

Hypopituitarism

Mechanisms, structural lesions, hormone deficits and clinicopathologic interpretation

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Learning objectives

- Localize hypopituitarism to pituitary or hypothalamic dysfunction.
- Explain how common destructive and vascular injuries reduce hormone secretion.
- Match missing pituitary hormones with organ-specific consequences.
- Distinguish posterior pituitary water-balance syndromes.

Definition: Deficient pituitary hormone secretion

- Hypopituitarism denotes reduced secretion of one or more pituitary hormones.
- The initiating lesion can involve the anterior pituitary itself or hypothalamic regulation.
- Clinical manifestations depend on which hormone axes are affected.

Deficient secretion is a functional diagnosis; The structural cause may differ.

Site of origin determines the mechanism

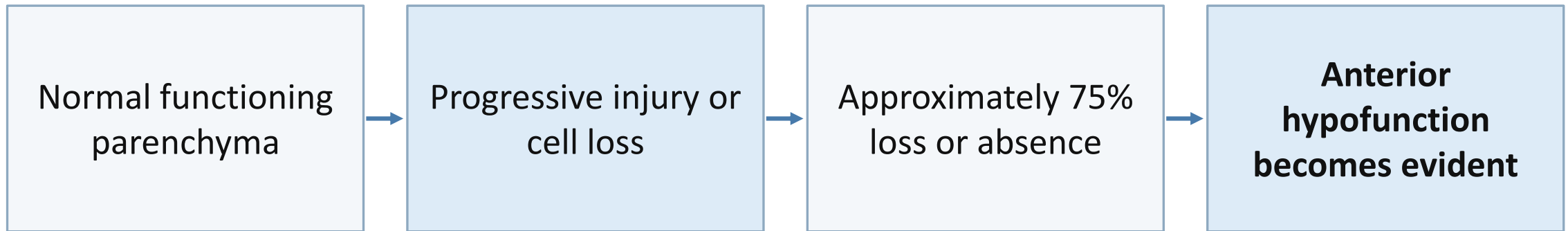
Pituitary disease

- Loss or damage of functional secretory parenchyma
- Direct impairment of trophic hormone production
- Often follows local destruction or compression

Hypothalamic disease

- Loss of releasing-factor stimulation
- May disturb posterior-pituitary vasopressin pathways
- Pituitary tissue may initially be structurally intact

Functional reserve of the anterior pituitary



The ~75% figure is a textbook approximation, not a patient-specific testing threshold.

Anterior and posterior pituitary are different organs

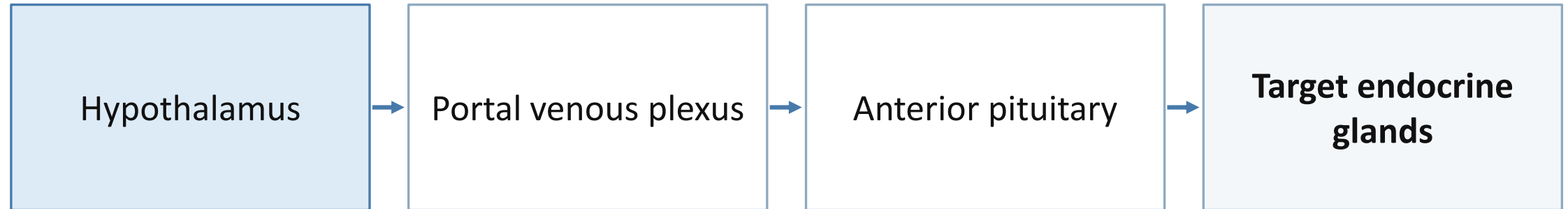
Adenohypophysis

- Epithelial glandular component
- Produces trophic hormones for endocrine targets
- Receives hypothalamic factors via portal vasculature

Neurohypophysis

- Neural extension of hypothalamus
- Stores and releases hypothalamus-synthesized ADH and oxytocin
- Different vulnerability to vascular injury

Hypothalamic–pituitary regulation



Releasing and inhibitory factors regulate secretion from anterior pituitary cells.

Anterior pituitary secretory cell populations

Cell population	Hormonal products
Somatotroph	GH
Mammosomatotroph	GH + prolactin
Lactotroph	Prolactin
Corticotroph	ACTH / corticotropin
Thyrotroph	TSH
Gonadotroph	FSH + LH

Trophic and direct-acting hormone consequences

Peripheral gland axes

- ACTH → adrenal cortex
- TSH → thyroid gland

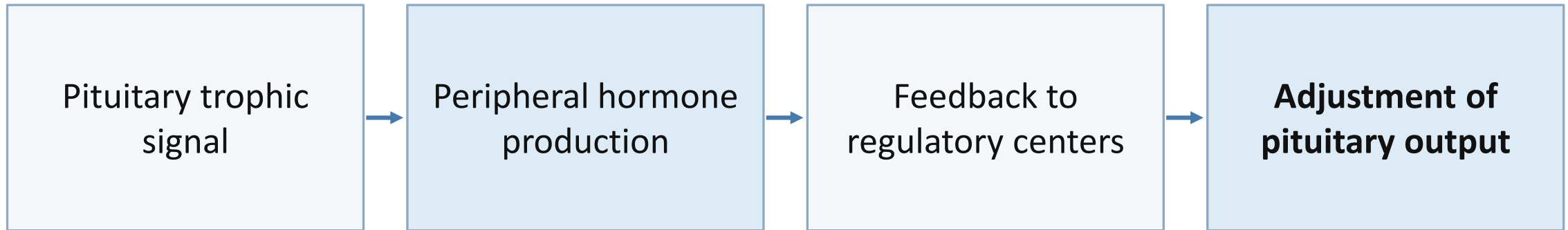
Gonadal axis

- FSH/LH → gonadal function
- Reproduction and sex steroids

Direct tissue effects

- GH → growth / body composition
- Prolactin → lactation

Negative feedback maintains endocrine balance



Assessment of gland failure requires considering the target-gland response, not only pituitary secretion.

