

Clinical Manifestations of Pituitary Disease

Endocrine excess • Hormonal deficiency • Local mass effects • Water balance

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Learning objectives

- Classify clinical presentations into endocrine excess, deficiency, local effects, and ADH disorders
- Explain the hypothalamic–pituitary relationships underlying characteristic syndromes
- Link optic chiasm compression and pituitary apoplexy to neurologic findings
- Use focused clinical patterns to distinguish common pituitary mechanisms

Clinical manifestations of pituitary disease

Hormone excess creates characteristic endocrine syndromes

Hormone deficiency produces loss of target-organ functions

Local expansion injures neighboring sellar and suprasellar structures

Posterior-pituitary disorders alter water and electrolyte homeostasis

Four questions organize clinical presentation

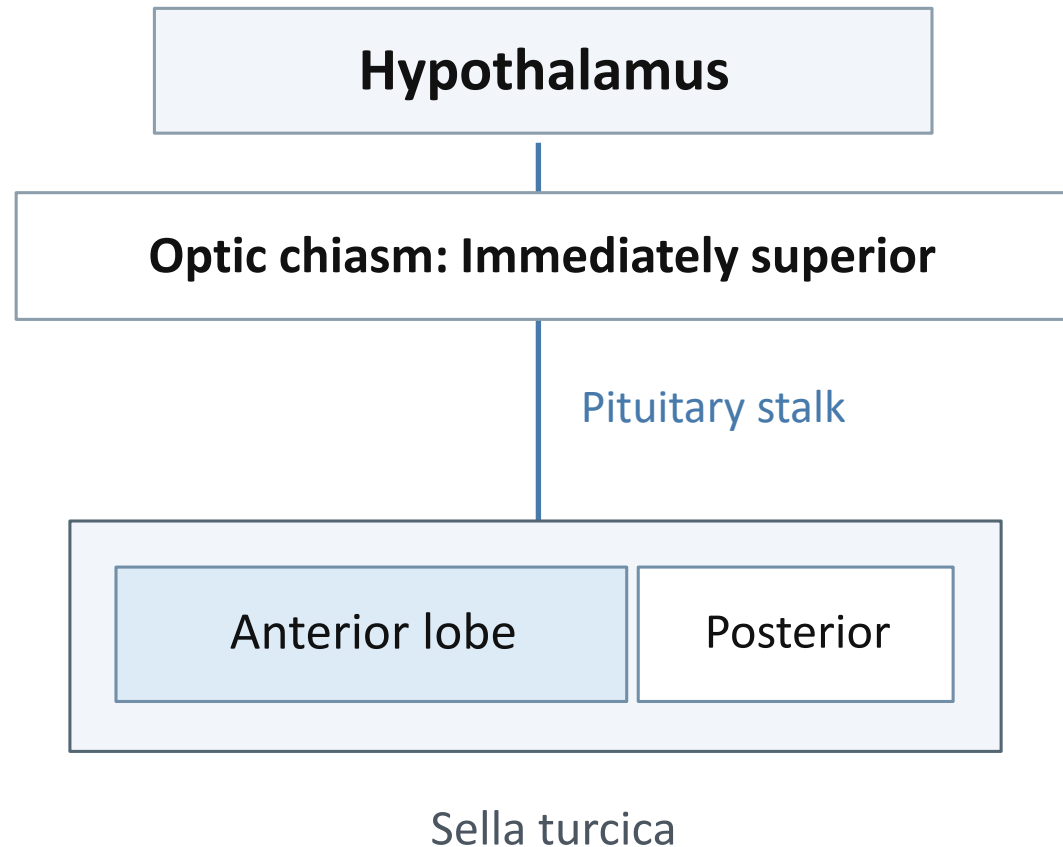
Is there a syndrome of hormone hypersecretion?

Is there clinical evidence of one or more hormone deficiencies?

Is there headache, visual loss, or another local mass effect?

Is the dominant problem polyuria or hyponatremia?

