PE1463/T

Royal College of Physicians Letter of 11 September 2013

Dear Mr Howlett

With reference to your correspondence, our response to the clinical thyroid situation(s) is on our website since July 2011:

http://www.rcplondon.ac.uk/sites/default/files/the-diagnosis-and-management-of-primary-hypothyroidism-revised-statement-14-june-2011_2.pdf

We have no plans to review our policy.

I am happy for the Committee to treat our 2011 statement and the article written by Professor John Wass (attached) as submissions.

We do not intend to respond to the petition. This is because we have already responded over a period of time in England, and produced our official response.

Yours sincerely

Sir Richard Thompson KCVO, DM, PRCP
The President
Royal College of Physicians
11 September 2013

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EDITORIALS

How to avoid precipitating an acute adrenal crisis

Most importantly, heed patients' requests for hydrocortisone

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There are two hormone deficiency syndromes that are rapidly fatal if untreated but which are quite easily managed. One is type 1 diabetes mellitus, commonly known to be treatable with insulin. The other is acute adrenocortical insufficiency (adrenal or so called addisonian crisis), which requires treatment with hydrocortisone. Unfortunately, too often, healthcare workers do not realise the urgency of treatment for acute adrenal crisis or fail to heed the requests of well informed patients for hydrocortisone.

Patients with adrenal insufficiency are at risk of developing life threatening adrenal crisis if steroids are reduced or stopped, or if glucocorticoid treatment is not increased during periods of increased stress (for example, illness, trauma, or surgery). The features of acute adrenal crisis include hypotension (particularly postural hypotension), shock, and hyponatraemia in 90% of patients. Hyperkalaemia is also a feature in 65% of patients. Fatal but avoidable addisonian crisis is the second most common cause of death in patients with known Addison's disease, accounting for 15% of deaths in patients with this disease.[1 2] Early treatment with parenteral hydrocortisone and intravenous rehydration with fluids are essential measures to avoid mortality. Why is this not always achieved?

The Addison's Disease Self Help Group (www.addisons.org.uk/), a charity that informs and supports patients with Addison's disease, has received numerous reports of doctors and nursing staff refusing requests for or delaying hydrocortisone administration in patients with Addison's disease who present unwell to healthcare services. One member of the group, a junior doctor with Addison's disease, reported a delay of more than 24 hours before being given steroids while she was an inpatient, even though she told healthcare staff that she needed hydrocortisone. Another member, a general practitioner, reported that his mother in law, who has established Addison's disease, repeatedly had to ask for parenteral steroids when she was admitted to hospital because she was severely unwell (G Moncrieff, 2012, personal communication). The Royal College of Physicians recently received correspondence from a deputy coroner about a patient with hypopituitarism who died after surgery because his care was not supervised by an endocrinologist and he received inadequate steroid replacement. The coroner expressed concern that no proper guidelines existed for what should have been a treatable problem. Deaths associated with inadequate steroid administration during surgery, for patients who require steroid replacement or need high doses of steroids that result in adrenal suppression, are common. This is despite guidelines for the perioperative management of these patients being available on the websites of the Society for Endocrinology (www.endocrinology.org/), the Addison's Disease Self Help Group, and the Pituitary Foundation (www.pituitary.org.uk/).

Extra steroids are needed for up to three days during periods of high stress in patients with adrenal failure or those receiving adrenal suppression therapy. Evidence from retrospective studies suggests that adrenal crisis is common in patients with primary adrenal failure.[3-5] The incidence is somewhat higher in patients with Addison's disease, who have combined glucocorticoid and mineralocorticoid deficiency, than in secondary adrenal failure,[3 4] in which patients have an intact renin-angiotensin-aldosterone system.[6] An international patient survey found that 8% of patients with a glucocorticoid insufficiency syndrome experience an adrenal crisis each year. The findings of a recent prospective study,[7] which recorded adrenal crises in 62 of 453 patients with known adrenal insufficiency over two years, including two deaths, support this. Adrenal crisis is also regularly seen in patients with congenital adrenal hyperplasia,[8] who cannot mount a normal cortisol response to stress because of genetic factors that impede the synthesis of cortisol. Importantly, adrenal crisis can occur in any patient treated with 5 mg or more of prednisolone (equivalent to 20 mg of hydrocortisone orally) for more than four weeks.[3] In addition, adrenal crises have even been reported in patients on long term inhaled steroids for asthma or high dose topical steroids (box).[9]