Mechanisms that produce hypopituitarism

Local destruction

- Mass lesion or infarction
- Surgery or irradiation

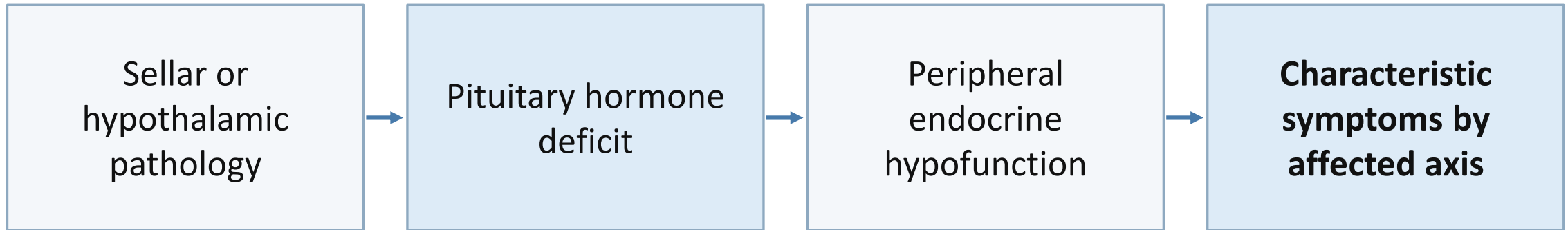
Upstream signaling loss

- Hypothalamic lesion
- Releasing-factor deficiency

Cell-intrinsic deficiency

- Congenital transcription-factor defect
- Selective hormone loss

One lesion can create several clinical syndromes

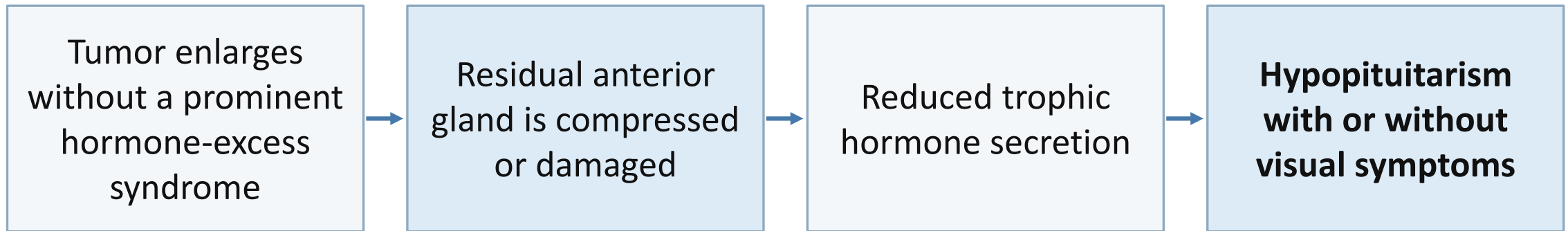


Different deficits may coexist in the same patient.

Sellar masses: Pressure damages normal cells

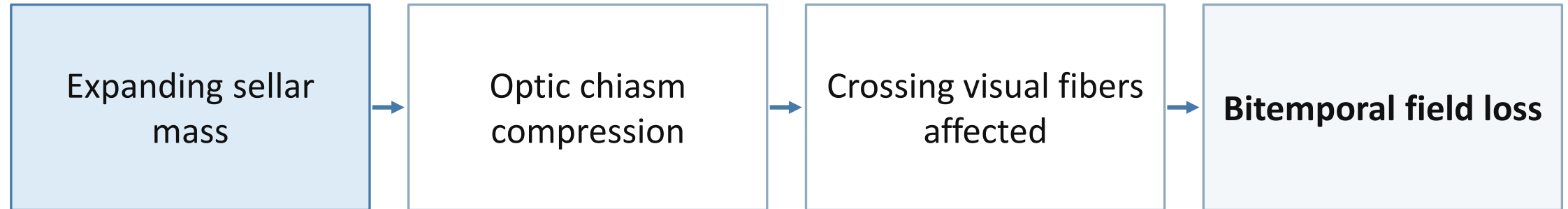
- Pituitary neuroendocrine tumors (PitNETs) may compress residual normal tissue.
- Other sellar neoplasms, malignancies and cysts may cause hypopituitarism.
- The endocrine outcome depends on the extent and location of injury.

Nonfunctioning PitNET: Endocrine silence is not benign



A nonfunctioning tumor can cause marked functional deficiency by mass effect.

Why sellar lesions disturb vision



Classical bitemporal hemianopsia results from chiasmal compression; It is not specific to hypopituitarism.

Two consequences of the same expanding sellar lesion

Hormonal effect

- Loss of pituitary secretory capacity
- Endocrine manifestations vary by lost hormones

Anatomic effect

- Compression of nearby optic structures
- Headache; Visual field impairment;
Possible elevated intracranial pressure

Traumatic brain injury and pituitary dysfunction

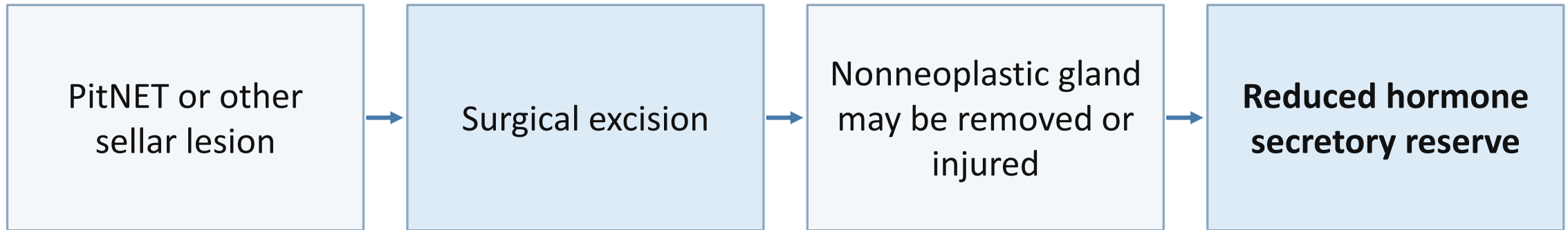
- Traumatic brain injury is a recognized important cause of pituitary hypofunction.
- Structural trauma may affect the pituitary–hypothalamic system.
- Consider endocrine insufficiency in the relevant clinical context.

History of central nervous system injury can be etiologically informative.

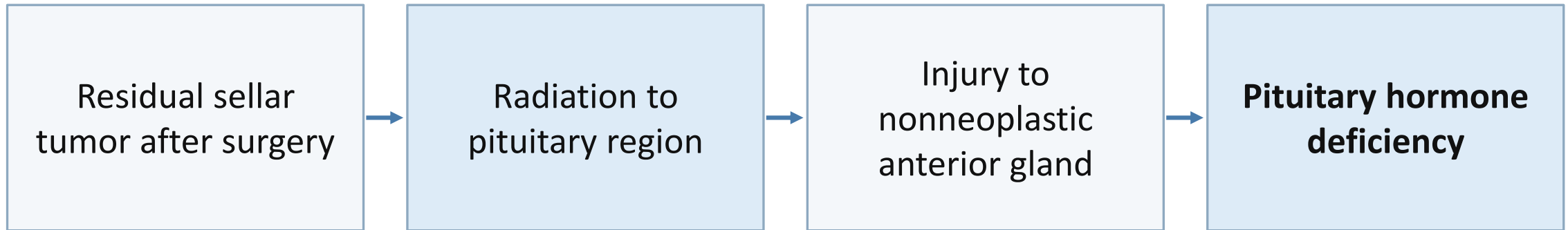
Subarachnoid hemorrhage is another major setting

- Subarachnoid hemorrhage is listed among common causes of pituitary hypofunction.
- The associated intracranial event may precede recognition of endocrine deficiency.
- An endocrine phenotype can therefore follow a nonendocrine neurologic presentation.

Pituitary surgery: Iatrogenic gland loss



Pituitary irradiation: Delayed gland damage



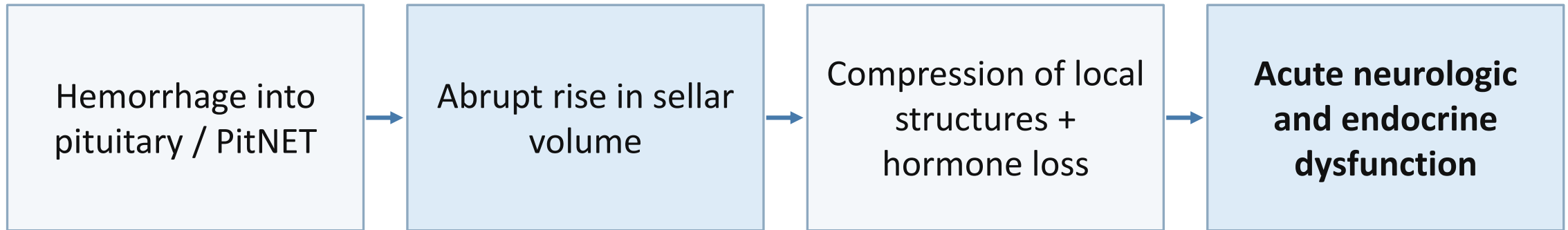
Antitumor treatment can itself contribute to later endocrine hypofunction.

