Hormonal Replacement in Hypopituitarism

Diagnosis and replacement therapy across the pituitary axes, hormone interactions, and over-replacement risk in adults.

2016 Endocrine Society
Hypopituitarism Hormonal Replacement Guideline
Fleseriu et al. · JCEM 2016;101:3888-3921

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

1 Diagnosis, by Axis

AXIS	TEST	DIAGNOSTIC THRESHOLD
Central AI	AM cortisol, 8–9 AM (not random)	<3 µg/dL → AI; >15 excludes; 3–15 → cosyntropin stim (peak <18.1 = AI); test ≥18–24h post HC dose
Central Hypothyroidism	Free T4 + TSH	Low fT4 + low/normal/mildly high TSH confirms; treat low-normal fT4 if symptomatic or falling ≥20%
GH Deficiency	GH stimulation test, BMI-adjusted cutoffs	Skip testing if ≥3 other axes deficient + classic features
Male Hypogonadism	AM total T, FSH, LH, prolactin (fasting, <10 AM, no acute illness)	—
Female Hypogonadism	E2, FSH, LH if oligo/amenorrhea	Exclude pregnancy & other causes; postmenopausal — low FSH/LH = gonadotrope dysfunction
Central DI	Simultaneous serum + urine osmolality	Polyuria + serum osm >295, urine osm ~600 (ratio ≥2), dipstick-negative glucose

2 Hormonal Replacement

1 **Glucocorticoid:** HC 15–20 mg/d divided (highest dose AM) or a longer-acting GC in select cases; teach stress-dosing + emergency kit/bracelet; against fludrocortisone in secondary AI. **Adrenal crisis:** immediate parenteral HC 50–100 mg.

1 **Thyroid:** L-T4 to mid-upper fT4 range (~1.6 µg/kg/d); against L-T3/thyroid extracts; do not titrate by TSH (central disease).

2 **Testosterone/Estrogen:** T replacement in men, gonadal hormone therapy in premenopausal women — both with central hypogonadism and no contraindications.

1 **GH:** offer to proven GHD, no contraindications; start 0.2–0.4 mg/d (<60y) or 0.1–0.2 mg/d (≥60y); titrate to IGF-1 below ULN. Against use for isolated low IGF-1 without pituitary disease, or for athletic enhancement.

GPS **DI:** individualize DDAVP dosing; a weekly polyuric "washout" limits hyponatremia risk; patients should wear an emergency bracelet/necklace.

3 Hormone Interactions & Over-Replacement

INTERACTION	MANAGEMENT
GC + GH	Test HPA axis before/after starting GH if not already on GC replacement
GC + Thyroid	Exclude/treat AI before starting L-T4 for CH; give empiric GC if AI evaluation isn't feasible yet
GC + Estrogen	Oral estrogen raises CBG → elevates total cortisol; interpret adrenal reserve testing with this in mind
GH + Thyroid	Monitor for new CH once GH starts; increase L-T4 if already replaced when GH begins
GC + DI	AI can mask partial DI — monitor for emergent DI after starting GC replacement
Over-replacement	Individualize/avoid GC excess (bone loss, CV risk) — use lowest tolerable HC dose; avoid thyroid over- or under-replacement

4 Perioperative Management

2 **Pituitary surgery:** stress-dose steroids periop, individualize postop GC until HPA axis is tested; preop L-T4 if CH, check fT4 6–8wk postop; retest all axes starting at 6wk. **DI:** short-acting sc ADH initially; avoid prescheduled DDAVP in week 1 (transient DI/SIADH risk); oral or intranasal DDAVP after discharge only if polyuria recurs.

2 **Non-pituitary surgery:** adjust GC to stress severity — minor/moderate stress: HC 25–75 mg/24h (1–2 days); major stress: 100 mg IV bolus + 200 mg/24h infusion (or 50 mg IV/IM q6h).

5 Pregnancy

GPS **HC** is the preferred GC; increase the dose per clinical course (often higher in the **third trimester**). Monitor closely for over-/under-replacement (weight gain, fatigue, postural BP changes, hyperglycemia). **Against dexamethasone** (not inactivated by the placenta). Use **stress-dose HC** during active labor.

6 Special Circumstances

1 **Cushing's disease:** GC replacement until full HPA recovery after ACTH-secreting tumor resection; retest thyroid & GH axes before replacing.

1 **Macroprolactinoma:** reassess all pituitary axes after successful dopamine-agonist treatment resolves central hypogonadism.

2 **Cured acromegaly:** low-dose GH replacement if GHD is documented and no contraindications exist.

1 **Pituitary apoplexy:** test all patients for acute AI; treat with GC until excluded; monitor axes over time regardless of surgical vs. conservative management.

2 **Enzyme-inducing AEDs:** educate on early AI signs; increase dexamethasone dose if coadministered; recheck fT4 6wk after starting an AED; adjust AED levels once estrogen starts; monitor/adjust DDAVP doses.

Fleseriu M, Hashim IA, Karavitaki N, et al. Hormonal Replacement in Hypopituitarism in Adults: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2016;101(11):3888-3921.