Prevention of adrenal crisis is better than cure. Patients on steroids with adrenal failure should carry a medical alert bracelet and a card stating that they take steroids daily. Advise patients to double their regular hydrocortisone replacement dose during intercurrent illness and to alert doctors and nurses to the need for early admission and parenteral steroid replacement during more severe illness and surgery. It is also recommended that patients carry the emergency information issued by the

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Situations in which acute adrenal crisis can occur

- Addison's disease or secondary (hypothalamic or pituitary) adrenal failure
- Patients on adrenal suppressive doses of prednisolone or other steroids, including dexamethasone in a prednisolone equivalence of greater than 5 mg for longer than one month
- Congenital adrenal hyperplasia
- Long term inhaled steroids
- High doses of topical steroids
- Precipitators include infection, major surgery, vomiting with inadequate steroid absorption, major stress

Addison's Self Help Group.[10] Patients might also benefit from having an ampoule of hydrocortisone at home or when travelling (together with appropriate syringe, needles, and instructions) for use in an emergency. Patients and their carers need to be trained in the use of emergency treatment. In acute illness, trauma (including surgery), or dehydration as a result of vomiting, start emergency parenteral administration of hydrocortisone 100 mg as soon as possible and repeat six hourly until the patient is stable.[10] In the short term this will cause no harm, but rapid treatment will save lives and may also shorten hospital admission time. Concurrent fluid resuscitation with intravenous normal saline is necessary to help normalise blood pressure. Always seek specialist endocrinology advice when treating a patient with adrenal insufficiency for another illness.

The Addison's Disease Self Help Group can issue hospital stickers to be put on to drug charts to draw attention to a patient's steroid dependency. Ideally, a red flag system on the electronic patient record should be developed (similar to the one that alerts healthcare professionals to patients with meticillin resistant *Staphylococcus aureus* infection) for those with steroid dependency to alert ancillary staff.

Last, but not least, listening to a well informed patient in adrenal crisis who says that he or she need steroids and taking urgent action will avoid unnecessary deaths from this eminently treatable medical problem.

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1 Erichsen MM, Løvås K, Fougner KJ, Svartberg J, Hauge ER, Bollerslev J, et al. Normal overall mortality rate in Addison's disease, but young patients are at risk of premature death. *Eur J Endocrinol* 2009;160:233-7.
2 Bergthorsdottir R, Leonsson-Zachrisson M, Odén A, Johannsson G. Premature mortality in patients with Addison's disease: a population-based study. *J Clin Endocrinol Metab* 2006;9:4849-53.
3 Arlt W, Allolio B. Adrenal insufficiency. *Lancet* 2003;61:1881-93.
4 Hahner S, Loeffler M, Bleicken B, Drechsler C, Milovanovic D, Fassnacht M, et al. Epidemiology of adrenal crisis in chronic adrenal insufficiency: the need for new prevention strategies. *Eur J Endocrinol* 2010;162:597-602.
5 White K, Arlt W. Adrenal crisis in treated Addison's disease: a predictable but under-managed event. *Eur J Endocrinol* 2010;162:115-20.
6 Arlt W. Adrenal insufficiency. In: Wass JAH, Stewart PM, eds. Oxford textbook of endocrinology and diabetes. 2nd ed. Oxford University Press, 2011:843-59.
7 Hahner S, Spinnler C, Beuschlein F, Fassnacht M, Lang K, Quinkler M, et al. Adrenal crisis and general morbidity in chronic adrenal insufficiency prospectively assessed in 472 patients [abstract]. *Endocr Abstracts* 2011;26:OC1.5. www.endocrine-abstracts.org/ea/0026/ea0026oc1.5.htm.
8 Reisch N, Willige M, Kohn D, Schwarz HP, Allolio B, Reincke M, et al. Frequency and causes of adrenal crises over lifetime in patients with 21-hydroxylase deficiency. *Eur J Endocrinol* 2012;167:35-42.
9 Zollner EW, Lombard C, Galal U, Hough S, Irusen E, Weinberg E. Hypothalamic-pituitary-adrenal axis suppression in asthmatic children on inhaled and nasal corticosteroids—more common than expected? *J Pediatr Endocrinol Metab* 2011;24:529-34.
10 Wass JAH, Howell TH, Arlt W, Pearce S. (2011). Addison's disease. Potentially life-threatening steroid dependency. Addison's Disease Self Help Group. 2011. www.addisons.org.uk/info/emergency/soscrisisletter.pdf.

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