Apoplexy: Abrupt hemorrhage into the pituitary

- Pituitary apoplexy is sudden hemorrhage into the gland, often within a PitNET.
- An acutely enlarged hemorrhagic lesion produces local mass effect.
- Rapid endocrine deterioration may occur simultaneously.

Pituitary apoplexy can be life-threatening.

Apoplexy: How a hemorrhage produces deterioration



Apoplexy: Three immediately relevant manifestations

Head pain

- Sudden severe headache
- Rapid sellar expansion

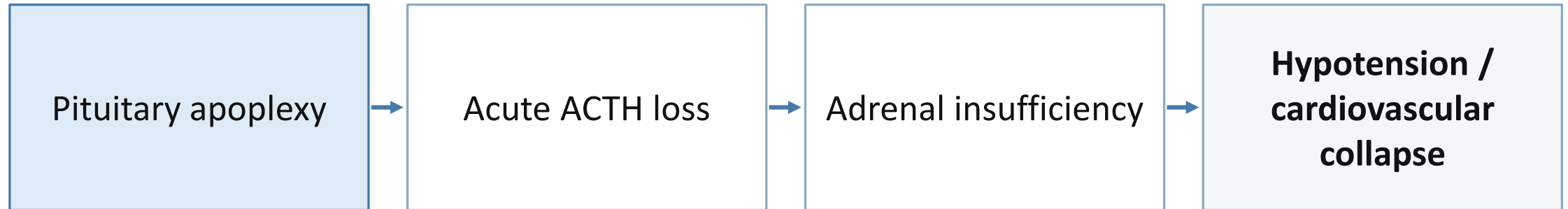
Cranial nerves

- Diplopia
- Oculomotor-nerve effects

Endocrine collapse

- Acute ACTH deficiency
- Hypotension / adrenal insufficiency

Why corticotropin loss threatens circulation



Loss of ACTH removes trophic support for adrenal glucocorticoid production.

Apoplexy is a neurosurgical emergency

- The hemorrhagic mass effect and acute endocrine failure can coexist.
- Severe cases may cause loss of consciousness or sudden death.
- Recognize the combination of sudden severe headache, diplopia and hypotension.

Urgent clinical assessment is indicated; This is not an isolated chronic endocrine disorder.

Acute apoplexy and slowly progressive mass effect

Apoplexy

- Abrupt hemorrhage and sellar enlargement
- Sudden headache; Possible diplopia
- Rapid hormone loss and hemodynamic compromise

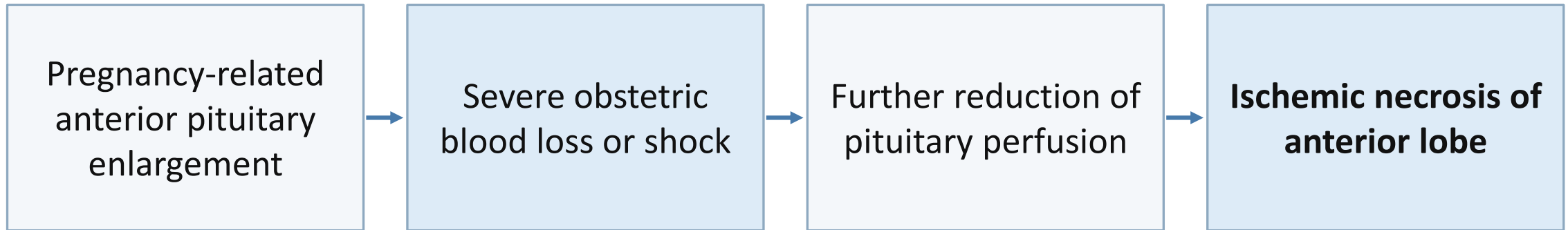
Progressive expansion

- Gradual compression of normal parenchyma
- Endocrine deficits and/or progressive visual effects
- May present without an acute collapse

Pregnancy enlarges the anterior pituitary

- During pregnancy the anterior lobe enlarges to almost twice its usual size.
- This physiologic enlargement is not matched by increased supply from the low-pressure vascular system.
- The enlarged gland is relatively vulnerable to impaired perfusion.

Sheehan syndrome: Mechanism of postpartum necrosis



Sheehan syndrome denotes postpartum ischemic necrosis of the pituitary.

Sheehan syndrome: Anterior selectivity

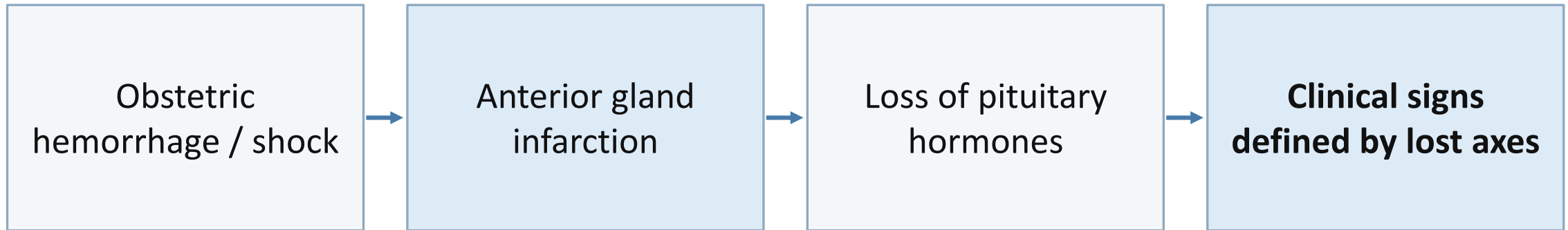
Anterior lobe

- Expands markedly in pregnancy
- Vulnerable to perfusion reduction
- Ischemic necrosis may cause hormone failure

Posterior lobe

- Receives direct arterial branches
- Usually less susceptible to ischemia
- Often remains unaffected in Sheehan syndrome

Postpartum hemorrhage to endocrine dysfunction



Failure of postpartum lactation is one potential clue to prolactin deficiency.

