PJ Nicholoff Steroid Protocol

About this Document

This document is meant for healthcare providers. For further explanation of steroids and adrenal crisis, please see the PPMD Steroid Care Page at parentprojectmd.org/steroids.

Background/Assessment

Normal basal secretion of cortisol from the adrenal gland is approximately 5-7 mg/m2/day or 8 -10 mg/day for adults. This amount increases during minor illnesses or surgery to approximately 50 mg/day (5x normal physiologic secretion). These small increases with uncomplicated surgery return to baseline in 24 hours. Procedures producing greater surgical stress, have been shown to increase cortisol responses to 75-150 mg/day (10x normal physiologic secretion), which return to baseline in about 5 days.

Corticosteroids are prescribed for multiple diagnoses to a wide variety of patients. Long term administration of corticosteroids may lead to suppression of the hypothalamic-pituitary-adrenal (HPA) axis. Rapid reduction or abrupt withdrawal of corticosteroid therapy that has been prolonged or at high doses can cause secondary adrenal insufficiency (suppression of the HPA axis), and steroid withdrawal or deprivation syndrome. Recovery from suppression of the HPA axis after discontinuing corticosteroids can be prolonged (possibly 6 to 12 months) and may vary based on doses, dosing schedules and duration of corticosteroid therapy. Since there is a great deal of individual variability in susceptibility to suppression of the HPA axis after chronic use of exogenous corticosteroids, it is not possible to predict with confidence which patients will be affected. Current practice is to administer supplemental (stress) doses of corticosteroids to patients with suspected suppression of the HPA axis in the perioperative period and during acute illness to prevent acute adrenal insufficiency, or adrenal crisis.

Defining HPA Suppressed Patients:

Recommendations differ slightly in defining a suppressed patient, but general guidelines are below (Table 1):

Table 1

Prednisone dose Equivalents/day - Adults	Prednisone Dose Equivalents/Day - Pediatric	Suppression of HPA axis?
5mg/day or less	3 mg/m2/day or less	Usually not suppressed.
5 – 20 mg/day	3-12 mg/m2/day	Possibly suppressed. ACTH stimulation test recommended or give supplemental dose.
20 mg/day for >10 days or more	12 mg/m2/day of prednisone for > 10 days or more	Suppressed. Give supplemental dose.

Patients receiving disease appropriate corticosteroid doses (at least 10 times above the physiologic cortisol dose) generally do not need stress doses if usual daily dose is continued. Patients who are on maintenance physiologic dose of hydrocortisone for primary disease of the HPA axis do require supplemental therapy.

Consultation with endocrinology is recommended for questions or concerns.

Recommendations for supplemental doses are generally divided by severity of stress the patient may experience (medical or surgical). Supplemental steroid doses are then based on degree of stress.

Corticosteroid Stress Doses:

Table 2

Medical/Surgical Stress	Corticosteroid Dosage DOS*	Postoperative Taper Regimen
Minor (local anesthesia, < 1 hour) (e.g. inguinal hernia, single tooth extraction, colonoscopy), mild febrile illness, mild, nausea/vomiting, mild diarrhea)	25mg or 30-50 mg/m2 po (if able to take po) or IV hydrocortisone (HC) or equivalent	None Resume maintenance physiologic dose of hydrocortisone when illness, pain or fever subsides
Moderate (e.g. multiple teeth extraction, fracture, pneumonia)	50mg or 50-75 mg/m2 IV hydrocortisone or equivalent	25 mg Q 8 or 50-75 mg/m2/day ÷ q 6 hours X 24 hour. Taper to baseline over 1-2 days.
Major (e.g. Septic shock, multiple trauma/fractures or severe burns, severe systemic infections, major surgery, pancreatitis, orthopedic surgery including open reduction, spinal fusion, etc.)	100mg or 100 mg/m2/dose IV hydrocortisone or equivalent	50 mg IV Q 8 or 100 mg/m2/day ÷ q 6 hours X 24-48hours. Taper to baseline over 1-3 days (continue stress dose if the physical stress (fever or pain) continues).

- DOS - Day of surgery

Patients using high dose twice-weekly corticosteroid-dosing schedule:

- If patients using a twice-weekly dosing schedule are unable to take corticosteroids by mouth during a time when they should be taking corticosteroids (due to nausea, vomiting, diarrhea, etc.), patients should take stress doses intravenously as indicated above.
- If patients using a twice weekly dosing schedule are undergoing/experiencing a moderate or major medical/surgical stressor in their life, cortisol level should be drawn and it is recommended that they follow the stress dosing recommendations in the above table.
- No literature exists for these recommendations. The recommendations are based on expert opinion and practice.