The sella determines the clinical anatomy



Clinical implications

- | | | |
|------------------------------|---|---------------------|
| Upward growth | → | Visual-field defect |
| Anterior destruction | → | Hormone deficiency |
| Functional neoplasm | → | Hormone excess |
| Hemorrhagic expansion | → | Acute apoplexy |

Anterior and posterior lobes have distinct roles

Mechanism / finding

- Adenohypophysis contains differentiated endocrine cell populations
- Anterior hormones regulate growth, gonadal function, thyroid, and adrenal cortex

Clinical implication

- Neurohypophysis stores and releases hypothalamic ADH and oxytocin
- Distinguishing lobes is essential for interpreting symptoms

Hypothalamic control precedes anterior pituitary secretion

Releasing factors travel to the anterior lobe through portal vessels



Dopamine inhibits lactotroph secretion of prolactin



Loss of a hypothalamic input can mimic primary pituitary dysfunction



A hypothalamic or stalk lesion may generate mixed endocrine signs

Hormone phenotype is not equivalent to tumor size

Mechanism / finding

- Small functioning tumors may generate conspicuous endocrine symptoms
- Clinically silent tumors can enlarge before being detected

Clinical implication

- A large lesion may cause hormone loss by compressing normal gland
- Endocrine output and local anatomy must be assessed separately

Clinical phenotypes reflect different causal routes

A secreting tumor can produce a hormone-excess syndrome



Destructive injury or mass compression can cause hypopituitarism



Chiasmal compression causes visual field loss independently of secretion



ADH imbalance produces renal water-handling manifestations

Hyperpituitarism is a hormone-excess state

- Excess trophic hormone secretion usually originates in a functioning PitNET
- Hypothalamic dysregulation is an additional, less frequent mechanism
- Nonpituitary hormone secretion can imitate a pituitary hypersecretory state
- Clinical phenotype depends on the particular hormone affected

Functional PitNETs produce recognizable syndromes

Lactotroph tumor

Hyperprolactinemia

Somatotroph tumor

GH excess with raised IGF-1

Corticotroph tumor

Excess corticotropin and Cushing disease

Thyrotroph tumor

TSH-mediated hyperthyroidism

Silent tumors may still express hormones

Mechanism / finding	Clinical implication
• Immunohistochemical hormone expression does not guarantee a clinical secretory syndrome • Some corticotroph and most gonadotroph tumors can be clinically silent	• Silent lesions frequently present with mass effect or hypopituitarism • A clinical label of “nonfunctioning” is not a histologic lineage diagnosis

PitNET classification follows cellular lineage

Lineage-associated transcription factors help identify pituitary tumor subtypes

PIT-1/POU1F1-related lineages include GH, PRL, and TSH tumors

TPIT/TBX19 lineage identifies corticotroph differentiation

SF-1 lineage identifies gonadotroph differentiation

Hyperprolactinemia primarily disrupts reproduction

- Amenorrhea and infertility may make hormone excess readily apparent
- Galactorrhea may accompany elevated prolactin concentrations
- Loss of libido and sexual dysfunction can affect either sex
- Presentation reflects hormone physiology rather than just tumor extent

Prolactin-related symptoms vary by sex and age

Mechanism / finding	Clinical implication
• Menstrual-cycle disturbance can reveal tumors early in younger women • Males and older women may have less conspicuous hormonal symptoms	• A clinically subtle lesion can enlarge before it is recognized • Large lesions may consequently present with visual or other mass effects