Other settings associated with pituitary necrosis

Coagulopathy

- Disseminated intravascular coagulation
- Impaired tissue perfusion

Vascular / hematologic

- Sickle cell anemia
- Shock of another origin

Intracranial / traumatic

- Elevated intracranial pressure
- Traumatic injury

Two vascular modes of gland injury

Ischemic necrosis

- Perfusion failure, classically postpartum hemorrhage
- Loss of viable anterior gland
- Deficits can persist after acute shock

Hemorrhagic apoplexy

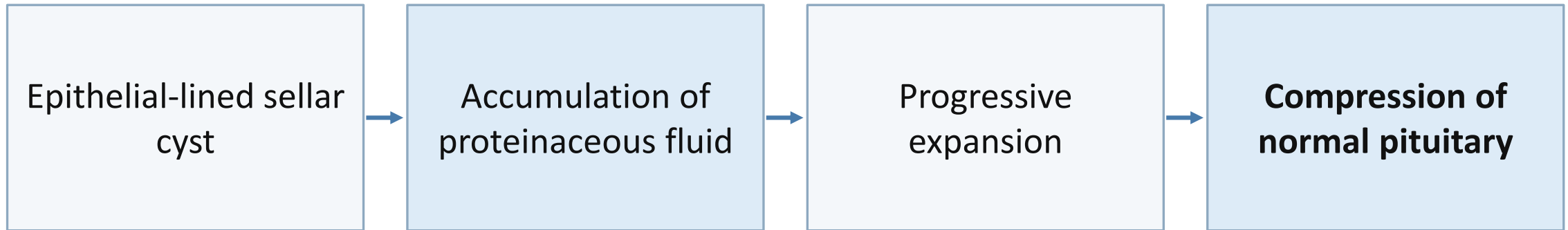
- Acute hemorrhage within pituitary, often PitNET
- Abrupt mass effect + pituitary injury
- Immediate neurologic and endocrine manifestations

Rathke cleft cyst: Pathology of a sellar cyst

- Rathke cleft cysts are lined by ciliated cuboidal epithelium.
- Occasional goblet cells and anterior pituitary cells may be present.
- Accumulating proteinaceous fluid allows cyst enlargement.

These are source-described morphologic features, not a clinical image.

Rathke cleft cyst: Functional consequence

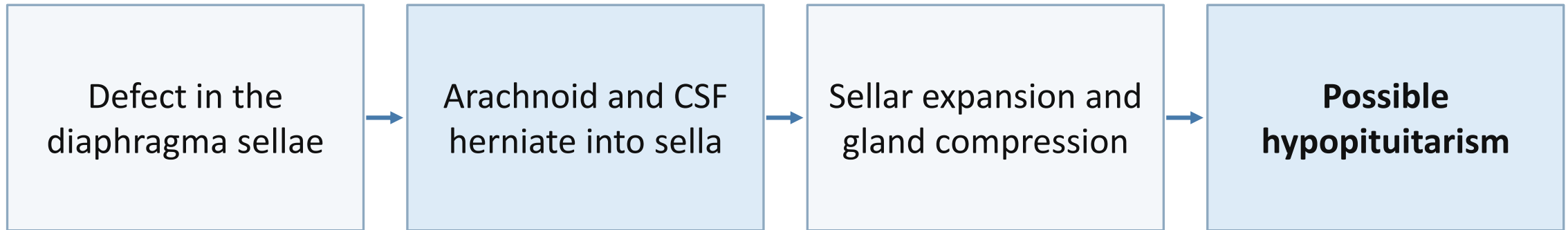


Functional compromise arises from loss of space for the normal gland.

Empty sella: The shared anatomic endpoint

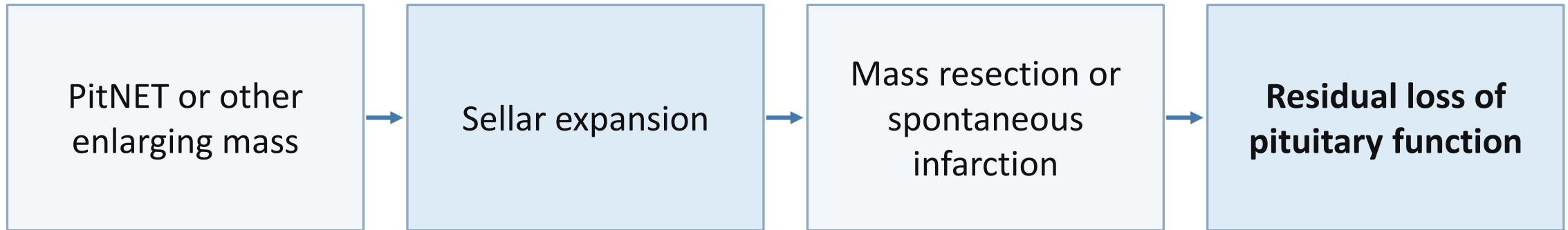
- The sella contains less functioning pituitary parenchyma or a compressed gland.
- It can follow destruction, ablation, infarction or displacement.
- An empty-sella appearance does not invariably signify hypopituitarism.

Primary empty sella: Cerebrospinal fluid entry



Hormone deficiency develops only if functioning tissue is sufficiently compromised.

Secondary empty sella: Loss after a preceding mass



Primary versus secondary empty sella

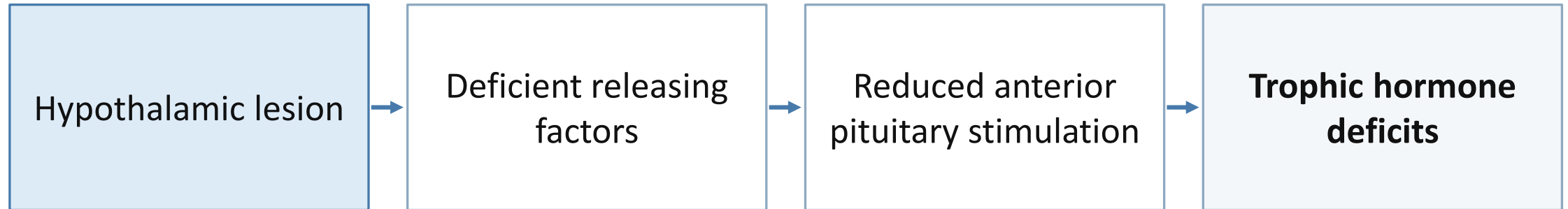
Primary empty sella

- Diaphragma sellae defect
- Arachnoid and CSF herniation
- Compressive change may reduce gland function

Secondary empty sella

- Preexisting mass or pituitary-directed intervention
- After tumor removal or infarction
- Functional tissue may be lost

Hypothalamic lesions can suppress anterior function



Localization upstream of the pituitary changes the mechanistic interpretation.

Hypothalamic tumors can cause pituitary hypofunction

- Both benign and malignant hypothalamic tumors may disrupt pituitary regulation.
- Many malignant lesions are metastases, including from breast and lung primaries.
- The endocrine result can involve more than one pituitary system.

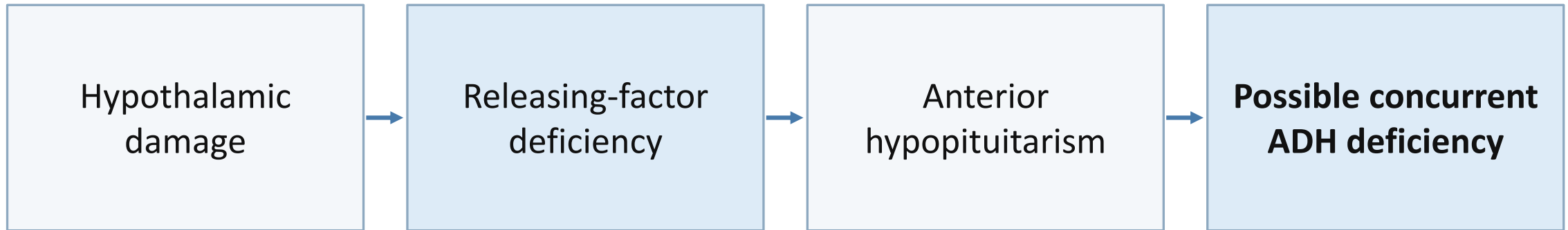
Cranial irradiation can impair hypothalamic control

- Brain irradiation may be followed by hypothalamic insufficiency.
- Releasing-factor loss can reduce anterior pituitary output.
- A treatment history can help localize a subsequent deficiency.

