

Following successful surgical treatment for Cushing's, most patients are adrenal insufficient (cannot make cortisol) for a period of time. Cortisol is essential to life so patients require replacement with a glucocorticoid, such as hydrocortisone. During times of illness and surgery the body requires additional cortisol, therefore, in these circumstances the replacement medication dose needs to be increased to prevent progressive symptoms of adrenal insufficiency or an adrenal crisis medical emergency. Precautions patients should take are summarized in Table I.

WHAT CHANGES SHOULD BE MADE TO REPLACEMENT MEDICATION DURING ILLNESS?

During times of illness, patients need to increase the replacement medication dose per the sick day rules below. Medication increase is needed in order to prevent worsening symptoms of adrenal insufficiency such as fatigue, dizziness or light-headedness on standing, reduced appetite, nausea, and abdominal discomfort. An increase in oral replacement medication during illness may prevent progression to life threatening adrenal crisis. While some patients may resist increasing their replacement dose, patients should err on the side of caution as increasing the replacement dose for a few days is not harmful while under dosing can be very dangerous.

In case oral medication cannot be tolerated due to vomiting or in a medical emergency, patients need to carry an emergency steroid injectable. The patient and others need to be educated on when and how to give an emergency injection. The injectable is usually 100mg of hydrocortisone and can be given at home with proper instruction. Usually the injection is given intramuscularly, however, subcutaneous injections have been shown to have only a slightly delayed onset and are easier for patients and caretakers to administer. Glucocorticoid suppositories are another option however these cannot be used when diarrhea is present.

Sick day rule 1: Home management of illness with fever¹

The standard daily replacement dose of oral glucocorticoids should be doubled when the patient experiences fever or illness requiring bed rest or antibiotics for an infection. More specifically, hydrocortisone replacement doses should be doubled when patients have a fever >38°C; 100.4°F. The dose should be tripled for fevers >39°C; 102.2°F. The dose increase should be sustained until recovery, usually 2 to 3 days. During this time, increased consumption of electrolyte-containing fluids as tolerated is recommended.

Sick day rule 2: Unable to tolerate oral medication due to gastroenteritis or trauma¹

In case of severe illness, trauma, persistent vomiting (as with gastroenteritis), and if needed when fasting for a procedure, adult and adolescent patients should inject 100mg of hydrocortisone intramuscularly or subcutaneously. Following the initial injection, patients should present to the Emergency Department (ED) as fluids are often needed.

Table I
Precautions Patients Should Take*

- Patients should carry an up to date medical ID card indicating adrenal insufficiency
- Patients should wear a medical alert bracelet or necklace stating "Adrenal insufficiency – needs steroids!" This is particularly useful if the patient is confused or unable to describe their need for a glucocorticoid injection.
- Patients should ensure that they always have a sufficient supply of hydrocortisone and fludrocortisone (accounting for possible sick days) and follow the sick day rules.
- Patients should carry a hydrocortisone emergency injection kit (vials of 100 mg hydrocortisone sodium, syringes, needles); alternatively, also hydrocortisone or prednisolone suppositories
- Patients (parents, partners) need to be taught to administer an injectable glucocorticoid preparation
- Patients should go to the hospital after emergency injection as fluids are almost always needed.
- Patients should carry a leaflet (or this pamphlet) with information on adrenal crisis and hospitalization to be shown to health care staff; clearly advise regarding the need to inject 100 mg hydrocortisone immediately IV or IM, followed by continuous infusion of 200 mg/24 h
- Patients should carry an emergency phone number for the endocrine specialist team
- Patients (or parent) should create emergency information in their cell phone (In Case of Emergency app or similar). Include medic alert information and contact numbers for family and endocrinologist.

**Modified with permission of The Endocrine Society from Table 4 in J Clin Endocrinol Metab, February 2016, 101(2):364–389 doi: 10.1210/jc.2015-1710 [Adapted from I. Bancos, et al: Diagnosis and management of adrenal insufficiency. Lancet Diabetes Endocrinol. 2015;3:216–226 (122), with permission. © Elsevier Limited.]*

WHAT CHANGES SHOULD BE MADE TO REPLACEMENT MEDICATION FOR SURGERY?

Increased replacement is also required for surgical procedures. Patients should alert their physician and anesthesiologist prior to any procedure. In cases of sedation, the patient should remain awake, if possible, until the increased dose is administered.