Dopamine normally restrains prolactin secretion

Hypothalamic dopamine provides tonic inhibition of lactotrophs



Disruption of the stalk reduces this inhibitory input



Prolactin may rise despite absence of a prolactin-secreting tumor



This mechanism underlies the clinically important stalk effect

Elevated prolactin does not always mean a prolactinoma

Pregnancy and breastfeeding are physiological settings of prolactin elevation

Dopamine receptor antagonism may elevate prolactin

Stalk injury or a suprasellar mass may cause disinhibition

Renal failure and hypothyroidism are other possible causes

The stalk effect is a diagnostic pitfall

A non-lactotroph sellar tumor can interfere with hypothalamic dopamine



Loss of tonic inhibition produces secondary hyperprolactinemia

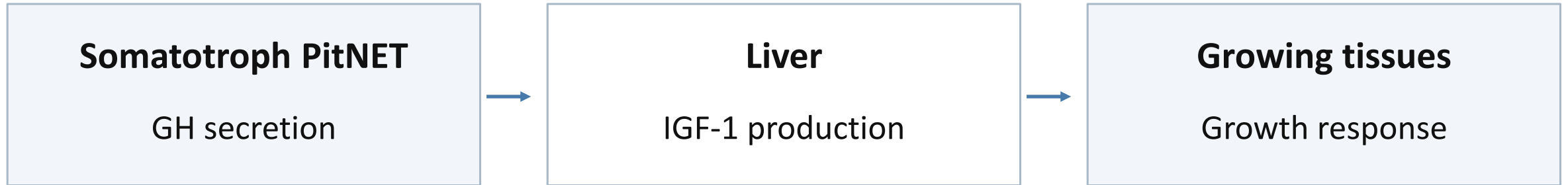


A mildly raised prolactin concentration alone does not identify lineage



Interpret biochemistry alongside symptoms and sellar anatomy

Growth hormone excess acts largely through IGF-1



Before epiphyseal closure

Gigantism: Excessive linear growth

After epiphyseal closure

Acromegaly: Soft tissue and acral growth

Gigantism reflects excess before epiphyseal closure

GH and IGF-1 promote excessive linear growth in children

Long bones can lengthen while growth plates remain open

Marked height and disproportionately long limbs are characteristic

Acromegalic soft-tissue changes may coexist

Acromegaly reflects excess after epiphyseal closure

- Linear growth is no longer possible once growth plates close
- Skin, soft tissues, viscera, and selected bones enlarge
- Facial coarsening and jaw protrusion are useful clinical clues
- The syndrome may evolve slowly and be recognized late

Acral and craniofacial findings provide diagnostic clues

Mechanism / finding	Clinical implication
• Hands and feet enlarge, with thickened digits • Mandibular growth causes prognathism and broadens the lower face	• Soft-tissue overgrowth changes facial and extremity contours • Slow progression can conceal the underlying hormone excess

GH excess has systemic consequences

Impaired glucose tolerance and diabetes may develop

Hypertension, cardiac failure, and skeletal-joint disease may occur

Muscle weakness and gonadal dysfunction are additional manifestations

Clinical burden extends beyond changes in facial appearance

Biochemistry confirms suspected acromegaly

Raised serum IGF-1 documents the sustained GH effect



Failure to suppress GH after oral glucose supports excess secretion



The relevant pituitary lesion must then be correlated with anatomy



Symptoms alone are insufficient to establish the biochemical disorder

Corticotroph tumors create an ACTH-excess phenotype

ACTH stimulates the adrenal cortex to produce glucocorticoids



Pituitary ACTH excess is specifically termed Cushing disease



Cushing syndrome has additional pituitary-independent causes



The pituitary origin cannot be assumed from hypercortisolism alone

Cushing disease is a subtype of Cushing syndrome

Mechanism / finding	Clinical implication
• Cushing syndrome describes the clinical state of glucocorticoid excess • Cushing disease specifies a pituitary corticotroph source of ACTH	• The distinction is etiologic rather than semantic • Pituitary-directed conclusions require demonstration of the source

Nelson syndrome combines tumor growth and pigmentation

After bilateral adrenalectomy, glucocorticoid negative feedback is lost



A corticotroph tumor may subsequently expand and cause mass effects



Skin hyperpigmentation can accompany increased POMC-derived peptides



Absence of adrenal glands prevents endogenous hypercortisolism

Thyrotroph tumors are a rare source of hyperthyroidism

An uncommon TSH-producing PitNET drives the thyroid gland



The hyperthyroid clinical phenotype results from excess thyroid stimulation



Pituitary etiology differs from primary thyroid hyperfunction



Interpretation requires considering the entire feedback axis

Gonadotroph tumors often present without excess symptoms

Mechanism / finding	Clinical implication
• Most secrete hormone amounts that do not cause a recognizable syndrome • They are commonly identified through visual or headache symptoms	• Deficiency of gonadal function may accompany normal-gland compression • Immunophenotype and clinical functionality must be distinguished