Inflammation and infection: An anatomic bridge

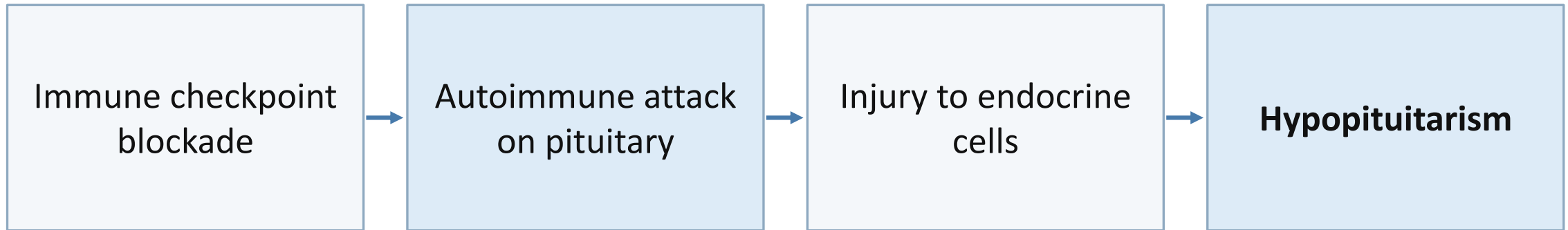
Granulomatous disease	Infection	Possible phenotype
• Sarcoidosis • Hypothalamic involvement	• Tuberculous meningitis • Hypothalamic involvement	• Anterior hormone deficiencies • Concurrent diabetes insipidus

Hypothalamic injury can affect two pathways



Combined anterior deficits and water-balance symptoms suggest broader hypothalamic involvement.

Cancer immunotherapy: Immune-mediated pituitary injury

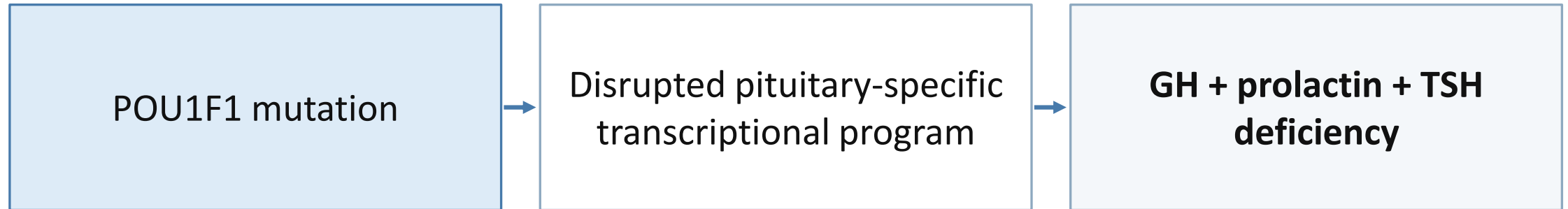


The primary tumor and its immunotherapy are distinct potential contributors to endocrine illness.

Genetic defects: Deficient pituitary development or function

- Congenital loss of transcription-factor function is a rare cause.
- The affected transcription factor helps determine which hormone-producing cell lines are deficient.
- A genetic mechanism can produce combined, rather than isolated, hormone deficits.

POU1F1 (PIT1): A characteristic combined deficit



This combination is explicitly; Do not generalize it to every congenital form.

Etiology classification by initiating injury

Mechanistic family	Examples
Compressive	PitNET, other sellar tumors, expanding cyst
Vascular	Apoplexy; Sheehan syndrome; shock-related necrosis
Traumatic	Traumatic brain injury; subarachnoid hemorrhage
Iatrogenic	Surgery; pituitary or brain irradiation
Hypothalamic / inflammatory	Tumor, metastasis, sarcoidosis, TB meningitis
Immune / congenital	Checkpoint therapy; transcription-factor defect

Clinical expression follows the missing hormone

- Patients with similar sellar pathology can have different endocrine presentations.
- Failure of several anterior pituitary cell types produces combined deficits.
- Look for a coherent pattern across growth, reproduction, thyroid, adrenal function and lactation.

Growth hormone loss varies by life stage

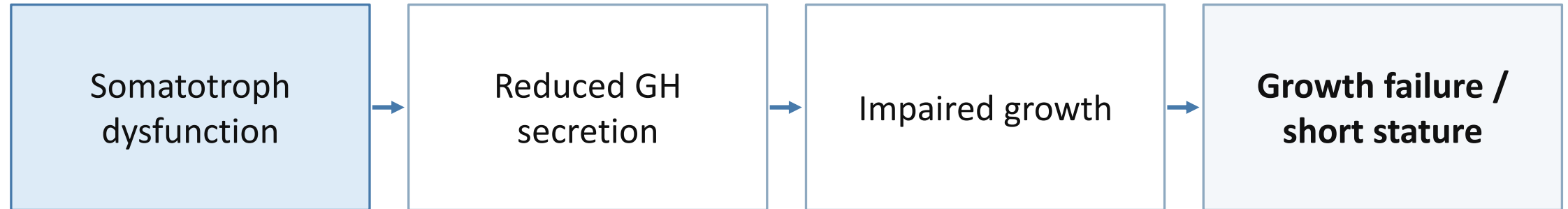
Children

- Growth failure
- Short stature
- Impaired somatic growth is the cardinal expression

Adults

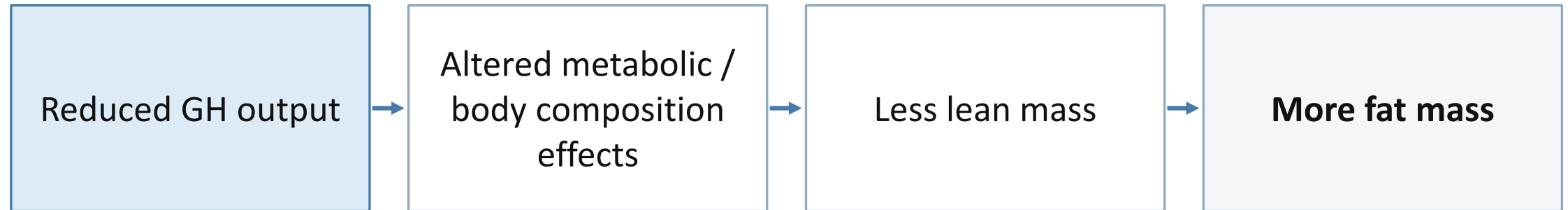
- Lower lean body mass
- Increased fat mass
- Manifestations differ from childhood growth failure

Growth-hormone deficit in childhood



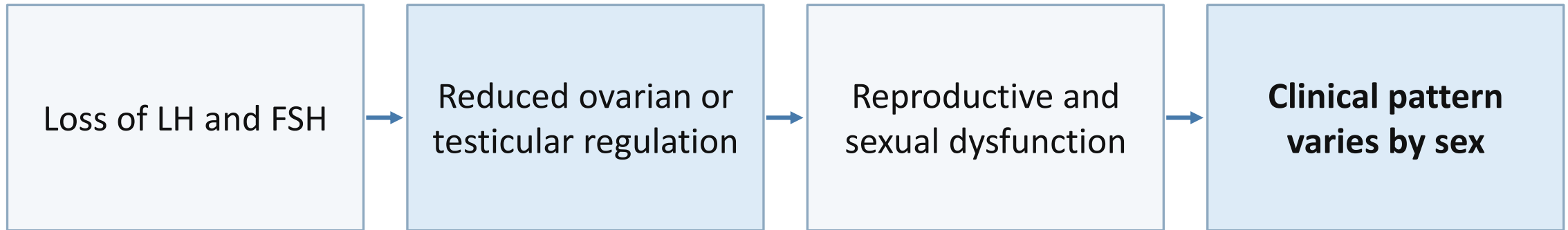
The growing skeleton makes linear-growth impairment prominent in children.

