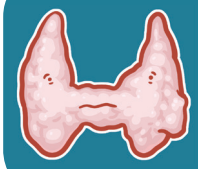

NOTES
HYPERPITUITARISM & HYPOPITUITARISM

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Disorders caused by excess/insufficient pituitary hormones, disruption in hypothalamic-pituitary axis function

CAUSES

Hyperpituitarism
- Genetic inheritance
- Secreting tumors (intracranial, ectopic)

Hypopituitarism
- Intracranial tumors, bleeding, infarction
- Neurosurgery, head trauma, infection
- Idiopathic

SIGNS & SYMPTOMS

- Disruption in growth, regulation; depends on affected hormones
- If pituitary adenoma, sequence of loss: "**G**o **L**ook **F**or **T**he **A**denoma" (see mnemonic)

MNEMONIC: Go Look For The Adenoma

Pituitary adenoma sequence of loss

Growth hormone (GH)

Luteinizing hormone (LH)

Follicle-stimulating hormone (FSH)

Thyroid-stimulating hormone (TSH)

Adrenocorticotropic hormone (ACTH)

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray, CT scan, MRI
- Intracranial, ectopic tumors; bleeding, infarction

LAB RESULTS
- Altered levels of pituitary, target tissue hormones

OTHER DIAGNOSTICS
- History, physical examination

TREATMENT

MEDICATIONS

Hyperpituitarism
- Somatostatin + dopamine agonists; GH receptor antagonists

Hypopituitarism
- Hormone replacement (e.g. glucocorticoids, thyroid hormone)

SURGERY
- Surgical excision of tumor

ACROMEGALY

osms.it/acromegaly

PATHOLOGY & CAUSES

- GH hypersecretion in adulthood after epiphyseal closure → enlargement of extremities, face

CAUSES

- Pituitary adenoma produces excess GH
- Nonpituitary tumors (pancreatic, lung, adrenal gland) produce ectopic GH

COMPLICATIONS

- Glucose intolerance to Type II diabetes, high blood pressure, respiratory problems, carpal tunnel syndrome, heart/kidney failure

SIGNS & SYMPTOMS

- Soft tissue, bone swelling
  - Hands, feet
  - *Skull:* jaw protrusion, enlargement (macrognathia), increased spacing of teeth; forehead, brow protrusion
  - *Organomegaly:* heart, kidneys; vocal cords → slow, deep voice
- Joint pain, headache, vision problems, thickened skin
- Excess sweating, hair growth, pigmentation

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI of sella turcica with gadolinium

- Somatotroph adenoma; tumoral location

CT scan of chest/abdomen

- Ectopic tumors

LAB RESULTS

Blood tests

- Acromegaly
  - ↑ insulin-like growth factor-1 (IGF-1) / somatomedin C
- Oral glucose tolerance test (OGTT)
  - Hyperglycemia

TREATMENT

MEDICATIONS

- Somatostatin agonists
  - Stop GH production
- Dopamine agonists, alternative to somatostatin agonists
  - For tumors that affect prolactin levels
- GH receptor antagonists
  - Blocks GH binding to receptors

SURGERY

- Transsphenoidal tumor resection

OTHER INTERVENTIONS

- Tumor radiation

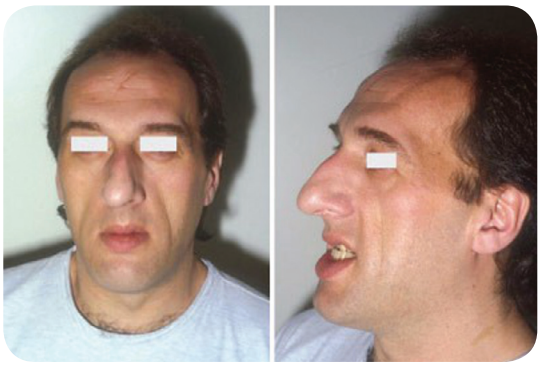

Figure 18.1 The clinical appearance of acromegaly. The facial features are coarse and mandibular overgrowth has lead to prognathism.

