A case of post-operative hypotension

TED GILES CLINICAL VIGNETTE

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Case

Case: Ms. M

- 18F healthy patient
- Admitted for arthroscopy and ulnar shortening osteotomy; history of multiple wrist fractures from figure skating
- Planned for regional anaesthesia; converted to GA due to significant anxiety
- Perioperatively required 10mg of IV ephedrine and 2100mL of crystalloid for perioperative hypotension

Case: Ms. M

- Following AM; increasing pain and disorientation, tremulousness, hypotension
- Moved to step-down unit
  - Further fluid resuscitation with total 4L crystalloid restores hemodynamic stability
- Provisional diagnosis: sensitivity to opioids

Case: Ms. M

- Further probing into the history and investigations:
- Patient was given diagnosis of “adrenal fatigue” by her family’s naturopathic practitioner; is receiving OTC supplements for treatment
  - “Adrenal Life Force” 2 tabs PO qAM
  - “HPA (axis) Life Force” 1 tab PO qAM
- This prompted a workup of her hypothalamic-pituitary-adrenal axis

Case: Ms. M

- HPA axis testing consistent with secondary adrenal insufficiency
- Advised to discontinue her supplements and watch for signs of adrenal insufficiency
- Has follow-up for repeated biochemical testing to ensure recovery of HPA axis

	0800h serum cortisol	Serum ACTH48h
48h	Undetectable (<28nmol/L)	2.1umol/L (suppressed)
72h	Undetectable	
7d	654nmol/L	8.5umol/L
Reference ranges	200-660nmol/L	Lower limit 14.0umol/L

What is “Adrenal Life Force”?

HPA (Axis) Life Force

- Manufactured by Physica Energetics

- Per product catalogue:
  - 100mg “adrenal tissue”
  - 100mg “pituitary tissue”

Supports High Endocrine Axis, Post Traumatic Stress, CFS, Fibromyalgia, Hormonal

90 Vegetarian Capsules

Dosage: 1-2 capsules 2x daily, or as directed by a Health Care Practitioner

Traditionally Supports:

- HPA axis support
- CFS
- Blood sugar
- Infertility
- Libido
- Digestive disturbances
- Post Traumatic Stress Disorders:
  Abuse, Accidents, Veterans, Surgery, Emotional, All Trauma
- Energy/Fatigue
- Fibromyalgia
- Hormonal insufficiencies
- Menstrual/Menopause
- Prostate
- Immune

From http://physicaenergetics.com/dv/products/HPA-(Axis)-Life-Force..html

Adrenal Life Force

- Manufactured by Physica Energetics

- Per product catalogue:
  - 250mg “adrenal tissue”
  - “Glandulars are from New Zealand/organic bovine”

Adrenal/Thyroid Insufficiencies, Fatigue, Hormonal Imbalances, Allergies, Anxiety, etc.

120 Vegetarian Capsules

Dosage: 1-2 capsules 2x daily, or as directed by a Health Care Practitioner

Traditionally Supports:

- Adrenal/Thyroid Insufficiencies
- Energy Depletion
- Immune support
- Libido
- PMS/Menopause
- Adjustments not holding
- Chronic Fatigue Syndrome
- Allergies
- Hormonal Imbalances
- Depression, Anxiety
- Blood Sugar Imbalances
- Arthritis

From http://physicaenergetics.com/dv/products/Adrenal-Life-Force..html

“Adrenal Fatigue” - Endocrine Society Opinion

- “Myth vs Fact” education material released by Hormone Health Network

› “Adrenal fatigue” is not a real medical condition. There are no scientific facts to support the theory that long-term mental, emotional, or physical stress drains the adrenal glands and causes many common symptoms.

› Adrenal insufficiency is a real disease diagnosed through blood tests.

› There is no test that can detect adrenal fatigue.

From http://www.hormone.org/hormones-and-health/myth-vs-fact

Is it plausible that an OTC supplement could lead to adrenal suppression?