The endocrine phenotype localizes the dominant axis

Prolactin excess

Menstrual, fertility, lactation, and sexual disturbances

GH/IGF-1 excess

Somatic overgrowth plus metabolic effects

ACTH excess

A pituitary cause of hypercortisolism

TSH excess

Thyroid hormone—excess manifestations

Hypopituitarism is failure of pituitary hormonal output

- Loss may involve a single anterior pituitary hormone or several
- Both pituitary and hypothalamic lesions can cause insufficient secretion
- The clinical phenotype depends on which trophic outputs fail
- A normal-sized or small lesion does not exclude clinically important loss

Hypopituitarism often reflects destructive pathology

Sellar masses can compress or replace functional parenchyma

Trauma and subarachnoid hemorrhage can impair secretion

Surgery, radiation, ischemia, and inflammation may damage gland

Recognition depends on connecting deficits to a plausible lesion or event

A mass can produce hypopituitarism by compression

Enlarging lesions exert pressure on adjacent normal anterior lobe



Reduced functioning tissue lowers one or more hormone outputs



Tumor tissue itself need not hypersecrete hormones



An expanding silent PitNET can cause both deficiency and headache

Traumatic and vascular injury are important etiologies

- Traumatic brain injury can impair hypothalamic or pituitary function
- Subarachnoid hemorrhage is another recognized cause
- Patterns of hormone loss may not coincide with obvious external injury
- The history of neurologic injury should enter endocrine assessment

Pituitary treatment can damage the normal gland

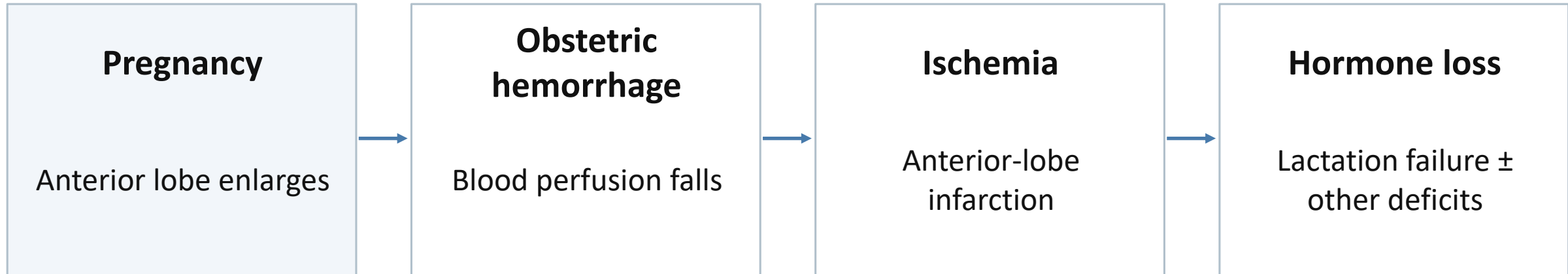
Surgery may remove some nonneoplastic pituitary parenchyma

Radiation can injure normal hormone-producing tissue

Deficiencies may coexist with treatment of a previously functional tumor

Clinical interpretation requires knowing the treatment history

Sheehan syndrome is postpartum ischemic necrosis



Posterior lobe is usually spared because of its direct arterial blood supply.

