

British Columbia's Children's Hospital Endocrinology & Diabetes Unit Daniel L. Metzger, MD, FAAP, FRCPC



# ADRENAL STEROID THERAPY AND WEANING

# PHYSIOLOGIC REPLACEMENT: usually given PO.

IV/IM: hydrocortisone sodium succinate: 6–8 mg/m<sup>2</sup>/d ÷ q 6 h IV/IM (Solu-Cortef<sup>®</sup> Act-O-Vials, A-Hydrocort<sup>®</sup> vials) comes as 100 mg/2 mL, 250 mg/2 mL, 500 mg/4 mL and 1000 mg/8 mL

methylprednisolone sodium succinate (Solu-Medrol<sup>®</sup>): 2 mg/m<sup>2</sup>/d  $\div$  q 6–8 h IV comes as 40 mg/1 mL, 125 mg/2 mL, 500 mg/4 mL and 1000 mg/8 mL Act-O-Vials

methylprednisolone acetate (Depo-Medrol<sup>®</sup>): 2 mg/m<sup>2</sup>/d  $\div$  q 24–72 h **IM** comes as 20 mg/mL, 40 mg/mL and 80 mg/mL suspension

dexame thasone sodium phosphate (Decadron®): 0.25 mg/m²/d  $\div$  q 12–24 h IV/IM comes as 4 mg/mL and 10 mg/mL solution

## PO: PO DOSES ARE GREATER THAN IV/IM BECAUSE OF INCOMPLETE ABSORPTION!

hydrocortisone (Cortef<sup>®</sup>): 8–12 mg/m<sup>2</sup>/d  $\div$  TID **PO** comes as 5-mg (Special Access Programme only), 10-mg and 20-mg tabs

cortisone acetate (Cortone®): 10–15 mg/m²/d  $\div$  TID PO comes as 25-mg tabs

prednisone: 2–3 mg/m<sup>2</sup>/d  $\div$  BID **PO** comes as 1-mg, 5-mg, and 50-mg tabs

prednisolone sodium phosphate (Pediapred<sup>®</sup>): 2–3 mg/m<sup>2</sup>/d  $\div$  BID **PO** comes as 1 mg/mL solution

dexamethasone (Decadron<sup>®</sup>): 0.2–0.3 mg/m<sup>2</sup>/d  $\div$  QD **PO** comes as 0.5-mg, 0.75-mg, 2-mg and 4-mg tabs and 0.1 mg/mL elixir

## **STRESS DOSE REPLACEMENT:** must be given **IM/IV** if any chance of vomiting or diarrhea.

- Minor stress (fever >38°C, flu, strep): use usual pills or parenteral hydrocortisone
  - $\circ$  2–3× replacement: 30–50 mg/m<sup>2</sup>/d ÷ TID–QID **PO/IM/IV**
  - $\circ$  Some patients are taught to follow with Depo-Medrol<sup>®</sup> 10 mg/m<sup>2</sup>/d IM q 24 hours.
- Major stress (surgery, MVA, meningitis): use parenteral hydrocortisone
  - Loading dose (age-based): IM/IV

<3 years: 25 mg/dose 3–9 years: 50 mg/dose ≥10 years: 100 mg/dose

- Follow with 5–6× replacement: 100 mg/m<sup>2</sup>/d  $\div$  TID–QID **IM/IV** or continuous drip **IV**
- IF IN DOUBT, GIVE STRESS DOSES!

**Drug-drug interactions:** increased catabolism of corticosteroids induced by barbiturates, carbamazepine, phenytoin, rifampin, primidone; as well as by hyperthyroidism or institution of L-thyroxine therapy in a hypothyroid state.

Adrenal replacement (hypopituitarism, adrenal insufficiency): give larger dose in the morning.

Adrenal suppression (congenital adrenal hyperplasia): give larger dose at HS.

