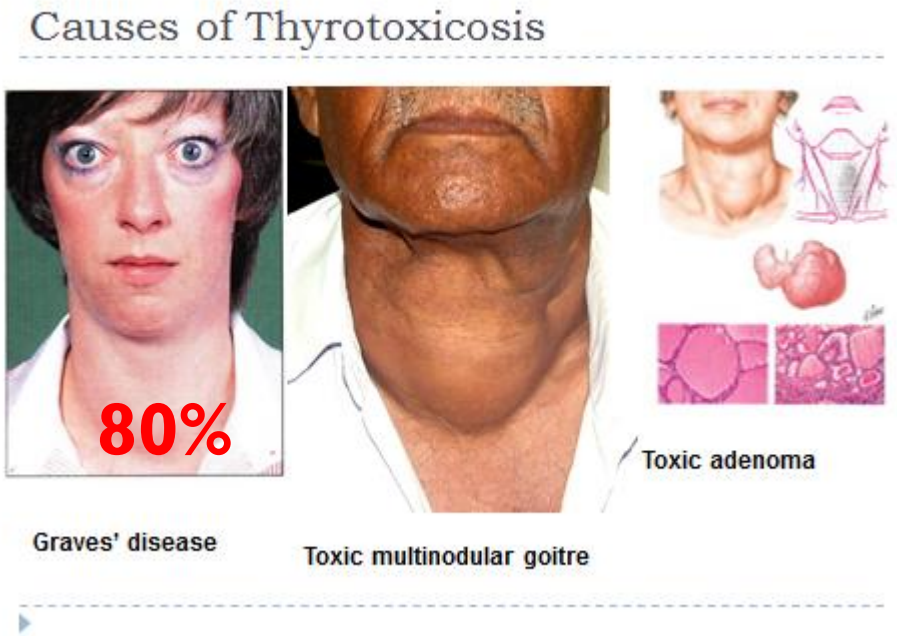

Pathogenesis

- Rapidity with which the TH rise rather than absolute level
  - Adrenergic receptor activation
  - Enhancement of cellular response to TH

Known Precipitants of Thyroid Storm	
Infection	Toxemia of pregnancy
Surgery – Thyroid, non-thyroid	Parturition
Iodinated contrast dyes	Severe emotional stress
Withdrawal of ATD	PE
RAI	CVA
TH ingestion	Bowel infarction
DKA or Hypoglycemia	Trauma, fractures
Amiodarone	Tooth extraction
CCF	Vigorous palpation of thyroid (!)

Burch et al 1993, Tietgens et al 1995, Hall et al 1999, Turner et al 2003, Greenspan et al 2004

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CE normal, ECG: Sinus tachycardia
CXR: Pulmonary congestion

Diagnosis

Thyroid Storm

- BWPS: 70

Graves' disease

Management

The most important determinants of survival in life-threatening thyrotoxicosis are early recognition and institution of appropriate therapy

Qns 2

- Which of the following drugs is used in the management of thyroid storm?

i. Propylthiouracil
ii. Sodium Iodide solution
iii. Hydrocortisone
iv. Propranolol

A. i, iii,iv
B. All of above
C. i, iv
D. None of above

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Management

- ABC important
- HD/ICU monitoring
- Medical management of Thyroid Storm
  - Inhibiting synthesis of new TH in the thyroid gland
    - Propylthiouracil, lugol's iodine/ IV sodium iodide
  - Inhibiting TH release
    - Lugol's iodine/ IV sodium iodide
  - Preventing conversion of T4 to T3
    - Propylthiouracil, IV hydrocortisone, Propranolol
  - Controlling adrenergic symptoms associated with thyrotoxicosis
    - Propranolol
  - Controlling systemic decompensation with supportive therapy

Nayak B, Burman K. Thyrotoxicosis and thyroid storm. Endocrinol Metab Clin North Am. 2006 Dec;35(4):663-86, vii

Caveats to use of B blockers

Case 1

- 32 year old male presented with SOB + LL edema 1 wk a/w heat intolerance and hand tremors
- Vitals:Afebrile, HR 134/min, BP 103/58 mmHg, SpO2 99%
- Clinically appeared anxious with exophthalmos, diffusely enlarged thyroid gland, bilateral LL pitting edema
- ECG showed atrial flutter, CXR cardiomegaly + mild fluid overload
- Propranolol started and patient admitted
- 4 hrs later developed SOB + chest discomfort
- BP unrecordable, weak pulse, narrow complex tachycardia
- He was cardioverted but remained hypotensive
- Intubated and started on inotropes