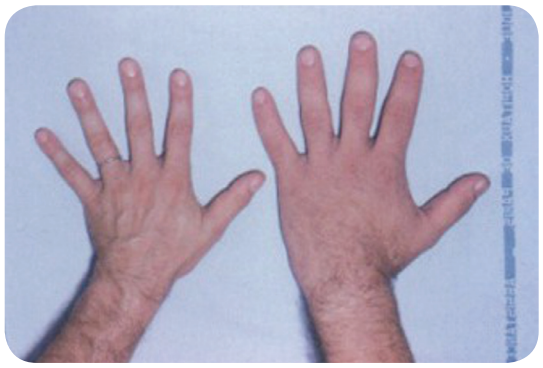

Figure 18.2 The appearance of the hands in the case of acromegaly. The acromegalic right hand is larger with expanded soft tissues and thickened, stubby fingers.

CONSTITUTIONAL GROWTH DELAY

osms.it/constitutional-growth-delay

PATHOLOGY & CAUSES

- Normal variation in rate of growth → temporary delay during early childhood, puberty
- Eventual adult height within normal range

CAUSES

- Alterations in hormones critical for growth, development
- GH axis: regulates bone, muscle growth
- ↓ GH → ↓ production of IGF-1/somatomedin C (prevents cell death), ↑ cellular metabolism, cell division, differentiation throughout body
- *Hypothalamic-pituitary-gonadal axis:* regulates sexual maturation
- ↓ gonadotropin-releasing hormone (GnRH) → ↓ anterior pituitary production of gonadotropins (LH, FSH) → ↓ production of sex hormones by gonads (estrogen, progesterone in individuals who are biologically female, testosterone in individuals biologically male) → delayed development of sex organs, secondary sexual characteristics

RISK FACTORS

- Family history of delayed growth

COMPLICATIONS

- Psychosocial stress

SIGNS & SYMPTOMS

- Normal size at birth
- Short preadolescent stature
- Delayed pubertal development, skeletal age

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray

- Delayed bone development

OTHER DIAGNOSTICS

- History, physical examination
- Height growth curve below, parallel to third percentile
- Delayed Tanner scale staging

TREATMENT

OTHER INTERVENTIONS

- Provide reassurance regarding eventual normal growth, development

DIABETES INSIPIDUS (DI)

osms.it/diabetes-insipidus

PATHOLOGY & CAUSES

- Disorder of fluid balance characterized by defect in urine concentration → excretion of large volumes of dilute urine
- *Diabetes* = to pass through; *insipidus* = tasteless

TYPES

Neurogenic (central) DI

- DI caused by absence/↓ secretion/production of antidiuretic hormone (ADH) by posterior pituitary

Nephrogenic DI

- Kidneys unresponsive to ADH secreted by posterior pituitary

CAUSES

Neurogenic DI

- Idiopathic (most common)
- Damage to hypothalamus/pituitary/supraoptico-hypophyseal tract (e.g. head trauma, pituitary adenoma), neurosurgery, infection (e.g. tuberculosis), infiltrative disease (e.g. Langerhans cell histiocytosis), hypoxic encephalopathy, ischemia
- Familial (familial neurohypophyseal DI)
  - Autosomal dominant gene mutation
- Congenital (e.g. septo-optic dysplasia)

Nephrogenic DI

- Hereditary
  - Defect in genes encoding for ADH receptor/aquaporin function
- Damage of renal tubules from systemic disease (e.g. polycystic kidney disease, pyelonephritis, amyloidosis)
- Lithium toxicity
  - Interferes with aquaporin function

SIGNS & SYMPTOMS

- Polyuria
  - *Neurogenic:* urine amount varies depending on degree of ADH production/secretion
  - *Nephrogenic:* daily output of > 3L in adults; > 2L/m2 in children
- Nocturia, polydipsia, dehydration, hypotension
- Neurogenic DI
  - Lack of other pituitary hormones

DIAGNOSIS

DIAGNOSTIC IMAGING

Cranial MRI (neurogenic DI)

