

- Tumoral masses in the sellar region with suprasellar extension can become manifest with visual impairment that is slowly progressive in most cases. Visual-field defects can present not only as classic bitemporal hemianopsia but also unilaterally in many cases. Usually, such defects remain unrecognised by patients until diagnosed by a doctor.
- Headaches can be an unspecific symptom of tumour masses. In case of lateral extension, rarely, signs of oculomotor nerve impairment and, even less common, additional damage to other cranial nerves within the cavernous sinus might arise.
- Hypopituitarism can be subclinical, indicated only by measurement of hormones, or its clinical onset might be acute and severe, necessitating admission and intensive care management. Shortages of adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), and antidiuretic hormone (ADH) are potentially life-threatening
- Gonadotropin and growth-hormone deficiencies, on the other hand, cause chronic morbidity. Raised prolactin concentrations sometimes accompany hypopituitarism because of disruption of inhibitory signals by the hypothalamus. This alteration can cause lactation, tenderness of the breast, and suppression of gonadotropins, leading to symptoms of hypogonadism.

clinical features

hormone tests

Criteria for hormone deficiency*	
Corticotrophic function	
Morning cortisol	<100 nmol/L: hypocortisolism; >500 nmol/L: hypocortisolism excluded
Morning ACTH	Below upper reference range: secondary adrenal insufficiency
Insulin tolerance test	Cortisol <500 nmol/L
250 µg ACTH test	Cortisol <500 nmol/L after 30 min
Thyrotrophic function	
Free thyroxine	Low (<11 pmol/L)
TSH	Low or normal (occasionally slightly raised)
Gonadotrophic function	
Women	
Clinical	Oligomenorrhoea, oestradiol <100 pmol/L, LH and FSH inappropriately low
Postmenopausal	LH and FSH inappropriately low
Men	
Testosterone	Low (<10-12 nmol/L), LH and FSH inappropriately low
Somatotrophic function	
IGF-I	Below or in the normal reference range
Insulin tolerance test	Adults: growth hormone ≤3 µg/L; Children: growth hormone ≤10 µg/L; Transition phase: growth hormone ≤5 µg/L
GHRH+ arginine test	Underweight or normal weight (BMI <25): 11.5 µg/L; Overweight (BMI ≥25 to <30): 8.0 µg/L; Obese (BMI ≥30): 4.2 µg/L
GHRH+ GHRP-6 test	Growth hormone ≤10 µg/L
Posterior pituitary function	
Basal urine and plasma sample	Urine volume (≥40 mL/kg bodyweight per day)+urine osmolality <300 mOsm/kg water+hyponatraemia
Water deprivation test	Urine osmolality <700 mOsm/kg; Ratio of urine to plasma osmolality <2

LH=luteinising hormone. FSH=follicle-stimulating hormone. ACTH=adrenocorticotropic hormone. TSH=thyrotrophic hormone. GHRH=growth hormone-releasing hormone. GHRP-6=growth hormone-releasing peptide 6. *Hormone levels might differ to the ones indicated, dependent on the laboratory and assay used.

Imaging

- Cranial MRI should be done to exclude tumours and other lesions of the sellar and parasellar region after hypopituitarism has been confirmed. Of sellar tumours, the pituitary adenoma is the most frequent. However, hypopituitarism is not excluded by normal MRI of the sellar and parasellar region.

investigation

hypopituitarism
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10/07/12]

general

Hypopituitarism is the inability of the pituitary gland to provide sufficient hormones adapted to the needs of the organism. It might be caused by either an inability of the gland itself to produce hormones or an insufficient supply of hypothalamic-releasing hormones.

epidemiology

- Incidence and prevalence of hypopituitarism are estimated to be 4.2 per 100 000 per year and 45.5 per 100 000, respectively.

