Summary of Recommendations

1.0 Diagnosis of hypopituitarism

Central adrenal insufficiency

1.1 We suggest measuring serum cortisol levels at 8–9 AM as the first-line test for diagnosing central adrenal insufficiency (AI). (2|⊕◯◯◯)

1.2 We recommend against using a random cortisol level to diagnose AI. (1|⊕⊕◯◯)

1.3 We suggest that a cortisol level <3 μg/dL is indicative of AI and a cortisol level >15 μg/dL likely excludes an AI diagnosis. (2|⊕◯◯◯)

1.4 We suggest performing a corticotropin stimulation test when morning cortisol values are between 3 and 15 μg/dL to diagnose AI. Peak cortisol levels <18.1 μg/dL (500 nmol/L) at 30 or 60 minutes indicate AI. (2|⊕⊕◯◯)

1.5 We suggest that clinicians perform biochemical testing for the hypothalamic-pituitary-adrenal (HPA) axis at least 18–24 hours after the last hydrocortisone (HC) dose or longer for synthetic glucocorticoids (GCs). (2|⊕⊕◯◯)

Central hypothyroidism

1.6 We recommend measuring serum free T_4 (fT4) and TSH to evaluate central hypothyroidism (CH). An fT4 level below the laboratory reference range in conjunction with a low, normal, or mildly elevated TSH in the setting of pituitary disease usually confirms a CH diagnosis. (1|⊕⊕⊕⊕)

1.7 In patients with pituitary disease and low-normal fT4 levels suspected to have mild CH, we suggest starting levothyroxine (L-T4) if suggestive symptoms are present or following fT4 levels over time and starting treatment if the fT4 level decreases by 20% or more. (2|⊕◯◯◯)

1.8 We suggest against using dynamic TSH-secretion testing to diagnose CH. (2|⊕⊕⊕◯)

GH deficiency

1.9 In patients with suspected GH deficiency (GHD), we recommend GH stimulation testing. Single GH measurements are not helpful. (1|⊕⊕⊕◯)

1.10 We recommend using appropriately controlled body mass index (BMI) cutoffs to assess peak GH values. (1|⊕⊕◯◯)

1.11 We suggest against biochemical testing for GHD in patients with clear-cut features of GHD and three other documented pituitary hormone deficits. (2|⊕⊕⊕◯)

Central hypogonadism in males

1.12 In males with suspected hypogonadism, we recommend measuring serum T, FSH, and LH to diagnose central hypogonadism. (1|⊕⊕◯◯)

1.13 We recommend that clinicians perform hormonal testing for central hypogonadism in males in the absence of acute/subacute illness and before 10 AM (after overnight fast) combined with serum prolactin (PRL). (1|⊕⊕◯◯)

Central hypogonadism in females

1.14 In the presence of oligomenorrhea or amenorrhea, we recommend measuring serum estradiol (E2), FSH, and LH. Clinicians should exclude other causes of menstrual irregularities related to impaired ovulation (hyperprolactinemia, hyperandrogenism, and thyroid disease), particularly if no other pituitary hormone deficits are present. In cases of amenorrhea, clinicians should also exclude pregnancy. (1|⊕⊕◯◯)

1.15 We suggest against dynamic testing with GnRH, which offers no useful diagnostic information. (2|⊕⊕◯◯)

1.16 We recommend that in postmenopausal women, the absence of high serum FSH and LH is sufficient for a diagnosis of gonadotrope dysfunction (provided the patient is not on hormonal replacement therapy [HRT]). (1|⊕⊕⊕◯)

Central diabetes insipidus

1.17 We recommend simultaneously measuring serum and urine osmolarity in patients with polyuria (more than 50 mL/kg of body weight/24 hours, 3.5 L/d in a 70-kg person). In the presence of high serum osmolarity (>295 mOsmol/L), urine osmolarity should reach approximately 600 mOsmol/L (urine osmolality/plasma osmolality ratio should be ≥2), whereas urine dipstick should be negative for glucose. (1|⊕⊕⊕◯)

2.0 Treatment

Hormonal replacement in panhypopituitarism

Glucocorticoid replacement

2.1 We recommend using HC, usually 15–20 mg total daily dose in single or divided doses. Patients using divided doses should take the highest dose in the morning at awakening and the second in the afternoon (two-dose regime) or the second and third at lunch and late afternoon, respectively (three-dose regime). (1|⊕⊕⊕◯)

2.2 We suggest using longer-acting GCs in selected cases (eg, nonavailability, poor compliance, convenience). (2|⊕◯◯◯)

2.3 We recommend that clinicians teach all patients with AI regarding stress-dose and emergency GC administration and instruct them to obtain an emergency card/bracelet/necklace regarding AI and an emergency kit containing injectable high-dose GC (1|⊕⊕⊕◯)

2.4 We recommend against using fludrocortisone in patients with secondary AI. (1|⊕⊕⊕◯)