- Hyperintensities, pituitary stalk thickening identifies signs of hypothalamic/pituitary dysfunction

LAB RESULTS

- ↓ ADH levels (neurogenic), urine osmolarity
- ↑ plasma osmolarity
- Hypernatremia
- *Water deprivation test (ADH stimulation test):* fluid deprivation → ADH (vasopressin) administered subcutaneously

- ↑ *urine osmolality:* confirms neurogenic DI
- *Little/no* ↑ *urine osmolality:* confirms nephrogenic DI

TREATMENT

MEDICATIONS

Neurogenic DI

- Desmopressin (dDAVP) (synthetic vasopressin)
- Chlorpropamide
  - Enhances renal response to low levels of ADH

Neurogenic/nephrogenic DI

- Nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g. indomethacin)
  - ↑ renal concentration of urine
- Thiazide diuretics (e.g. hydrochlorothiazide) + low sodium diet
  - ↓ polyuria (↑ water permeability to collecting tubules)

OTHER INTERVENTIONS

- Fluid replacement
- Diet
  - Low solute (low sodium, low protein)

GIGANTISM

osms.it/gigantism

PATHOLOGY & CAUSES

- GH hypersecretion during childhood → rapid, excessive linear growth

CAUSES

- Excessive secretion of GH, GHRH, IGF-1
- Tumor in pituitary gland
- Tumors outside pituitary, secrete GH
- Hereditary
  - Gene mutation (e.g. McCune Albright syndrome, multiple endocrine neoplasia Type I)

COMPLICATIONS

- *Cardiovascular conditions:* hypertension in children
- *Bone conditions:* osteoarthritis
- *Diabetes mellitus:* insulin resistance

SIGNS & SYMPTOMS

- Height significantly above standard deviations
- Obesity
- Overgrowth of face, extremities
- Headaches
- Maxilla/mandible protrusion

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- Pituitary tumors

CT scan

- Tumors in other organs, might secrete GH/GHRH

X-ray

- Assess bones

LAB RESULTS

Blood tests

- OGTT
  - Hyperglycemia
  - Elevated IGF-1

TREATMENT

MEDICATIONS

- Somatostatin agonists
  - Shrink pituitary tumors, stop GH production
- Dopamine agonists
  - If somatostatin agonists not effective
  - Effective in tumors producing hyperprolactinemia
- Somatostatin + dopamine agonists
- GH receptor antagonists

SURGERY

- For small pituitary adenomas
  - Transsphenoidal surgical approach

OTHER INTERVENTIONS

- Radiation (not recommended for children)
  - Can produce panhypopituitarism (decreased secretion in most pituitary hormones) → learning disabilities, obesity

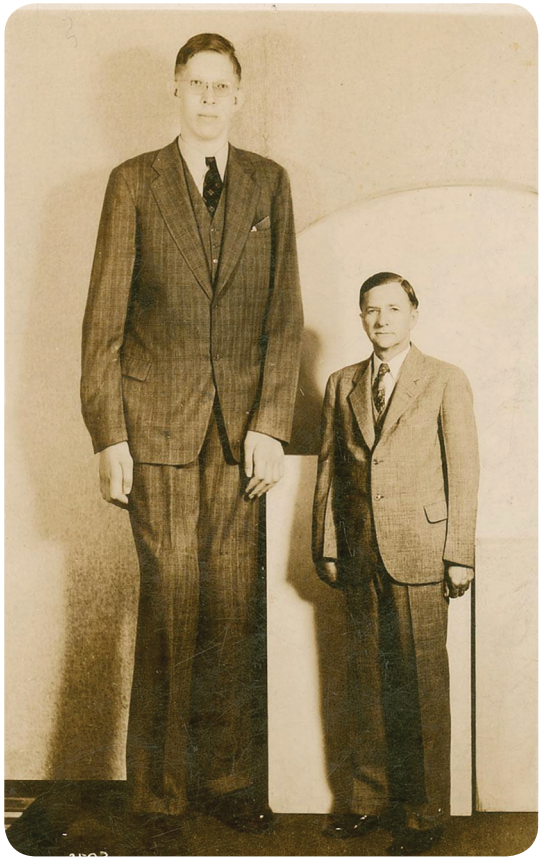

Figure 18.3 The worlds tallest ever recorded man, Robert Wadlow, was diagnosed with from gigantism as a consequence of pituitary hyperplasia. He stood at 2.27m/8ft 11in and wore a size 37 shoe.