Case 2

- 28 year old man p/w SOB, orthopnea, generalised edema 1 week
- Clinically in fluid overload with elevated JVP, bilateral basal creps, scrotal and bilateral LL edema
- Vitals: Afebrile, HR 173/min, BP 103/73mmHg, SpO2 100%
- ECG showed AF, CXR showed cardiomegaly and CCF
- IV diltiazem started for AF control and admitted
- In ward, patient developed recurrent rapid AF
- Both digoxin and propranolol were commenced but he subsequently collapsed from cardiogenic shock

- Long standing thyrotoxicosis induces dilated CMP
- Young individuals with severe and long standing hyperthyroidism
- Avoid use of B blockers or Calcium channel blockers in these patients

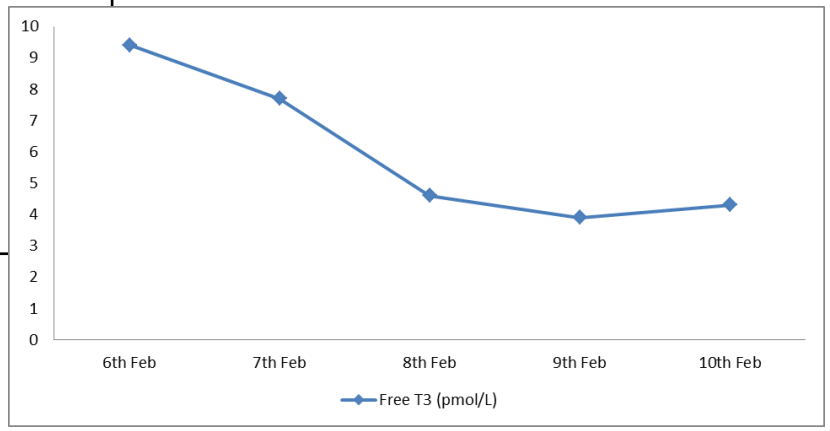
When the storm passes unnoticed- A case series of thyroid storm. Su Yin Adeline Ngo et al. 2007

An example of Storm Treatment

Date	6th Feb (at presentation)	7th Feb	8th Feb	9th Feb	10th Feb
FreeT3 (pmol/L)	9.4 ↑	7.7 ↑	4.6 ↑	3.9	4.3
Drug Therapy Given	IV Hydrocortisone 100mg 6H PO PTU 200mg 6H	IV Hydrocortisone 100mg 6H IV NaI 1g 12H PO PTU 200mg 6H	IV Hydrocortisone 50mg 6H IV NaI 1g 12H PO PTU 200mg 6H PO Bisoprolol 2.5mg om	PO PTU 200mg 6H PO Bisoprolol 5mg om	PO PTU 100mg 8H PO Bisoprolol 5mg om
Drug Therapy Discontinued				Hydrocortisone and NaI	

- Monitor clinical improvement
  - HR, BP, improvement of CCF
- FT3 levels

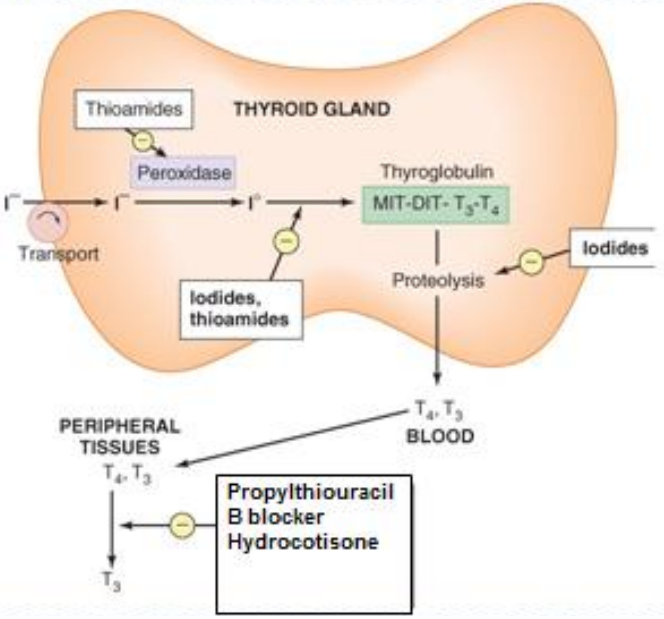
Figure 3. Graph of free T3 level and drug therapy