Postpartum lactation failure can signal pituitary damage

Prolactin deficiency can impair milk production after delivery



A history of obstetric hemorrhage supports ischemic pituitary injury



Other anterior hormone deficiencies may accompany lactation failure



The key link is postpartum ischemia followed by loss of pituitary output

An empty sella can have different mechanisms

Mechanism / finding	Clinical implication
• Primary empty sella follows herniation of meninges and CSF through a diaphragmatic defect • Compression and flattening of the gland may impair function	• Secondary empty sella follows loss or removal of an earlier sellar mass • Imaging appearance alone does not establish the endocrine state

Rathke cleft cysts can compromise pituitary function

A cyst can accumulate fluid and expand within the sellar region



Expansion displaces normal hormone-producing parenchyma



The mechanism of dysfunction is mass compression rather than secretion



Cystic pathology belongs in the differential of a sellar mass

Hypothalamic disease may mimic primary pituitary failure

- Reduced releasing factors can decrease anterior pituitary secretion
- Lesions can also compromise ADH production or delivery
- Tumors, radiation injury, inflammatory disorders, and infections are causes
- Mixed anterior and posterior deficits suggest broader axis involvement

Inflammatory and immune injury may reduce hormone output

Sarcoidosis and tuberculous meningitis may affect the hypothalamus

Immune checkpoint therapy can precipitate autoimmune pituitary injury

The clinical consequences reflect the hormonal deficits produced

Pathologic mechanism may be inflammatory rather than neoplastic

Inherited lineage defects can produce combined deficiency

Developmental transcription factors establish anterior pituitary cell types



POU1F1/PIT-1 defects may impair GH, prolactin, and TSH output



A combination of deficits can indicate shared developmental lineage



These causes are rare compared with acquired destructive disorders

Growth hormone deficiency changes with age

Mechanism / finding	Clinical implication
• In children, impaired GH output causes growth failure and short stature • In adults, reduced lean body mass and increased fat mass may occur	• Clinical consequences reflect the normal age-dependent role of GH • Isolated height is not the appropriate adult screening clue

Gonadotropin deficiency affects reproductive function

Mechanism / finding	Clinical implication
• Reduced LH and FSH compromise gonadal stimulation • In women, menstrual disruption, amenorrhea, and infertility may follow	• In men, reduced libido, impotence, and androgen-dependent hair loss may occur • The phenotype reflects downstream sex-steroid deficiency

TSH deficiency causes a central thyroid deficit

Pituitary failure reduces trophic stimulation of the thyroid



Insufficient thyroid output causes hypothyroid manifestations



The relevant abnormality lies upstream of an otherwise responsive gland



Interpret the thyroid phenotype in its pituitary context

ACTH deficiency can cause adrenal insufficiency

Loss of corticotropin reduces adrenal cortical stimulation



Adrenal insufficiency may contribute to hypotension and systemic illness



Acute loss during pituitary apoplexy can cause circulatory collapse



This deficit makes abrupt pituitary failure especially dangerous

Prolactin deficiency is distinctive after childbirth

Mechanism / finding

- Prolactin supports mammary milk production
- Pituitary lactotroph failure may lead to postpartum lactation failure

Clinical implication

- Its absence is a deficiency phenotype, unlike galactorrhea in excess
- Clinical relevance depends on pregnancy and postpartum context

Multiple hormone losses create a compound syndrome

Compression, infarction, or inflammation can affect several lineages

Symptoms may combine gonadal, thyroid, adrenal, and growth-related deficits

The dominant complaint need not reveal every missing hormone

Evaluation of an injured pituitary cannot focus on a single axis

The sellar location links mass size to symptoms

An enlarging lesion may extend superiorly toward the optic chiasm



Compression can disturb vision before other neurological findings occur



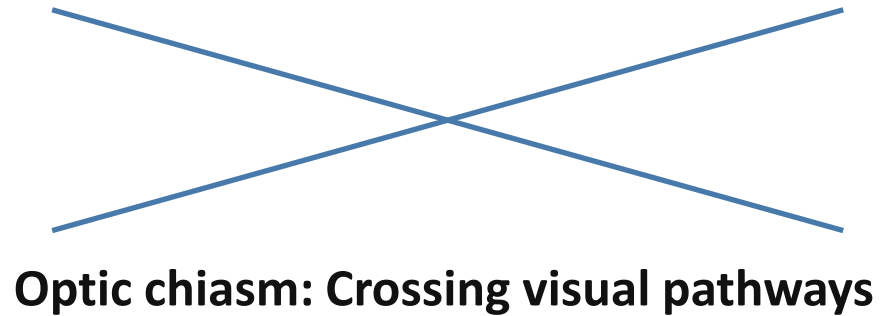
Further expansion may produce headache and additional neurologic signs