Mineralocorticoid replacement: fludrocortisone (Florinef®, 0.1 mg tabs)

- Only form available, must be given PO/NG
- Doses:
  - $\circ$  0.1–0.2 mg/d ÷ QD–BID for babies
  - $\circ$  0.05–0.1 mg/d ÷ QD–BID for little kids
  - $\circ$  0.1–0.2 mg/d ÷ QD–BID for older kids, adults
- Follow electrolytes, BP
- Patients who are NPO and on stress doses of hydrocortisone or cortisone (**not** others) are usually getting enough mineralocorticoid coverage without Florinef<sup>®</sup>, but you should probably watch electrolytes.

Salt replacement: mineralocorticoid-deficient infants may also require oral NaCl replacement

- Usual dose is ~1 gram/day
- Can use salt packets from restaurant-supply store, which contain 0.7–1.0 g NaCl
- Mix 1 gram NaCl into 120 mL (4 oz) breast milk or formula and give 30 mL (1 oz) with feeds QID
- Can use 23.4% (4.0 mEq/mL) pharmacy-supplied liquid: 4.3 mL = 1 gram NaCl
- Can use homemade salt solution [I teaspoon (6 gram) NaCl in 120 mL (4 oz) sterile water]: 50 mg/mL (0.856 mEq/mL), 20 mL = 1 gram NaCl)

Medication	Glucocorticoid	Mineralocorticoid
cortisone	100 mg	100 mg
hydrocortisone	80 mg	80 mg
prednisone, prednisolone	20 mg	100 mg
methylprednisolone	16 mg	none
9α-fluorohydrocortisone	5 mg	0.2 mg
dexamethasone	1–2 mg	none

#### When weaning patients off steroids, remember:

- Hypothalamic-pituitary axis is first to be suppressed and first to recover.
- Amount of suppression depends on dose, duration and time of day given. There is also a large inter-individual variation in this.
- A 2-week course of high-dose steroids can have detectable effects up to 1 year.
- Patients on a weaning schedule may not be able to handle a new stress and will require going back up on the dose for at least a while.
- Rate of weaning is also dependent on underlying process being treated.
- Look for signs of withdrawal: anorexia, myalgia, nausea, emesis, lethargy, headache, fever, desquamation, arthralgia, weight loss, postural hypotension.

#### Weaning schedules: fairly empirical.

- High-dose "pulse" steroids (often ~10× maintenance), given for ≤7 days: no weaning necessary if patient **not** recently treated with steroids.
- High-dose steroids, given for 1–4 weeks: cut by ~25% every 4–7 days.
- High-dose steroids given for ≥1 month: wean rapidly to "stress doses", then cut by ~10–25% every 1–2 weeks, until dose is <50% of physiologic replacement. Probably should then be tested for suppression (see below).</li>
- On long treatment/weaning schedules, can try to get all of dose to once in the morning, or once every other day, to allow HPA axis to recover and minimize growth-retarding effects.

#### **Testing for suppression:**

- Whenever in doubt if patient is "crashing", send off a cortisol level and treat **STAT** pending results.
- Insulin tolerance test: gold standard, but has some risk and is thus not performed routinely at BCCH.
- A 0600- to 0800-h cortisol level 24 h after the last dose of glucocorticoid is a fair screen for ability to produce basal (not stress) amount of cortisol: should be ≥200 nmol/L.
- Low-dose ACTH test: tests whether adrenals can respond to stress signal from pituitary. Since pituitary–adrenal axis is the last to recover, if a patient passes this test, s/he should theoretically not be suppressed. Very safe test.

Give synthetic  $\alpha^{1-24}$ -ACTH (cosyntropin, Cortrosyn<sup>®</sup>), 1 µg/m<sup>2</sup> **IV push**, preferably at 0800 h. Draw a cortisol level at baseline (normal 276–690 nmol/L at 0800 h), 20 min and 30 min (normal response: rise in cortisol to ≥450 nmol/L at 20 and/or 30 min).



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www.bcchildrens.ca/endocrinology-diabetes-site/documents/cortmgmt.pdf