Clinical Pearls

- Diagnosis of TS is clinical, BWPS serves as a guide
- The heart is sensitive to the action of TH and most patients have CVS manifestations

Multimodality treatment approach



Thyrotoxicosis and Thyroid Storm. Bindu N et al. 2006

Case Scenario (2)

39 year old Chinese lady presented with 5 days of nausea associated with one day of diarrhoea, LOA and LOW 2-3kg over 1 week. Past medical history include Hashimoto's thyroiditis diagnosed two years ago treated with thyroxine. She also noted oligomenorrhoea two years ago, was investigated in a private gynecology clinic which she refused hormone replacement. Investigations then revealed:

FSH	18.5 U/L	1.0-14.0
LH	39.3 U/L	1.0-24.0
Estradiol	<18.4 pmol/L	37.0-1284

Examination: Afebrile, lethargic, BP 80/50 mmHg, HR 100/min, SpO_2 100% RA. Alert and oriented. Rest of examination was unremarkable

Urea	2.6 mmol/L	2.8-7.7	**TSH**	6.49 mU/L	0.65-3.70
Na	101 mmol/L	135-145	**FT4**	14.4 pmol/L	8.8-14.4
K	4.6 mmol/L	3.3-4.9	**Hb**	13.6 g/dL	12.0-16.0
Cl	73 mmol/L	96-108	**TW**	5.56 x 10(9)/L	4.0-10.0
HCO3	16.1 mmol/L	19.0-31.0	**Plt**	285 x 10(9)/L	140-440
Glucose	5.1 mmol/L	3.9-11.0	**Eosinophils**	7.2 %	0-6
Creatinine	39 mmol/L	40-85			

Qns 3

Which of the following is the most important investigation to consider?

A. Serum cortisol
B. Serum and urine osmolality
C. Plasma renin activity
D. Serum calcium

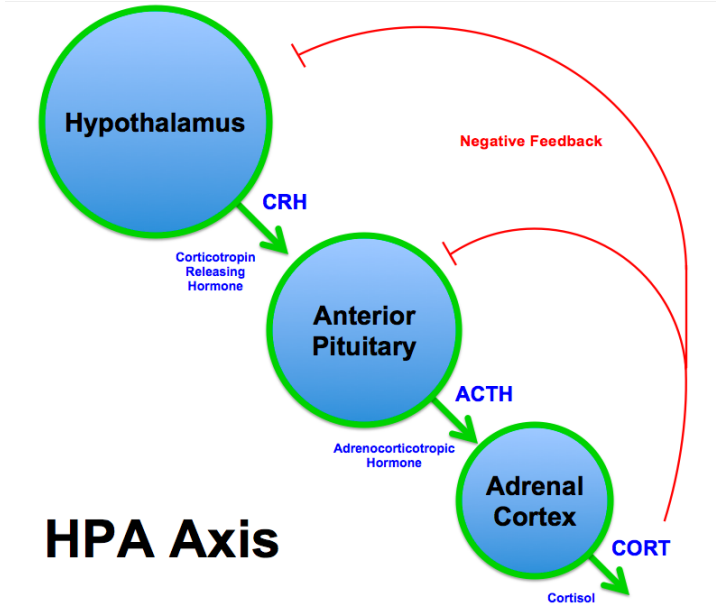
Qns 3

Which of the following is the most important investigation to consider?