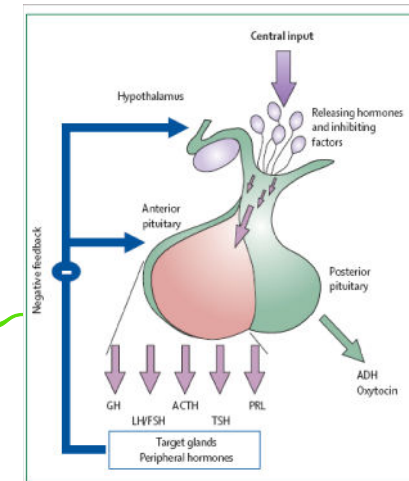


Figure 1: Regulation of hypothalamic-pituitary-peripheral function
The anterior pituitary produces adrenocorticotropic hormone (ACTH), thyrotrophic hormone (TSH), luteinising hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), and growth hormone (GH). Their secretion is regulated by hypothalamic releasing and inhibiting factors and by negative feedback inhibition of their peripheral hormones. The posterior pituitary is a storage organ for the hypothalamic hormones antidiuretic hormone (ADH) and oxytocin. Hypopituitarism can arise at hypothalamic, stalk or pituitary level.

physiology

aetiology

- Brain damage***
 - Traumatic brain injury
 - Subarachnoid haemorrhage
 - Neurosurgery
 - Irradiation
 - Stroke
- Pituitary tumours***
 - Adenomas
 - Others
- Non-pituitary tumours**
 - Craniopharyngiomas
 - Meningiomas
 - Gliomas
 - Chordomas
 - Ependymomas
 - Metastases
- Infections**
 - Abscess
 - Hypophysitis
 - Meningitis
 - Encephalitis
- Infarction**
 - Apoplexia
 - Sheehan's syndrome
- Autoimmune disorders**
 - Lymphocytic hypophysitis
- Haemochromatosis, granulomatous diseases, histiocytosis**
- Empty sella**
- Perinatal insults**
- Pituitary hypoplasia or aplasia**
- Genetic causes**
- Idiopathic causes**

*Pituitary tumours are classically the most common cause of hypopituitarism. However, new findings imply that causes related to brain damage might outnumber pituitary adenomas in causing hypopituitarism.

treatment

Treatment	Monitoring and dose adjustment
ACTH⁴⁴⁶	10-25 mg hydrocortisone per day (2-3 doses per day) or 25-37.5 mg cortisone acetate Stress (surgery, infection, etc): increase dose up to 100-150 mg/day ⁴⁴
TSH	L-thyroxine mean dose after initial up-titration: ⁴³ >60 years: 1.1 µg/kg bodyweight; <60 years: 1.3 µg/kg bodyweight Adjust to free thyroxine (target: middle-upper normal range) and normal tri-iodothyronine Further adjustments to cholesterol and clinical symptoms; Increase might be necessary during pregnancy or new oestrogen or growth hormone replacement ⁴⁵⁻⁴⁹
LH/FSH	
Women ^{45,49}	Oral contraceptive (20-35 µg ethinyl oestradiol) or oestradiol valerate 2-4 mg/day or equine oestrogens 0.626-1.250 mg/day or transdermal oestradiol patch or gel (four times less risk of thrombosis); Unless hysterectomised, additional gestagen replacement necessary Induction of fertility: FSH or pulsatile gonadotropin-releasing hormone (the latter only in hypothalamic dysfunction) ⁴⁹
Men	Testosterone gel 25-50 mg/day ^{44,45} or testosterone undecanoate 1000 mg intramuscularly all 12 weeks ⁴⁵ or buccal testosterone pellet 30 mg twice a day ^{45,49} or testosterone enanthate 250 mg intramuscularly all 2-4 weeks (causes fluctuating testosterone concentrations); Induction of fertility: human chorionic gonadotropin, human menopausal gonadotropin FSH or pulsatile gonadotropin-releasing hormone (the latter only in hypothalamic dysfunction) ^{45,44}
Growth hormone	Growth hormone dose after up-titration; Children: 25-50 µg/kg per day; Adults: 0.2-1 mg/day Adjust to normal IGF-I concentrations; Further adjustments to beneficial and unwanted effects (oedema, arthralgias, carpal tunnel syndrome)
ADH	Desmopressin oral (0.3-1.2 mg/day) or intranasal (10-40 µg/day) in 1-4 doses per day ^{44,45} Adjust dose to normalisation of fluid intake

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