GROWTH HORMONE DEFICIENCY (GHD)

osms.it/growth-hormone-deficiency

PATHOLOGY & CAUSES

- Conditions caused by decreased production of GH (AKA somatotropin)
- Partial/complete, permanent/transient

CAUSES

- Hypothalamic/pituitary dysfunction
  - Tumors (e.g. pituitary/parasellar adenomas); radiation; traumatic injury; autoimmune disease; genetic mutations (e.g. PROP1); congenital structural defects of brain (e.g. Prader–Willi, Turner syndrome); idiopathic

SIGNS & SYMPTOMS

- Newborns
  - Hypoglycemia, micropenis, excessive jaundice
- Children
  - Stunted growth/short stature, delayed puberty
  - Nystagmus, hypoglycemia, retinal defects, midfacial defects (e.g. cleft lip)
  - *Severe cases:* delayed basic motor skills (e.g. standing, walking)
  - Moderately overweight (rare—severely obese)
- Adults
  - Decreased muscle mass, decreased bone mineral density, high 5-alpha reductase, baldness, cardiac conditions
  - Psychological issues (memory problems, social issues, depression)

DIAGNOSIS

LAB RESULTS

- Serum GH levels < 1ng/mL
  - Nonspecific test for GH deficiency: affected by circadian rhythms, food intake, stress
- Serum IGF-1
  - More accurate assessment of GH secretion; not affected by external factors
  - Less than standard gender-specific levels → confirms diagnosis
- Insulin tolerance test
  - Regular insulin administered via intravenous (IV) → measure blood at 30 minute intervals
  - Subnormal increase in serum GH confirms diagnosis

TREATMENT

MEDICATIONS

- Daily injections with recombinant growth hormone (rGH)
  - *Childhood:* GH daily injections; stature monitoring throughout growth period
  - *Adulthood:* 25% treatment for children

HYPERPITUITARISM

osms.it/hyperpituitarism

PATHOLOGY & CAUSES

- Disorders caused by pituitary hormones hypersecretion

CAUSES

- Pituitary adenoma (most common)
- Genetic mutation from single cell (monoclonal) → tumorigenesis → tumor secretes hormones
  - Prolactin → prolactinoma
  - ACTH → Cushing's disease
  - GH → acromegaly (occurs during adulthood after epiphyseal closure), gigantism (during childhood before epiphyseal closure)

SIGNS & SYMPTOMS

- Diaphoresis; visual field problems; headaches; lethargy; excessive hair growth; larger organs, extremities, facial components

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray

- Sella turcica, pituitary glands

LAB RESULTS

- Elevated hormone levels in serum

TREATMENT

MEDICATIONS

- *Dopamine agonists:* gonadal dysfunctions
  - Inhibit prolactin secretion
  - Inhibitors of tumoral cells division

SURGERY

- Total/partial removal of pituitary/tumor
  - Endonasal transsphenoidal surgery (most common)

HYPERPROLACTINEMIA

osms.it/hyperprolactinemia

PATHOLOGY & CAUSES

- Disorder caused by high blood levels of pituitary hormone prolactin
- *Prolactin:* secreted by lactotroph cells in anterior segment of pituitary

CAUSES

- Prolactinoma/lactotroph adenoma (prolactin-secreting tumor)
- Pregnancy
- Damage to hypothalamic-pituitary stalk
- Disorders affecting hypothalamus
- Drugs, medication, heavy metal poisoning
  - Inhibits dopamine production
  - Dopamine receptor antagonists, synthesis inhibitors → pituitary overproduces prolactin
- Renal failure
- Primary hypothyroidism