A. Serum cortisol - 90 nmol/L
B. Serum and urine osmolality - 214 mmol/kg (275-301), 30 mmol/Kg (50-1200)
C. Plasma renin activity – 7.57 ug/L/hr (0.66-3.08)
D. Serum calcium - normal

Adrenal crisis

- Life threatening emergency
- Half of patients with Addison's disease report at least one previous crisis
- Precipitant – Sepsis, trauma, dental procedure, psychological distress



Clinical manifestations

Symptoms	Pathophysiology	Prevalence (100%)
Fatigue, lack of energy	GC, adrenal androgen deficiency	100
Anorexia, weight loss	GC deficiency	100
N/V, gastric pain (most common in primary)	GC, MC deficiency	92
Myalgia, joint pain	GC deficiency	6-13
Dizziness	MC, GC deficiency	12
Salt craving (primary only)	MC deficiency	16
Signs		
Skin hyperpigmentation (primary only, chronic)	Activation of skin melanocortin-1 receptors by high ACTH	94
Low BP, postural hypotension, dehydration (pronounced in primary)	MC, GC deficiency	88-94
Biochemical		
Hyponatremia	MC, GC deficiency	88
Hyperkalemia (primary only)	MC deficiency	64
Hypercalcemia (primary only)	GC deficiency (mostly with concurrent hyperthyroidism)	6
Anemia, Lymphocytosis, eosinophilia, Hypoglycemia	GC deficiency	

E Charmandari. Adrenal insufficiency. Lancet. 2014 Jun 21;383(9935):2152-67

Diagnosis of adrenal insufficiency

- Confirm **inappropriately low** cortisol secretion
  - BP 80/60mmHg, random cortisol 90 nmol/L
- Primary or central adrenal insufficiency
  - Clinical suspicion, ACTH 182 ng/L (10-60), High renin
- Underlying pathological process

Management

- Intravenous hydrocortisone without delay
  - IV 100mg stat followed by 6hourly
- Intravenous fluid resuscitation
- Paired random cortisol and ACTH before treatment
- When in doubt, treat first!
- Treat adrenal insufficiency before hypothyroidism

Management

Patient's Progress

Date	22 July	23 July	24 July	25 July	26 July	11 Aug
Serum Na	101	116	126	131	133	137
Treatment	IV Hydrocort 100mg 8H IV N/S 1L/day LT4	IV Hydrocort 100mg 8H IV N/S 1L/day LT4	IV Hydrocort 50mg 8H LT4	PO Hydrocort 40 mg OM 20mg at 4pm LT4	PO Hydrocort 20mg OM 10mg at 4pm LT4	PO Hydrocort 10mg OM 5mg 4PM Fludrocort 0.05mg OM LT4 Progyluton

Diagnosis of adrenal insufficiency

- Confirm **inappropriately low** cortisol secretion
  - BP 80/60mmHg, random cortisol 90 nmol/L
- Primary or central adrenal insufficiency
  - Clinical suspicion, ACTH 182 ng/L (10-60), High renin
- Underlying pathological process
  - Primary hypothyroidism, premature ovarian failure (Primary)

	Pathogenetic mechanisms	Clinical manifestations in addition to adrenal insufficiency
Autoimmune adrenalitis		
Isolated	Associations with HLA-DR3-DQ2, HLA-DR4-DQ8, MICA, CTLA-4, PTPN22, CIITA, CLEC16A, vitamin D receptor	None
APS type 1 (APECED)	*AIRE* gene mutations	Chronic mucocutaneous candidosis, hypoparathyroidism, other autoimmune diseases
APS type 2	Associations with HLA-DR3, HLA-DR4, CTLA-4	Thyroid autoimmune disease, type 1 diabetes, other autoimmune diseases
APS type 4	Associations with HLA-DR3, CTLA-4	Other autoimmune diseases (autoimmune gastritis, vitiligo, coeliac disease, alopecia), excluding thyroid disease and type 1 diabetes
Infectious adrenalitis		
Tuberculous adrenalitis	Tuberculosis	Tuberculosis-associated manifestations in other organs
AIDS	HIV-1	Other AIDS-associated diseases
Fungal adrenalitis	Histoplasmosis, cryptococcosis, coccidioidomycosis	Opportunistic infections
Syphilis	*Treponema pallidum*	Other syphilis-associated organ involvement

Clinical Pearls

- Adrenal crisis is life threatening
- Early recognition and treatment is key to survival
- Diagnosis of adrenal insufficiency
  - Confirm inappropriately low cortisol secretion
  - Primary or central adrenal insufficiency
  - Underlying pathological process
- When in doubt (but clinical suspicion high), treat 1st!
- Prevention and Education

The End