Hormone secretion and local mass effects are separate dimensions

Optic chiasm compression causes temporal visual loss

Bitemporal hemianopsia: Outer visual-field loss



Sellar mass ↑

Bitemporal hemianopsia is a localizing clinical pattern

Mechanism / finding	Clinical implication
• Patients lose the outer visual fields in both eyes • The defect arises from disruption of crossing chiasmal fibers	• A suprasellar component of a sellar lesion should be considered • The precise field pattern depends on anatomical involvement

Expanding pituitary masses can cause headache

Like other intracranial masses, they may increase intracranial pressure

Headache can accompany nausea and vomiting

These symptoms are less anatomically specific than chiasmal field loss

Clinical severity may reflect compression rather than endocrine function

Some sellar tumors cause diplopia

Mechanism / finding	Clinical implication
• Neurologic symptoms can include double vision from ocular motor involvement • This can accompany an expanding lesion or hemorrhagic complication	• Diplopia is distinct from bitemporal visual field loss • Its appearance demands assessment for acute or progressive local effects

Pituitary apoplexy is acute hemorrhagic expansion

Hemorrhage may occur in a pre-existing pituitary tumor



Sudden enlargement causes abrupt worsening of local compression



Normal pituitary tissue may lose function rapidly



It can be a life-threatening neurosurgical emergency

Apoplexy combines neurologic and endocrine danger

Sudden severe headache and diplopia may accompany acute enlargement

Acute loss of ACTH may cause adrenal insufficiency and hypotension

Severe presentations include altered consciousness and cardiovascular collapse

The syndrome should not be interpreted as headache alone

Silent PitNETs may declare themselves late

A hormonally silent lesion lacks an early conspicuous endocrine signature



Continued growth may produce visual symptoms or headache



Compression of adjacent anterior lobe causes hormone deficiencies



A single lesion can therefore present with mass effect and hypopituitarism

Endocrine signs and mass effects may coexist

A functioning tumor can secrete hormone while also enlarging

A nonfunctioning tumor can compress the pituitary and chiasm

Apoplexy can convert a chronic mass into acute hormone failure

The clinical assessment must integrate all three presentations

Posterior-pituitary disorders center on ADH

ADH is synthesized in hypothalamic neurons



The posterior lobe stores and releases transported ADH



ADH restricts urinary free-water loss during dehydration



Too little or too much activity disrupts water and sodium balance

Physiologic ADH release responds to body fluids

High plasma osmolality stimulates ADH secretion



Low circulating pressure or volume also favors ADH release



Increased atrial distention inhibits ADH release



The normal response conserves water when needed

Central diabetes insipidus reflects AVP deficiency

ADH deficiency is also termed arginine vasopressin deficiency (AVP-D)



The kidney cannot conserve water appropriately when ADH signal is lacking



High volumes of dilute urine are produced



The major clinical risks arise from ongoing free-water loss

AVP deficiency produces thirst and polyuria

- Urine output is increased and urine is relatively dilute
- Free-water loss provokes thirst and compensatory polydipsia
- Serum sodium and osmolality may rise if losses are not replaced
- Access to water strongly modifies clinical severity

Restricted water access raises dehydration risk

Mechanism / finding

- Alert patients can often replace losses by drinking water
- Obtunded or bedridden patients may not access adequate water

Clinical implication

- Unreplaced free-water loss can cause dangerous dehydration
- The same physiological defect may have different clinical severity

Central and nephrogenic diabetes insipidus differ

Mechanism / finding	Clinical implication
• Central diabetes insipidus = insufficient AVP production or release • Nephrogenic diabetes insipidus = renal resistance to circulating AVP	• Both produce large volumes of dilute urine and thirst • The primary defect is different despite a shared clinical presentation