Recovery of the Hypothalamic-Pituitary-Adrenal (HPA) Axis in Patients With Rheumatic Diseases Receiving Low-Dose Prednisone

GERALD E. LA ROCHELLE, JR., M.D., ANNE G. LA ROCHELLE, M.D.,
ROBERT E. RATNER, M.D. F.A.C.P., DAVID G. BORENSTEIN, M.D. F.A.C.P., *Washington, D.C.*

- Dose-response study published in American Journal of Medicine 1993

- Retrospective analysis of 50 rheumatology patients receiving ≤10mg of prednisone
- ACTH stim test performed to assess adrenal reserve

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- Level of suppression categorized as normal, intermediate, and suppressed
- No patients showed overt suppressed at doses lower than 5mg/day
  - However 3 patients had "intermediate" responses

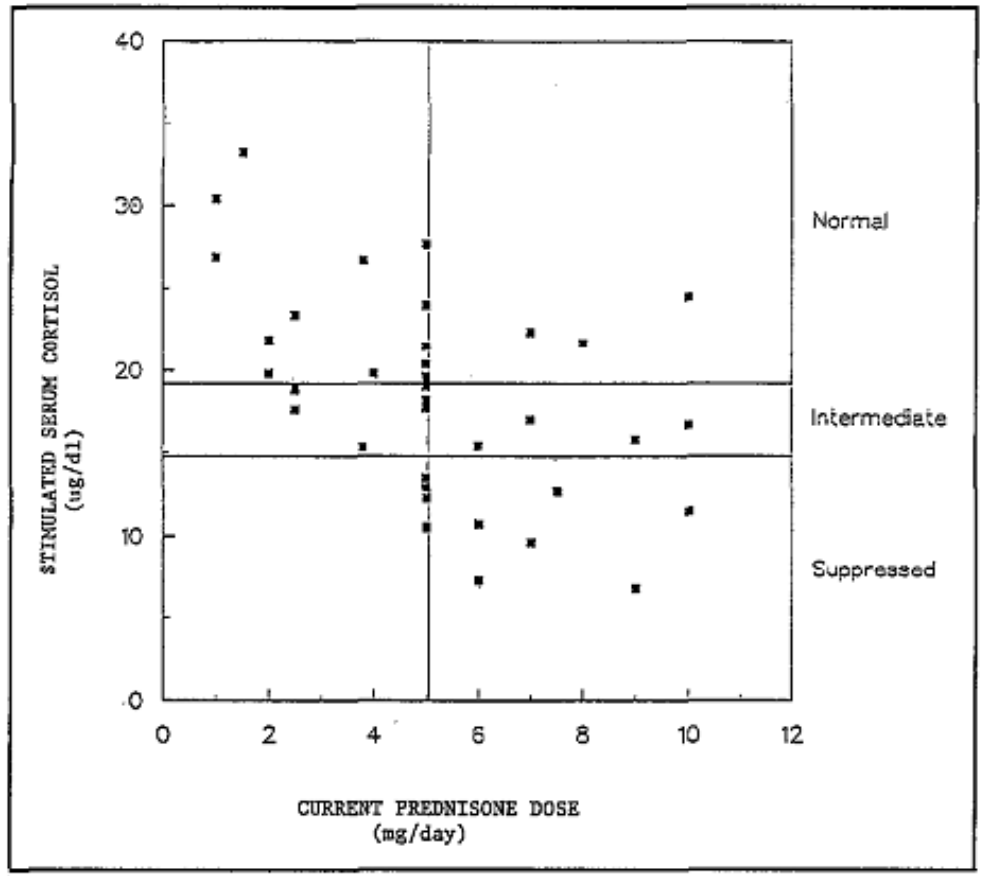

Figure 1. Serum cortisol levels after stimulation with adrenocorticotropic hormone for each patient plotted as a function of the prednisone dose of that patient at the time of the study.

Have OTC medications been reported to cause adrenal suppression?