Adult GH deficiency: Changed body composition



Body-composition changes rather than short stature in adults.

Gonadotropin loss: The reproductive axis



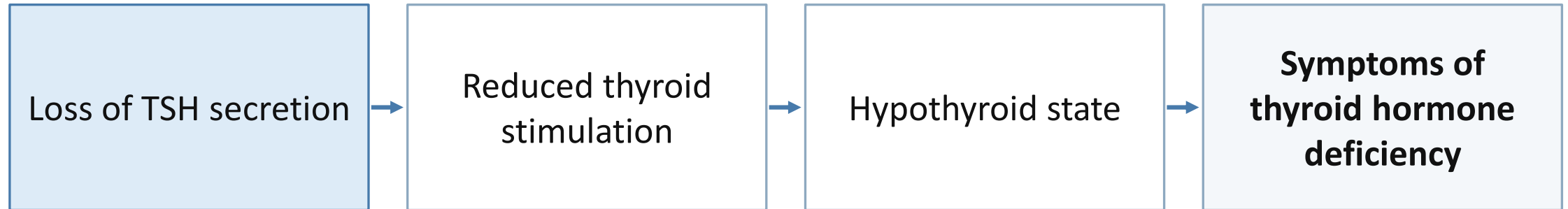
Gonadotropin deficiency in females

- FSH and LH regulate ovarian follicular maturation and ovulation.
- Deficiency is associated with amenorrhea and infertility.
- Interpret the symptom pattern as a failure of pituitary gonadal support.

Gonadotropin deficiency in males

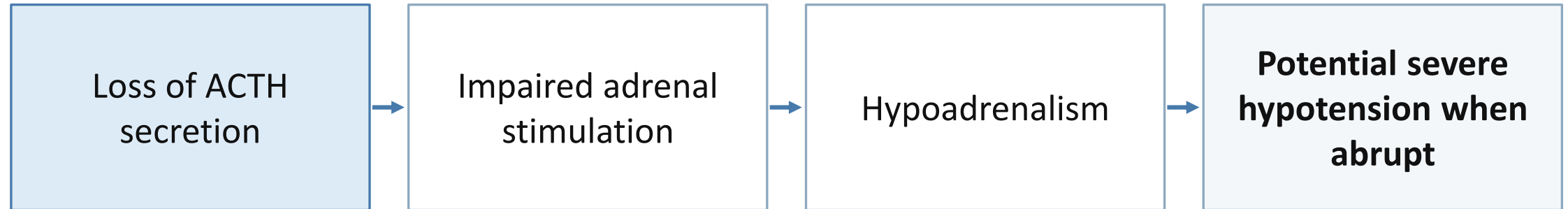
- Deficient gonadotropins impair normal testicular function.
- Reduced libido and impotence may occur.
- Loss of pubic and axillary hair is another recognized manifestation.

Thyrotropin deficiency: An upstream thyroid problem



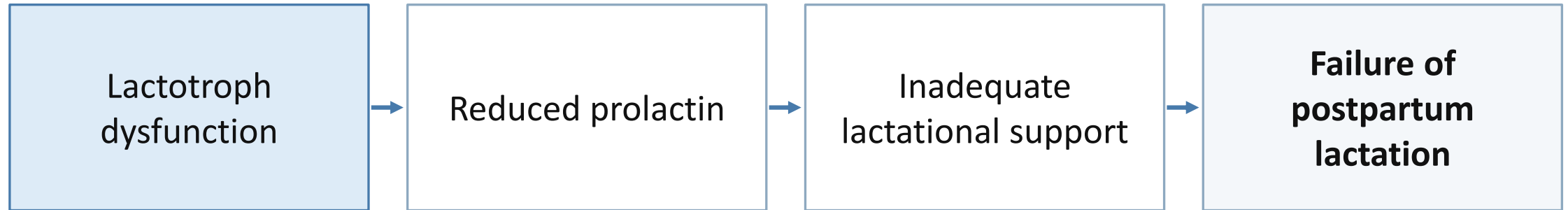
The initiating defect is pituitary rather than a primary thyroid gland lesion.

Corticotropin deficiency: An upstream adrenal problem



The acute apoplexy setting highlights the clinical importance of corticotropin deficiency.

Prolactin deficiency: Postpartum lactation failure



This is particularly relevant when assessing postpartum pituitary injury.

Match missing hormone with main clinical clue

Pituitary hormone	Characteristic manifestation
GH in children	Growth failure, short stature
GH in adults	Reduced lean mass, increased fat mass
LH / FSH in females	Amenorrhea, infertility
LH / FSH in males	Sexual dysfunction, loss of body hair
TSH	Hypothyroid manifestations
ACTH	Hypoadrenalism; acute hypotension possible
Prolactin	Failure of postpartum lactation

Hormone failure and mass effect are distinct axes

Endocrine deficiency

- Growth, reproductive, thyroid or adrenal consequences
- Deficit may be selective or combined

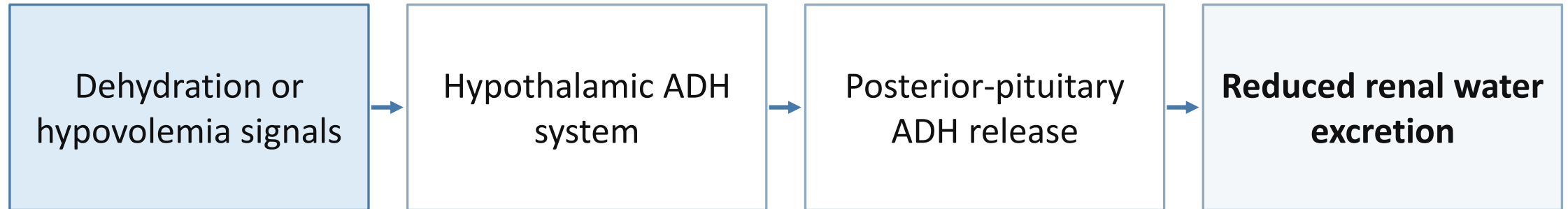
Local structural effects

- Headache or visual disturbances from sellar expansion
- Acute hemorrhage can cause cranial-nerve symptoms

Posterior pituitary: Scope of water-balance disease

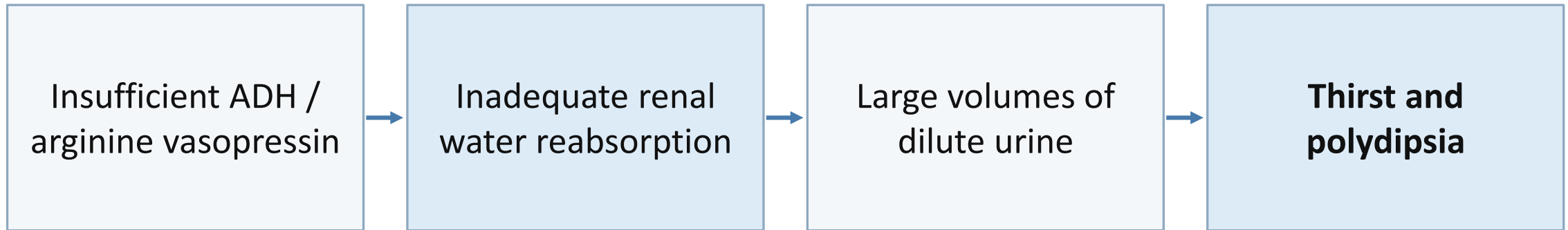
- The neurohypophysis releases ADH (arginine vasopressin) and oxytocin.
- Clinically important posterior syndromes center on too little or too much ADH.
- These disorders should be distinguished from deficits of anterior trophic hormones.