Minor to moderate surgical stress¹

Prior to minor surgical procedures, such as dental procedures with local anesthesia, the patient can double the daily replacement dose. For dental work requiring sedation, the doubled daily dose can be administered intravenously prior to the procedure. For moderate surgical procedures, such as cholecystectomy or joint replacement a hydrocortisone dose of 50–75 mg/24 hours should be maintained in adults and adolescents usually for 1 to 2 days.

Major surgery with general anesthesia, trauma, delivery, or disease that requires intensive care¹

Prior to major surgery, such as cardiopulmonary bypass 100mg of hydrocortisone should be injected intravenously (IV), followed by continuous IV infusion of 200 mg hydrocortisone/24h; alternatively 50 mg every 6 hours IV or intramuscularly (IM). The same applies to trauma or very serious illness. Weight-appropriate continuous IV fluids with 5% dextrose and 0.2 or 0.45% NaCl should be continued. Depending on the clinical state, rapid tapering of the replacement hydrocortisone dose and a switch to oral replacement is recommended.

ADRENAL CRISIS MANAGEMENT

An adrenal crisis denotes a much more severe situation, a medical emergency, where there is an abrupt development of severe weakness, a tendency to fall on standing, nausea, vomiting, abdominal pain, back pain, confusion and hypotension (low blood pressure) consistent with shock. The blood sodium and potassium abnormalities are much more frequent than is seen in adrenal insufficiency. The treatment of adrenal crisis is urgent and the administration of a glucocorticoid, usually hydrocortisone 100mg, is generally given IV or IM. Such treatment is life-saving. If an adrenal crisis develops, the patient should inject 100mg of hydrocortisone intramuscularly or subcutaneously and present to the ED immediately, as fluids are almost always needed. In some cases, treatment in the ER can be delayed and the below information on the treatment of adrenal crisis in a hospital setting can be shared with medical personnel.

Management of Acute Adrenal Crisis²

- Rapid infusion of 1000 mL isotonic saline within the first hour or 5% glucose in isotonic saline, followed by continuous IV isotonic saline guided by individual patient needs
- Hydrocortisone 100 mg IV immediately followed by hydrocortisone 200 mg/d as a continuous infusion for 24 h; alternately hydrocortisone 50mg q6h IV for 24 h, then reduced to hydrocortisone 100 mg/d the following day
- Children, rapid bolus of normal saline (0.9%) 20 mL/kg. Can repeat up to a total of 60 mL/kg within 1 h for shock
- Children, hydrocortisone 50–100 mg/m² bolus followed by hydrocortisone 50–100 mg/m²/d divided q 6 h
- For hypoglycemia: dextrose 0.5–1 g/kg of dextrose or 2–4 mL/kg of D25W (maximum single dose 25 g) infused slowly at rate of 2 to 3 mL/min. Alternatively, 5–10 mL/kg of D10W for children <12 y old
- Cardiac monitoring: Rapid tapering and switch to oral regimen depending on clinical state

Note: The information in this pamphlet is based on the Endocrine Society Guideline on the Treatment of Primary Adrenal Insufficiency published in *J Clin Endocrinol Metab*, February 2016, 101(2):364–389 doi: 10.1210/jc.2015-1710. Since doses differ for children, please refer to the complete guideline. This pamphlet was reviewed by Dr. David Torpy, Royal Adelaide Hospital, Australia and Dr. Meg Keil, NIH.

¹I. Bancos, et al: *Diagnosis and management of adrenal insufficiency. Lancet Diabetes Endocrinol.* 2015;3:216–226 (122), with permission. © Elsevier Limited and from B. Allolio: *Extensive expertise in endocrinology: adrenal crisis. Eur J Endocrinol.* 2015;172:R115–R124 (126), with permission. © Endocrine Society] Abbreviation: D10W, 10% dextrose solution; D25W, 25% dextrose solution.

²Table reprinted in part with permission of The Endocrine Society from Table 3 in *J Clin Endocrinol Metab*, February 2016, 101(2):364–389 doi: 10.1210/jc.2015-1710 [Adapted from B. Allolio: *Extensive expertise in endocrinology: adrenal crisis. Eur J Endocrinol.* 2015;172:R115–R124 (126), with permission. © Endocrine Society.]