SIGNS & SYMPTOMS

- Individuals who are biologically male
  - Impaired genital activity (hypogonadism) → infertility, impotence
  - Decreased libido
  - Overdevelopment of mammary glands (gynecomastia)
  - Spontaneous secretion, flow of breast milk (galactorrhea)
- Individuals who are biologically female
  - *Irregular menstrual cycles:* sometimes complete lack of menstruation (amenorrhoea); no ovulation → infertility
  - Galactorrhea
  - Painful breasts
- Visual impairment, headaches when pituitary adenoma presses on optic nerve

DIAGNOSIS

DIAGNOSTIC IMAGING

Head MRI/CT scan

- Tumors/lesions in hypothalamic-pituitary area: if none + high serum levels: idiopathic hyperprolactinemia

LAB RESULTS

- High serum prolactin levels

OTHER DIAGNOSTICS

- Lower bone density
- Pregnancy/hypothyroidism

TREATMENT

MEDICATIONS

- *Tumor:* dopamine agonist (inhibit prolactin production, secretion)
  - Bromocriptine/cabergoline

SURGERY

- Surgical removal of tumor
  - High rate recurrence

HYPOPITUITARISM

osms.it/hypopituitarism

PATHOLOGY & CAUSES

- Disorders caused by complete/partial lack of pituitary hormone production, secretion

CAUSES

- Tumors
  - Pituitary adenomas → compression → intracranial pressure → destruction of pituitary
  - Brain (e.g. metastatic cancer)
  - Body
- Traumatic injury, shock, stroke → ischemia
- Vascular
  - Hemorrhages (e.g. aneurysms, subarachnoid hemorrhage)
- Radiation
- Infections
  - Brain (e.g. meningitis)
  - Abnormal brain cells/substance infiltrations (e.g. hemochromatosis)
  - Autoimmune disorders (e.g. autoimmune hypophysitis)
- Congenital (defect in transcription factors)
  - *PROP1* gene mutation → hormone deficiency (most common)
  - Pituitary transcription factor 1 (*PIT-1*) mutation → GH, prolactin, TSH deficiencies
- Hypothalamic dysfunction, decrease in releasing hormones

SIGNS & SYMPTOMS

- Occur when ≥ 75% of anterior pituitary nonfunctional
- Vary depending on hormone affected
- Sequence of loss: "**G**o **L**ook **F**or **T**he **A**denoma" (see mnemonic)
- If tumor present
  - Pressure on optic chiasm → visual disturbances
  - Increased intracranial pressure → headache

MNEMONIC: Go Look For The Adenoma

Pituitary adenoma sequence of loss

Growth hormone (GH)

Luteinizing hormone (LH)

Follicle-stimulating hormone (FSH)

Thyroid-stimulating hormone (TSH)

Adrenocorticotropic hormone (ACTH)

DIAGNOSIS

LAB RESULTS

- Blood tests
  - Serum thyroid levels (T_3/T_4)
  - ACTH secretion (measure serum cortisol in the morning)

TREATMENT

MEDICATIONS

- Hormone replacement
  - *ACTH deficiency:* hydrocortisone
  - *TSH deficiency:* levothyroxine
  - *FSH/LH deficiency:* testosterone (for individuals who are biologically male); estrogen-progestin (for premenopausal individuals who are biologically female)

SURGERY

- Surgical excision of tumors

HYPOPROLACTINEMIA

osms.it/hypoprolactinemia

PATHOLOGY & CAUSES

- Low serum prolactin levels due to damaged lactotroph cells in anterior pituitary

CAUSES

- Sheehan's syndrome
  - Postpartum hemorrhage → hypotension, decreased circulation to pituitary, ischemia, damaged lactotroph cells
- Medications
  - Dopamine, dopamine agonists; inhibit prolactin release
- Tumors
  - Pressure on pituitary/hypothalamus → damage lactotroph cells

SIGNS & SYMPTOMS

- Individuals who are biologically female and breastfeeding
  - Decreased lactation (agalactorrhea)

