Primary Adrenal Insufficiency

Diagnosis, glucocorticoid/mineralocorticoid/DHEA replacement, and management in special populations.

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Primary Adrenal Insufficiency Guideline
Bornstein et al. · JCEM 2016;101:364-389

GRADE — 1 · Strong For | 2 · Suggest For | 2- · Suggest Against | 3 · Strong Against | Ungraded / Best Practice

1 Diagnosis & Testing

1	Test acutely ill patients with unexplained volume depletion, hypotension, hyponatremia, hyperkalemia, fever, abdominal pain, hyperpigmentation, or (in children) hypoglycemia. Confirm with a **corticotropin (ACTH) stimulation test** when condition allows; give **immediate IV hydrocortisone** stress dosing first if adrenal crisis is suspected — don't wait for results.
2	**Standard-dose (250 µg) ACTH stimulation** test preferred; peak cortisol <500 nmol/L (18 µg/dL) at 30–60 min indicates PAI. Low-dose (1 µg) test only if standard dose is unavailable; morning cortisol <140 nmol/L (5 µg/dL) + ACTH is a preliminary alternative if stimulation testing isn't feasible.
1	Measure **plasma ACTH** (>2× ULN with confirmed cortisol deficiency = PAI) and **simultaneous renin + aldosterone** to assess mineralocorticoid deficiency. Determine the **etiology** in all confirmed cases (ungraded).

2 Glucocorticoid Replacement

1	Glucocorticoid therapy for **all confirmed PAI**. Use **hydrocortisone 15–25 mg** or cortisone acetate 20–35 mg in 2–3 divided daily doses (largest dose on waking); **prednisolone 3–5 mg/day** is an alternative for reduced compliance.
2-	**Against dexamethasone** (Cushingoid risk from difficult dose titration) and **against routine hormonal monitoring** — titrate on clinical assessment (weight, postural BP, energy, signs of excess) instead.

3 Mineralocorticoid & DHEA Replacement

1	**Fludrocortisone** (starting 50–100 µg) for all with confirmed aldosterone deficiency; do not restrict salt. Monitor clinically (salt craving, postural hypotension, edema) plus electrolytes. If hypertension develops, reduce fludrocortisone before adding an antihypertensive.
2	Consider a **6-month DHEA trial** in women with low libido, depressive symptoms, or low energy despite optimized GC/MC replacement; monitor with morning DHEAS; discontinue if no sustained benefit.

4 Pregnancy

2	Review each trimester for over-/under-replacement; increase hydrocortisone, particularly in the **third trimester** (ungraded). Prefer **hydrocortisone** over cortisone acetate/prednisolone/prednisone; **against dexamethasone** (not inactivated by the placenta). Use **stress dosing** during active labor.

5 Pediatric Management

2	**Hydrocortisone**, 3–4 divided doses (starting ~8 mg/m²/day), preferred over other glucocorticoids; **avoid** long-acting synthetics (prednisolone, dexamethasone). Monitor growth velocity, weight, BP, energy (ungraded).
1	**Fludrocortisone** (starting 100 µg/day) for confirmed aldosterone deficiency; **sodium chloride supplements** in infants through 12 months.

6 Adrenal Crisis — Management & Prevention

1	**Immediate parenteral hydrocortisone 100 mg** (50 mg/m² in children), then fluid resuscitation and **200 mg/24h** hydrocortisone (continuous IV or 6-hourly); age/BSA-appropriate dosing in children. **Prednisolone** if hydrocortisone unavailable — dexamethasone is least preferred.
2	**Sick-day dosing:** adjust glucocorticoid dose to illness severity/stressor magnitude. Educate patients on stress dosing and crisis prevention, including self/lay parenteral administration (ungraded).
1	Equip every patient with a **steroid emergency card**, medical alert ID, and a **glucocorticoid injection kit**, with training on its use.

7 Ongoing Monitoring

2	Endocrinology review **at least annually** (infants every 3–4 months); assess yearly for over-/under-replacement; screen periodically for associated **autoimmune disease** (thyroid, T1DM, premature ovarian failure, celiac, autoimmune gastritis/B12 deficiency) if autoimmune PAI isn't excluded.
2	Educate on **increasing glucocorticoid doses** during intercurrent illness, fever, or stress; offer **genetic counseling** when PAI is due to a monogenic disorder.

Remember — Every PAI patient needs three things at all times: a steroid emergency card, an injection kit, and sick-day dosing education. Suspected adrenal crisis is treated with immediate parenteral hydrocortisone — never delay treatment to wait for confirmatory labs.

Bornstein SR, Allolio B, Arlt W, et al. Diagnosis and Treatment of Primary Adrenal Insufficiency: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2016;101(2):364-389.