Hypoadrenalism secondary to topical corticosteroid-containing skin-lightening cream: danger of over-the-counter cosmetic agents

Angela Shiao Ting Lee
BSc(Med) MB BS[1]

Nimalie J Perera
MB BS(Hons), FRACP, FRCPA[1]

Elizabeth L Chua
MB BS, FRACP, PhD[2]

- Case report published in Medical Journal of Australia Oct 2015

- 26 year old Sudanese woman seen in endocrinology clinic for investigation of decreased fertility
- Using “skin lightening cream” x years
  - Fluocinonine 0.075%, hydrocortisone acetate 1% purchased OTC

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Patient's pathology results

Test	During cream use	After stopping cream use	Reference interval
Serum sodium	140 mmol/L		135–145 mmol/L
Serum potassium	4.2 mmol/L		3.5–5.0 mmol/L
Serum cortisol (repeated samples on separate days)	62 nmol/L (7.30 am) 116 nmol/L (8.40 am) < 28 nmol/L (8.50 am)		200–600 nmol/L
Serum ACTH	3.1 pmol/L		< 10 pmol/L
24-hour urine free cortisol	33 nmol/24 hours		50–250 nmol/24hours
Serum cortisol after 250 µ synacthen (short synacthen test)		153 nmol/L (0 min) (9.00 am) 448 nmol/L (30 min) 621 nmol/L (60 min)	> 550 nmol/L after synacthen stimulation

ACTH = adrenocorticotropic hormone. ◆

Corticosteroid adulteration in proprietary Chinese medicines: a recurring problem

YK Chong, CK Ching, SW Ng, Tony WL Mak *

- Case series published in the Hong Kong Medical Journal October 2015

- Retrospectively looked at 61 patients referred to a tertiary clinical toxicology lab and found to be taking herbal supplements adulterated with corticosteroids

Corticosteroid adulteration in proprietary Chinese medicines: a recurring problem

YK Chong, CK Ching, SW Ng, Tony WL Mak *

TABLE 1. Corticosteroids used to adulterate the proprietary Chinese medicines (pCMs) taken by patients in this study (n=61)

Corticosteroids (and its conjugates)	No. (%) of pCMs
Dexamethasone	25 (41.0)
Prednisone	20 (32.8)
Betamethasone	5 (8.2)
Prednisolone	4 (6.6)
Clobetasol, fluocinonide	2 (3.3)
Dexamethasone, prednisolone	2 (3.3)
Dexamethasone, prednisone	1 (1.6)
Dexamethasone, triamcinolone, fluocinonide	1 (1.6)
Triamcinolone	1 (1.6)

Corticosteroid adulteration in proprietary Chinese medicines: a recurring problem

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TABLE 3. Complications attributable to exogenous corticosteroids in the proprietary Chinese medicines (pCMs) taken by patients in this study (n=61)

Classification	Complications	No. (%) of pCMs
Attributable	Cushing's syndrome	18 (29.5)
	Adrenal insufficiency	17 (27.9)
	Cataract occurring in paediatric patient	1 (1.6)
Potentially attributable	Sepsis	5 (8.2)
	Reactivation of tuberculosis	2 (3.3)
	Helicobacter pylori–negative gastritis	6 (9.8)
	Exacerbation of underlying hepatitis B	3 (4.9)
	Exacerbation of underlying hepatitis C	1 (1.6)
	Transient diabetes	1 (1.6)

Overall 38 of 61 had complications at least potentially attributable to their adulterated OTC remedy

Conclusion

Take-home points

- Importance of eliciting full medical history and drug history, including OTC
- Advise patients seek information on what their supplements actually contain
- Risk of non-specific labels like adrenal fatigue, Wilson's temperature syndrome, male menopause, etc.
- Must be careful not to ostracize patients who increasingly seek help from alternative medicine practitioners

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Why not other causes of secondary adrenal insufficiency?