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- Tumor confirmation

LAB RESULTS

- Low prolactin levels despite receiving thyrotropin-releasing hormone (TRH)
  - Individuals who are biologically female: < 3µg/L
  - Individuals who are biologically male: < 5µg/L

TREATMENT

MEDICATIONS

- Dopamine antagonists
  - Oppose dopamine in individuals who want to breastfeed

SURGERY

- Surgical removal of tumor

PITUITARY APOPLEXY

osms.it/pituitary-apoplexy

PATHOLOGY & CAUSES

- Pituitary function impaired due to hemorrhage into gland
- Hemorrhage → blood collects within pituitary interstitium → swelling → infarction, loss of pituitary function → compression of surrounding structures

RISK FACTORS

- Intracranial tumors, head trauma, neurosurgery, Sheehan's syndrome (postpartum pituitary necrosis)

COMPLICATIONS

- Hypopituitarism, neuronal damage

SIGNS & SYMPTOMS

- Meningeal stretching
  - Severe headache
- Optic chiasm compression
  - Diplopia, bitemporal hemianopia
- Parenchymal compression
  - Mental status changes
- Clinical manifestations of hypopituitarism (e.g. ↓ ACTH → ↓ cortisol → hypoglycemia, hypotension, adrenal crisis)

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/MRI

- Enlarged pituitary gland; hyperintense blood-filled center

LAB RESULTS

- ↓ pituitary hormone levels, target tissue hormones

TREATMENT

MEDICATIONS

- Hormone replacement
  - Glucocorticoids (emergent), levothyroxine

SURGERY

- Surgical decompression
- Transphenoidal resection of pituitary gland

SHEEHAN'S SYNDROME

osms.it/sheehans-syndrome

PATHOLOGY & CAUSES

- AKA postpartum pituitary gland necrosis
- Destruction of lactotroph cells of anterior pituitary in setting of postpartum hemorrhage

CAUSES

- Pituitary increases in size during gestation → metabolic activity of lactotrophs increase, blood supply does not → pituitary vulnerable to perfusion decrease → hypovolemia, hypotension, shock → pituitary infarction, necrosis

SIGNS & SYMPTOMS

- Pituitary dysfunction

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- Pituitary ring sign (halo around empty sella)

LAB RESULTS

- Pituitary hormone levels

OTHER DIAGNOSTICS

- Obstetric history

TREATMENT

MEDICATIONS

- Glucocorticoid replacement (emergent) if adrenal insufficiency
- Ongoing hormone replacement as needed

SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION (SIADH)

osms.it/SIADH

PATHOLOGY & CAUSES

- Inappropriate ADH secretion → ↓ water excretion
  - ADH overproduced, secreted → highly concentrated urine, ↓ volume
  - ↑ intake of fluids, ADH secretion → water retention → dilutes plasma sodium levels → hyponatremia

CAUSES

- Central nervous system (CNS) disorders enhance ADH production, release
  - Trauma, stroke, hemorrhage, infection
  - Mental illness, though carbamazepine effects
- Ectopic production of ADH
  - *Lung malignancies:* e.g. small cell carcinoma

- *Nonmalignant lung disorders:* pneumonia, tuberculosis, cystic fibrosis (CF)
- Medications
  - Anticonvulsants, opioids, sulfonylureas
- Injury/surgical removal of pituitary

SIGNS & SYMPTOMS

- Body weakness
  - Fatigue, dizziness, confusion, nausea, lethargy; anorexia
- Muscle cramps
  - Myoclonus,tremors
- Seizures

DIAGNOSIS

LAB RESULTS

- Urinalysis
  - Highly concentrated urine
- Serum tests
  - Hyponatremia, low plasma osmolarity

TREATMENT

MEDICATIONS

- ADH receptor antagonist (e.g. tolvaptan)

OTHER INTERVENTIONS

- Water restriction
  - < 800mL daily
  - If SIADH associated with subarachnoid hemorrhage, fluid restriction not recommended
- IV hypertonic saline administration for severe cases, oral salt tablets, loop diuretics
- Urea administration
  - Increases urine output