Normal vasopressin conserves free water



ADH secretion rises with osmotic or pressure-related stimuli.

AVP deficiency: Central diabetes insipidus



The terminology “arginine vasopressin deficiency” (AVP-D).

Central AVP deficiency versus renal resistance

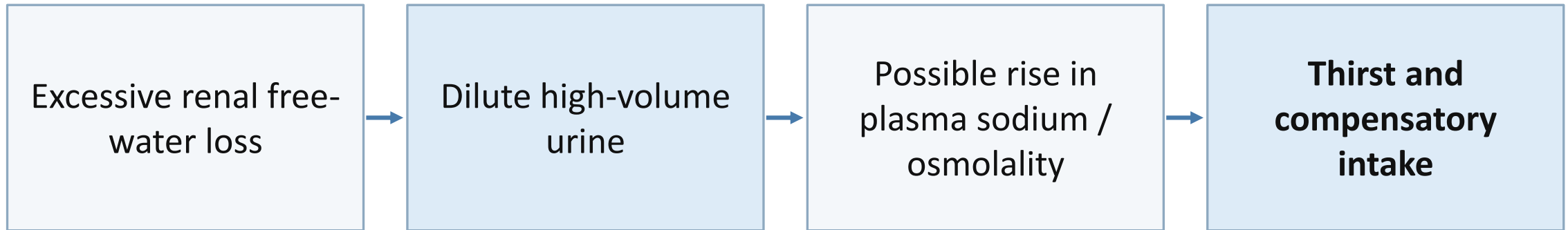
Central AVP deficiency

- Impaired vasopressin supply or release
- Hypothalamic–pituitary origin
- Formerly central diabetes insipidus

AVP resistance

- Kidney tubules fail to respond to circulating ADH
- Renal target-tissue origin
- Formerly nephrogenic diabetes insipidus

Polyuria causes water depletion

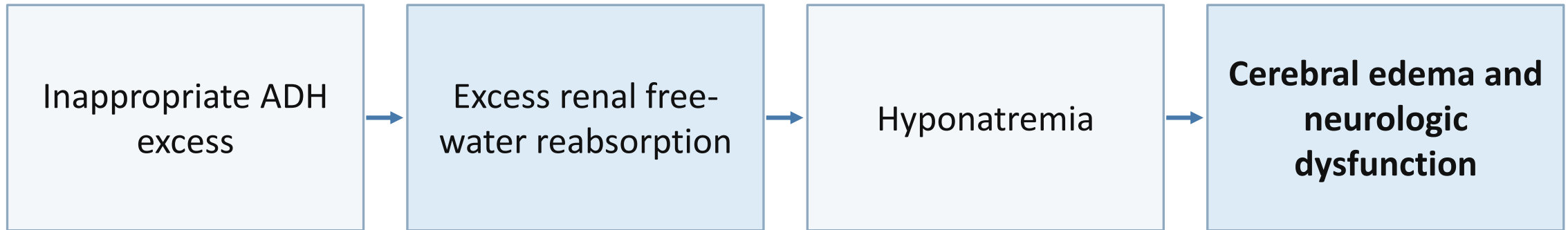


Patients with access to drinking water can often compensate for urinary losses.

Who is vulnerable to severe dehydration?

- An alert patient with free access to water often compensates by drinking.
- An obtunded or bedridden patient may be unable to replace the water lost.
- Restricted access to fluids can turn AVP deficiency into life-threatening dehydration.

SIADH: The opposite water-balance disturbance



Common cause groups of SIADH

Ectopic production

- Malignant neoplasms
- Particularly small-cell lung carcinoma

Medication effects

- Drugs that increase ADH secretion

CNS disease

- Central nervous system infection
- Trauma

Vasopressin deficiency versus SIADH

ADH deficiency (AVP-D)

- Impaired water retention
- Large volume of dilute urine
- Possible high sodium / osmolality

ADH excess (SIADH)

- Excess free-water retention
- Hyponatremia
- Neurologic dysfunction from cerebral edema

SIADH: Fluid retention without typical edema

- Total body water is increased as free water is retained.
- Circulating blood volume often remains near normal.
- Peripheral edema generally does not develop despite hyponatremia.

Etiologic clues can help localize the lesion

Sellar lesion

- Visual-field changes
- Mass effect + hormonal loss

Postpartum ischemia

- Obstetric hemorrhage
- Lactation failure

Hypothalamic involvement

- Anterior hormonal loss
- Possible AVP deficiency

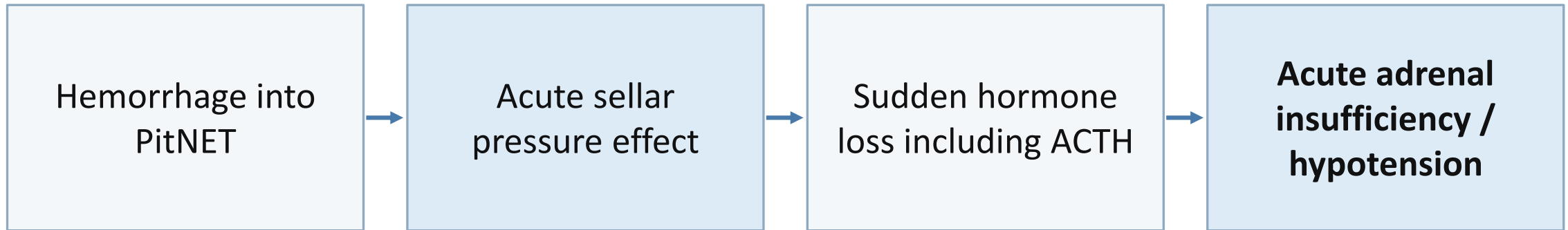
Case 1: Sudden deterioration in a sellar tumor

A patient with a known pituitary mass develops an abrupt severe headache, double vision and hypotension.

Reasoning questions

- What event explains both the neurologic and endocrine changes?
- Which deficient anterior hormone best explains hypotension?

Case 1 resolution: Apoplexy with ACTH loss



This presentation requires emergency assessment, not elective endocrine follow-up.