- Why not primary adrenal insufficiency?
  - ACTH suppressed; would be elevated in primary adrenal insufficiency ie. Addison's disease
- No clinical signs of chronic secondary adrenal insufficiency were noted
  - No polyuria, normal baseline blood pressure, normal sodium and potassium at baseline
- Recovery of HPA axis within 1 week of discontinuation of supplements
  - Would expect no recovery if endogenous process was implicated
- Parsimony
  - Iatrogenic adrenal insufficiency most common etiology
    - ICH, pituitary apoplexy, pituitary/hypothalamic tumor, etc, not suggested by the history
  - Known history of taking supplement containing adrenal tissue

Why was the steroid in supplement undetectable?

The complexity of laboratory testing and diagnosis of steroid excess syndromes associated with herbal remedy use[1]

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- Letter to the Editor of Clinical Endocrinology 2011
- Typical assays used for detection of serum free cortisol are most specific for cortisol
- Have SOME cross-reactivity to
  - Prednisolone, methylprednisolone, prednisone, corticosterone, cortisone
- Have NO cross-reactivity with
  - Dexamethasone, beclomethasone, androstenedione, dehydroepiandrosterone sulphate
- Report includes a case of clear Cushing's syndrome with completely suppressed ACTH and undetectable 0800h serum free cortisol
  - Secondary to herbal supplements *"Mustika Dewa"* and *"Raja Syifa"*

The diagnosis and investigation of adrenal insufficiency in adults

Ian Wallace[1], Sean Cunningham[2] and John Lindsay[1]

Annals of Clinical Biochemistry Volume 46 September 2009

- AM serum cortisol
  - 0700-0900h; >500nmol/L indicates good adrenal reserve
  - <100nmol/L is definite adrenal insufficiency; 100-500 generally require repeat testing
- ACTH stimulation test
  - ACTH 250ug; baseline, 30m, 60m serum cortisol values taken
  - Peak cortisol should be >500-600nmol/L
- Metyrapone test
  - 30mg/kg administered at 0000h, cortisol and 11-deoxycortisol measured 8am
  - Serum cortisol <200nmol/L or 11-deoxycortisol levels <200nmol/L consistent w insufficiency
- Insulin tolerance test
  - Administration of 0.15u/kg insulin IV with goal of serum glucose <2.2
  - Serum cortisol values above 500-600nol/L consistent with adequate adrenal reserve
  - Plasma glucose response

Role of IV dexamethasone

- Although thought of as “long-acting” steroid, short half-life for elimination
  - 1.88-2.23h per Micromedex
- Our patient received dexamethasone at 1300h on day 0, with first measurement of serum cortisol ~36h later, and still suppressed 60h after dose
- Limited information on duration of adrenal/pituitary suppression past the 8-12h period from dexamethasone
  - Indirectly studied in a number of very old psychiatry papers investigating link b/t depression and HPA axis

NUMBER OF CORTISOL TIME-POINTS AND DEXAMETHASONE SUPPRESSION TEST SENSITIVITY FOR MAJOR DEPRESSION

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(*Received* 24 *June* 1983; *in final form* 14 *November* 1984)

- Groups of patient ssuppressed with 2mg dexamethasone, non-suppression (serum cortisol >5ug/dL or ~137nmol/L measured
  - Healthy controls only 5% non-suppressed at 24h
  - No measurements beyond this; unclear how diurnal variation in cortisol would affect result at following 0800h interval

TABLE 1. DISTRIBUTION OF DST NON-SUPPRESSION IN DEPRESSED PATIENTS AND CONTROLS: ANALYSIS OF SIX POST-DEXAMETHASONE CORTISOL TIME-POINTS

				Percent non-suppressors (cortisol ⩾ 5.0 μg %)					
Diagnostic group	*N*	Sex (M/F)	Age (years)	0800 h	1200 h	1600 h	2000 h	2200 h	Midnight
Normal volunteers	20	6/14	29 ± 1	0	5	5	10	5	5
Non-major depression	13	5/8	30 ± 4	0	0	8	15	8	8
Primary major depression	65	21/44	36 ± 2	12	16	26	29	26	20