SIADH is excess water retention from ADH

Inappropriate ADH activity increases renal free-water reabsorption



Retained water dilutes serum sodium concentration



Neurologic manifestations relate to hyponatremia and cerebral edema



Peripheral edema is generally absent despite increased body water

SIADH often originates outside the pituitary

Ectopic ADH from malignant tumors is a major cause

Small-cell lung carcinoma is a classic neoplastic example

Drugs and CNS disorders can also provoke ADH excess

An ADH phenotype does not automatically localize disease to the sella

The neurologic phenotype of SIADH reflects hyponatremia

Water retention lowers plasma sodium concentration



Reduced extracellular tonicity promotes cerebral water accumulation



Neurologic dysfunction may arise from cerebral edema



The clinical risk differs fundamentally from water-loss disorders

AVP deficiency and SIADH are opposite water states

Arginine vasopressin deficiency

Insufficient ADH signal



Reduced renal water reabsorption



Large volumes of dilute urine



Thirst; Hypernatremia if water lost

Inappropriate ADH secretion

Excess ADH activity



Excess renal free-water retention



Dilutional hyponatremia



Cerebral edema; Neurologic signs

Case: Amenorrhea and galactorrhea

A reproductive-age patient develops menstrual cessation and galactorrhea

- The phenotype directs attention to prolactin excess
- A lactotroph PitNET is one possibility, not the only cause
- Exclude physiological, medication, stalk, thyroid, and renal explanations

Case: Progressive enlargement of hands and jaw

An adult reports larger shoe size and progressive prognathism

- The phenotype suggests acquired GH/IGF-1 excess
- A raised IGF-1 and failure of GH suppression support acromegaly
- A somatotroph PitNET is an important pituitary cause

Case: Postpartum hemorrhage and failed lactation

After severe obstetric bleeding, milk production is absent

- Postpartum ischemic necrosis of the anterior pituitary is a concern
- Other trophic hormone deficits may accompany prolactin loss
- The chronology distinguishes this from hyperprolactinemic galactorrhea

Case: Headache with bilateral temporal field loss

Visual field testing reveals reduced temporal fields in both eyes

- The pattern localizes to the optic chiasm
- An expanding sellar mass may also impair anterior pituitary secretion
- Neurologic localization and endocrine characterization are both necessary

Case: Sudden headache, diplopia, hypotension

Abrupt deterioration can reflect hemorrhage into a pituitary lesion

- Acute compression explains headache and ocular symptoms
- ACTH loss may produce adrenal insufficiency and hypotension
- The constellation warrants recognition as pituitary apoplexy

A concise clinical classification

Endocrine hyperfunction: Symptoms of the overproduced hormone

Endocrine hypofunction: Impaired target-organ or reproductive function

Local mass effects: Visual, headache, cranial nerve, or acute apoplexy signs

Posterior disorders: Changes in urine concentration and sodium balance

Integrate localization with physiology

A bitemporal field defect implicates chiasmal compression

A postpartum deficit suggests vascular anterior-pituitary injury

Polyuria with thirst suggests AVP deficiency or resistance

Hyponatremic neurologic dysfunction suggests excess ADH activity

Essential diagnostic distinctions

Mechanism / finding	Clinical implication
• Hyperprolactinemia ≠ necessarily a prolactin-secreting PitNET • Cushing disease ≠ all forms of Cushing syndrome	• Clinically nonfunctioning ≠ negative for lineage-marker expression • Central diabetes insipidus ≠ renal vasopressin resistance

Clinicopathologic conclusions

- Hormone excess and loss are mechanistically different but may coexist
- Anatomic compression explains the characteristic optic-chiasm phenotype
- Acute hemorrhage can rapidly combine neurologic and endocrine failure
- ADH dysregulation produces opposite fluid-balance syndromes

Principal reference and source boundaries

Robbins, Cotran & Kumar: Pathologic Basis of Disease

11th edition (2026), Chapter 24 — The Endocrine System

Primary heading: Clinical Manifestations of Pituitary Disease, p. 972

Supporting context: pituitary anatomy and related syndromes, pp. 971–978

Illustrations in this lecture are original editable explanatory schematics.