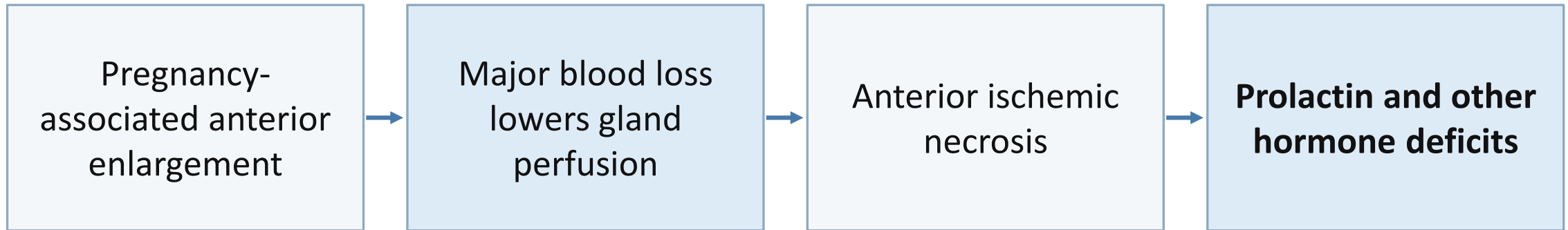
Case 2: Postpartum endocrine failure

Following major obstetric hemorrhage and shock, a patient cannot establish lactation and subsequently has manifestations of pituitary hormone deficiency.

Reasoning questions

- What specific vascular pathology is suggested?
- Why is the anterior lobe preferentially involved?

Case 2 resolution: Sheehan syndrome



The posterior lobe is relatively protected by its direct arterial supply.

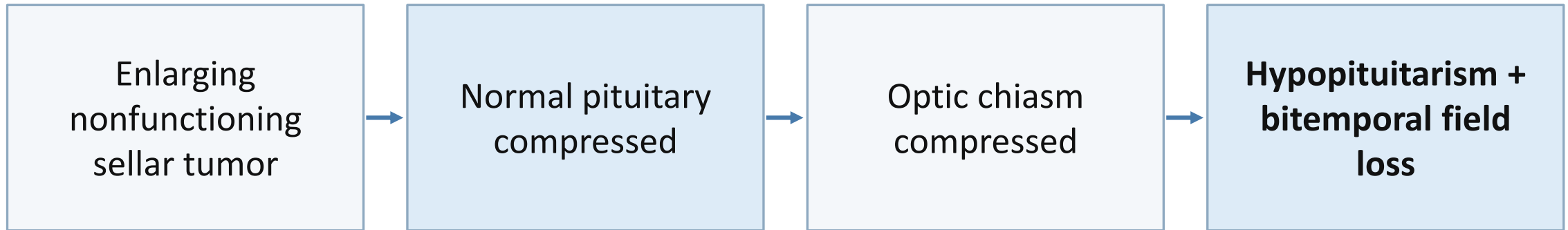
Case 3: Growing sellar lesion

A sellar mass enlarges without a clear hypersecretion syndrome. The patient develops bilateral temporal visual-field loss and endocrine insufficiency.

Reasoning questions

- How can a nonfunctioning lesion produce severe illness?
- What nearby neural structure explains the field defect?

Case 3 resolution: Two forms of mass effect



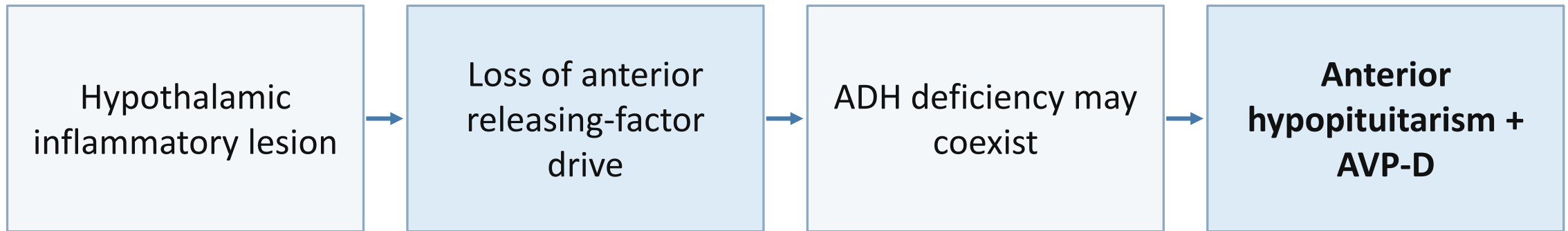
Case 4: Mixed endocrine and water-balance symptoms

A patient with a hypothalamic inflammatory disorder has anterior endocrine deficiencies, polyuria and intense thirst.

Reasoning questions

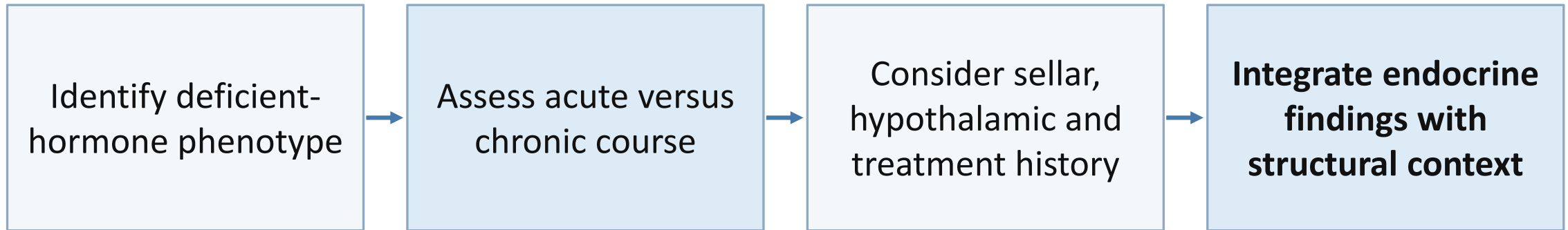
- Which two physiologic systems may be affected?
- What does the combined presentation suggest about localization?

Case 4 resolution: Hypothalamic combined injury



Sarcoidosis and tuberculous meningitis are two Robbins examples.

Clinical reasoning: From phenotype to cause



This is a source-based reasoning framework, not a prescriptive diagnostic protocol.

Two diagnostic pitfalls

Assuming mass effects imply hypersecretion

- Nonfunctional PitNETs may instead compress normal gland
- Visual abnormalities and hormone deficiency can coexist

Assuming all polyuria is anterior failure

- ADH deficiency is a posterior / hypothalamic system problem
- Separate AVP-D from anterior tropic-hormone deficiency

Mechanism-to-presentation synthesis

Mechanism	Characteristic clue	Functional consequence
Sellar compression	Mass effect, visual symptoms	Anterior hormone loss
Pituitary apoplexy	Abrupt headache, diplopia, hypotension	Acute ACTH loss possible
Sheehan syndrome	Postpartum blood loss / shock	Anterior ischemic necrosis
Primary empty sella	CSF herniation into sella	Sometimes gland compression
Hypothalamic inflammation	Anterior deficits $\pm$ polyuria	Releasing factors $\pm$ AVP affected
POU1F1 defect	Congenital combined deficit	GH, PRL and TSH loss

Major clinicopathologic conclusions

- Hypopituitarism is decreased pituitary hormone output from diverse local or upstream causes.
- Apoplexy and postpartum infarction illustrate different mechanisms of acute gland injury.
- Hormone-deficiency manifestations depend on the specific secretory cell populations affected.
- Posterior AVP syndromes are separate water-balance disorders and may coexist with hypothalamic disease.

Principal references

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 24: The Endocrine System. Hypopituitarism, p. 977.
- Adjacent source material: Pituitary gland / clinical manifestations, pp. 971–973; posterior pituitary syndromes, pp. 977–978.
- Topic register: RCK-0777, provided source extraction from robbins.md.