Clinical update no. 544
4 September 2019

23yr-yr F, unwell for about 6 months with malaise and general lack of energy.

Sodium	113L
Potassium	6.6H
Chloride	86L
Bicarbonate	16L
Anion Gap	18H
Urea	7.9H
Creatinine	94H
Est. of GFR	74L
Glucose	3.9
Osmol-meas	246L
Osmol-calc	243L

URINE	
Na Conc	71
Osmolality	297

Random cortisol (4pm) within normal range –

ACTH/Cortisol Studies (Plasma/Serum)
Cortisol 191

Cortisol Reference Interval
100 - 540 nmol/L (before 10am)
80 - 480 nmol/L (after 5pm)

A short synacthen test –

Short Synacthen Test				
Relative Time (mins):	*	*	60	90
Time:				13:46
Cortisol (nmol/L)	139	*	165	142

A normal cortisol response (suggesting adequate reserve) is:

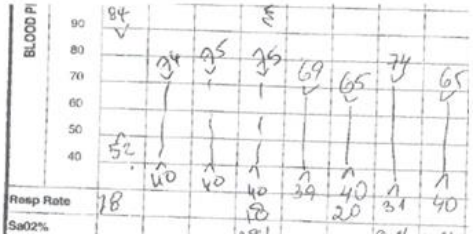
- a rise of greater than 220 nmol/l and/or
- a rise to an absolute level of greater than 550 nmol/l

Synacthen test: adrenal insufficiency with minimal rise of cortisol.

32yr-F with fever, headache, vomiting and lethargy. Temp 40.1 HR 104 RR 22 BP 110/70

Blood Chemistry	
Sodium	142 mmol/L
Potassium	# (c) 2.8 mmol/L
Chloride	103 mmol/L
Bicarbonate	27 mmol/L
Urea	3.4 mmol/L
Creatinine	83 µmol/L
Estimated Glomerular Filtration Rate	* >60 mL/min/1.
Glucose Random	4.0 mmol/L

No clear infective focus, and subsequently hypotensive. Lactate 1.3, CRP 5. Admitted ICU



ACTH Level	* <2.3 pmol/L
Cortisol Level.	* 4 nmol/L

She quickly improved with hydrocortisone IV. Further history that she had been unwell 6mth

An adrenal crisis precipitated by infection, this time with low K, not high as expected.

22yr-M presented unwell from GP with malaise, dizziness, vomiting, myalgia. Unwell 6mth, multiple visits to GP; he had marked salt craving and increasing pigmentation.

Background of Graves' disease age 17, complicated by agranulocytosis from carbimazole. Subsequent I 131 thyroid ablation and thyroxine replacement.

Na 120 K 3.8 Urine Na 112 osmolarity 873

Diagnosing SIADH requires exclusion of thyroid and adrenal insufficiency; 0640 level

Cortisol	<30

Prompt improvement with hydrocortisone.

The NEW ENGLAND JOURNAL of MEDICINE

Adrenal Crisis

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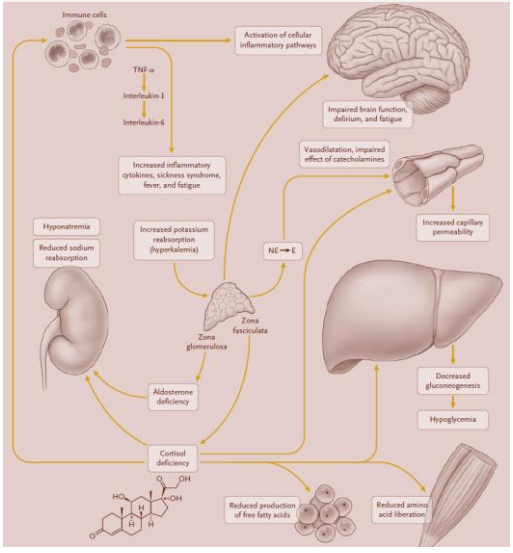
Figure 1. Pathophysiology of Adrenal Crisis.



Adrenal crisis appears to be increasing in frequency. There is no universally accepted definition and assessment is mainly clinical, relating to the multiple organ systems involved. A pragmatic definition is an acute deterioration associated with hypotension,

either absolute (SBP <100 mm Hg) or relative (SBP ≥20 mm Hg lower than usual), with features that resolve within 1 - 2 hours after parenteral glucocorticoid administration, generally hypotension resolving within 1hr and symptoms within 2hr.

For children definition is HR/BP outside aged based norms; hypo-Na, hyper-K or hypoglycaemia without other cause and resolution with glucocorticoid replacement.

Features at all ages include acute abdominal symptoms; delirium, obtundation; hypo-Na, hyper-K, hypoglycaemia, and fever. Look for another cause if BP does not respond to glucocorticoid replacement.

Low cortisol results in elevated cytokine levels giving fever, malaise, anorexia, myalgia, neutropenia, and lymphocytosis.

Milder hypo adrenal states may present with anorexia, nausea, vomiting, fatigue, postural dizziness, abdominal pain, limb and back pain, and impaired consciousness; and biochemical derangement as described.

Marked symptoms without hypotension signal an incipient adrenal crisis, and treatment with hydrocortisone and IV fluids may avert the development of an actual adrenal crisis.

EVENTS THAT PRECIPITATE ADRENAL CRISIS

Infections, gastroenteritis, trauma and major surgery, non-compliance with treatment and other stressors can precipitate a crisis, and prior to a crisis a need to increase replacement dosing. Thyrotoxicosis, or thyroxine therapy, can also precipitate. A variety of drug can alter response.

Table 2. Management of Adrenal Crisis.

Adults	
Hydrocortisone*	100 mg IV (or IM if no access) then 200mg/24hr as infusion or 50mg q. 6hr, then oral after 24hr
Fluids	0.9% saline 1L IV over 1hr; add 5% dextrose if hypoglycaemic, then titrate to response
Children	
Hydrocortisone	50 mg/sq m * IV then 50-100 mg/sq m each24hr (infusion, or q 6hr divided dosing, and transition to oral after 24hr.
Fluids	IV 0.9% saline 20 ml/kg + dextrose, and titrate to response.

* 50 – 100 mg/sq m approximates to 2-4 mg/kg

Hydrocortisone is preferred due to its glucocorticoid and mineralocorticoid effects, but if unavailable use dexamethasone or prednisolone. Fludrocortisone is not needed acutely if hydrocortisone dose is >50mg/24hr, however is part or maintenance therapy when stable and able to take orally (is no IV form).

MANAGEMENT ISSUES

HEALTH CARE MILIEU

Lack of awareness and a reluctance to give hydrocortisone can lead to adverse events. Initial diagnosis is often delayed.

A doubling or tripling of dosing may be required for intercurrent stressors such as infection to prevent a crisis.

Maximal adrenal secretory output is 200 mg/24hr of hydrocortisone (8.5 times baseline) and may be need to be matched for major surgery and other stress. Self-administered parenteral dosing may be needed, including off label sc injection.

Case vignette: 18yr-M with known primary adrenal insufficiency presented with fatigue, postural dizziness, several days diarrhoea with nausea. He had increased his hydrocortisone dose from 14/8/8mg to 40/20/20 mg for one day at onset of diarrhoea and then 20mg tds. He deteriorated markedly with BP 100/65. Na 133, K 4.5. He responded promptly to IV treatment. Oral supplementation had been inadequate. Parenteral replacement may have helped given he had reduced GI absorption.