ACUTE ADRENAL INSUFFICIENCY
Supporting information

This guideline has been prepared with reference to the following:

NICE. Adrenal insufficiency: identification and management. 2024. London. NICE

https://www.nice.org.uk/guidance/ng243

Evans L, Rhodes A, Alhazzani W et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47:1181-1247

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8486643/

Marik PE, Pastores SM, Annane D, et al. Recommendations for the diagnosis and management of corticosteroid insufficiency in critically ill adult patients: Consensus statements from an international task force by the American College of Critical Care Medicine. Crit Care Med 2008; 36:1937-49

Immediate treatment

100 mg of hydrocortisone given as an IV bolus, followed by 100 mg IV 6 hrly, improves the outcome?
A 2019 review of the evidence concluded that treatment should include prompt administration of intravenous hydrocortisone, given as a 100-mg bolus, followed by 200 mg every 24 hours, administered as a continuous infusion or as frequent intravenous (or intramuscular) boluses (50 mg) every 6 hours, with subsequent doses tailored to the clinical response (Rushworth, 2019).

Rushworth L, Torpy DJ & Falhammar H. Adrenal Crisis. N Engl J Med 2019;381:852-861

Evidence Level: V

Rehydration with sodium chloride 0.9% at the rate of 1 litre IV over 30-60 min, followed by 3-4 litre over the next 24 hr, improves the outcome?
Fluid and sodium depletion (hypovolaemia and hyponatraemia) are key features of acute adrenal insufficiency and rapid rehydration is essential to correct these. Opinion differs as to what quantity of sodium chloride 0.9% over what period of time is necessary: up to 3 litres within the first 2 hours (Shenker, 2001; Vallotton, 1992); a total of 3-4 litres in the first 24 hours, rapidly at first and more slowly as improvement occurs (Dunlop, 1963). One authority (Grossman, 1998) is more conservative and advises that “hypovolaemia is rarely as severe as it might seem”, going on to suggest 1 litre over 4 hours followed by “additional fluids as appropriate.”

Dunlop D. Eighty-six cases of Addison’s disease. BMJ 1963;ii:887-91
http://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC1873052&blobtype=pdf

Grossman A. Clinical endocrinology, 2nd ed. Oxford: Blackwell Science, 1998. p.479

Shenker Y, Skatrud JB. Adrenal insufficiency in critically ill patients. Am J Respir Crit Care Med 2001;163:1520-3

Vallotton MB. Disorders of the adrenal cortex. Baill Clin Endocrinol Metab 1992;6:41-56

Evidence Level: V

Glucagon is unhelpful in the presence of hypoglycaemia, but IV glucose infusion improves the outcome?
The action of glucagon relies upon the patient having adequate hepatic glycogen stores, so is not effective in adrenal insufficiency, when “marked depletion” of these stores occurs (Sweetman, 2011). Lack of glucocorticoid secretion causes impaired carbohydrate metabolism and a marked tendency to hypoglycaemia (Dunlop, 1963). A 5% glucose infusion is indicated in order to prevent this developing (Cooper, 2003).

Cooper MS, Stewart PM. Corticosteroid insufficiency in acutely ill patients. N Engl J Med 2003;348:727-34

Dunlop D. Eighty-six cases of Addison's disease. BMJ 1963;ii:887-91
http://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC1873052&blobtype=pdf

Sweetman SC (ed). Martindale: the complete drug reference, 37th ed. London: Pharmaceutical Press, 2011

Evidence Level: V

Subsequent management

Oral hydrocortisone (20 mg 8 hrly) is appropriate once the patient is improving?
Most patients presenting with adrenal crisis have primary adrenal insufficiency and require lifelong mineralocorticoid replacement as well as emergency treatment (Oki, 2007). It is usual, in the absence of a major precipitating or complicating illness, to taper the dose of hydrocortisone over 1 to 3 days until an oral maintenance dose is substituted. The usual maintenance dose is 25 – 37.5 mg daily (Coursin, 2002), or, according to some sources, 12 – 15 mg/m² daily (Werbel, 1993), which mimics the natural output of the body.

Coursin DB, Wood KE. Corticosteroid supplementation for adrenal insufficiency. JAMA 2002;287:236-40

Oki K, Yamane K. Therapies for adrenal insufficiency. Expert Opin Pharmacother 2007;8:1283-91

Werbel SS, Ober KP. Acute adrenal insufficiency. Endocrinol Metab Clin N Am 1993;22:303-27

Evidence Level: V

On discharge, the 12-hrly dose of hydrocortisone should be larger in the morning than in the evening?
The total daily dosage of hydrocortisone (usually 30 mg) is usually divided into 20 mg being given in the morning and 10 mg in the evening. This results in more stable concentrations (and effects) of cortisol (Plat, 1999).

Plat L, Leproult R, L'Hermite-Baleriaux M, et al. Metabolic effects of short-term elevations of plasma cortisol are more pronounced in the evening than in the morning. J Clin Endocrinol Metab 1999;84:3082-92

Evidence Level: V

Oral fludrocortisone 50 – 100 mcg daily improves the outcome in primary adrenal failure?
In primary adrenal failure, hydrocortisone alone does not usually provide sufficient mineralocorticoid activity for complete replacement (Coursin, 2002). Fludrocortisone is more than 100 times as potent (Sweetman, 2011) and is given in combination with hydrocortisone to guard against sodium and water depletion. Although 100mcg daily is the generally recommended dose, a small study of 10 patients with Addison's disease (Smith, 1984) found that all of them exhibited signs of sodium and water depletion (very high levels of plasma-renin activity), despite being on standard fludrocortisone treatment. These patients needed maintenance doses of 200 mcg daily in order to restore sodium balance.

Coursin DB, Wood KE. Corticosteroid supplementation for adrenal insufficiency. JAMA 2002;287:236-40

Smith SJ, Markandu ND, Banks RA, et al. Evidence that patients with Addison's disease are undertreated with fludrocortisone. Lancet 1984;i:11-14

Sweetman SC (ed). Martindale: the complete drug reference, 37th ed. London: Pharmaceutical Press, 2011

Evidence Level: V

Last amended August 2024
Last reviewed January 2026