Recommendation for Corticosteroid Therapy Withdraw:

Below is one recommendation for tapering chronic corticosteroids (generally managed in an outpatient setting):

- Start on a Monday, giving 20-25% lower corticosteroid dose for 2 weeks (or longer)
- If multiple doses are taken, start first to reduce multiple daily doses to a single morning dose
    - Cut the dose 20-25% again for 2 weeks (or longer); continue this schedule
    - Continue until dose is near physiologic dose (3mg/m2/day of prednisone or 3.6mg/m2/day of Deflazacort)
- When near physiologic dose, substitute corticosteroids with short acting form of corticosteroid or hydrocortisone (12 mg/m2/day of hydrocortisone)
- This will also enable the patient to have a supply of hydrocortisone to be used for stress doses if needed in times of stress after coming off steroids
    - Continue to taper off by 20-25% each week (or longer)
    - Give every other day for 2 weeks (or longer)
    - Stop
    - WATCH VERY CAREFULLY FOR SIGNS OF ADRENAL CRISIS (see below)
- Alert parents to signs/symptoms of adrenal crisis
- If patients have symptoms of adrenal insufficiency during the taper, the steroid dose prior to the taper should be maintained for longer

IF THE PATIENT HAS A SERIOUS ILLNESS/INJURY DURING THE TAPER, THEY MAY NEED A "STRESS DOSE" OF CORTICOSTEROIDS:

- Encourage parents to continue to report any serious events until 1 year post-taper
    - The stress doses of hydrocortisone is 30-50 mg/m2/day, or higher, for major stress (see Table 2)
    - Patients need to go to the emergency room if having signs or symptoms of adrenal crisis. Serum electrolytes with blood glucose and cortisol level should be obtained.
    - Patients should see a pediatric endocrinologist for evaluation of HPA axis during the process of corticosteroid therapy withdrawal.

Patients using high dose twice-weekly corticosteroid-dosing schedule:

- It is recommended that patients electing to discontinue the use of twice weekly corticosteroids, do so under the guidance of a neuromuscular provider and/or endocrinologist.
- No literature exists for these recommendations. The recommendations are based on expert opinion and practice

Testing HPA axis:

- After reaching half the physiological dose (5-6 mg/m2/day of hydrocortisone or 1-1.5 mg/m2/day of prednisone), morning serum cortisol and ACTH should be assayed monthly (may do less frequently), until they reach normal levels.
- When baseline morning serum ACTH and cortisol are normal, discontinue the corticosteroid and carry out the rapid ACTH stimulation test monthly until post-stimulation cortisol response is normal (post-stimulus level > 20 mcg/dL). When this point is reached, it can be considered that the HPA axis has recovered

Modification of above protocol:

- Omit monthly AM cortisol and ACTH and perform an ACTH stimulation test in 3 months after discontinuation of corticosteroids
- During this time (3 months before getting ACTH stimulation test), patients will need to take stress dose at the time of stress
- If ACTH stimulation test result is abnormal (peak cortisol <20), patients will need to continue taking stress doses of hydrocortisone at the time of stress. (Patients Repeat ACTH stimulation test again in 1-2 months later and families would need to have teaching on this with an endocrine nurse.)

Alternatively, when laboratory tests cannot be carried out:

- Patients who have used corticosteroids for prolonged periods can be considered as having suppression of the HPA axis up to 1 year after discontinuation of corticosteroid therapy and therefore need hydrocortisone stress dose coverage

during the time of stress

Risk factors for adrenal crisis include:

- Dehydration
- Infection and other physical stress
- Injury to the adrenal or pituitary gland
- Stopping treatment too suddenly with glucocorticoid medications such as prednisone hydrocortisone
- Surgery
- Trauma

Symptoms of adrenal crisis can include any of the following:

- Abdominal pain
- Shock
- Confusion or coma
- Dehydration
- Dizziness or light-headedness
- Fatigue
- Flank pain
- Headache
- High fever
- Loss of appetite
- Loss of consciousness
- Low blood pressure
- Nausea
- Profound weakness
- Rapid heart rate
- Rapid respiratory rate (see tachypnea)
- Slow, sluggish movement
- Unusual and excessive sweating on face or palms
- Vomiting

Exams and Tests

Tests that may be ordered to help diagnose acute adrenal crisis include:

- ACTH (cosyntropin) stimulation test
- Cortisol level
- Blood sugar
- Serum potassium
- Serum sodium
- Serum pH

Corticosteroid Conversion Table

Table 3

Medication	Equivalent doses
Cortisone	25 mg
Hydrocortisone	20 mg
Deflazacort	6 mg
Prednisone	5 mg
Methyl prednisone	4 mg
Triamcinolone	4 mg
Betamethasone	0.75 mg
Dexamethasone	0.75 mg

References

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In honor of the late Philip James "PJ" Nicholoff, for his contribution to the global Duchenne community.