

Hypothalamic Suprasellar Tumors

A clinicopathologic lecture

Anatomy • morphology • molecular pathology • clinical effects

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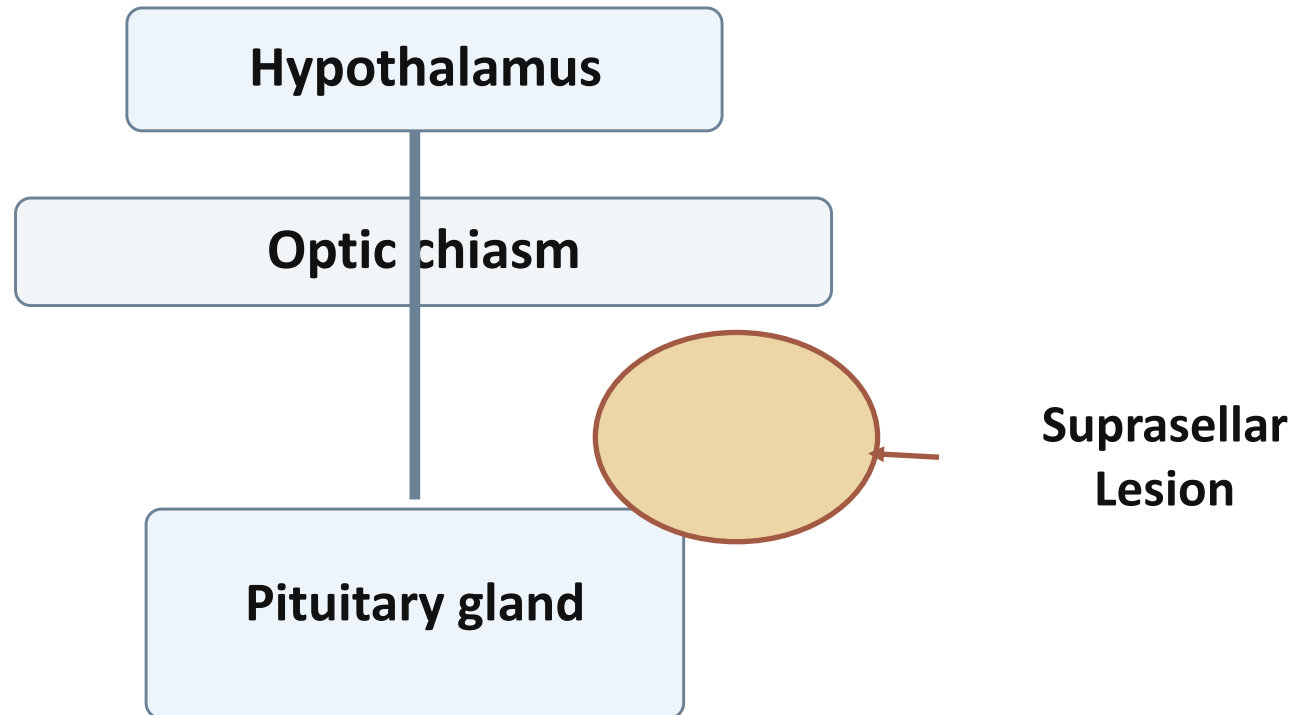
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Learning objectives

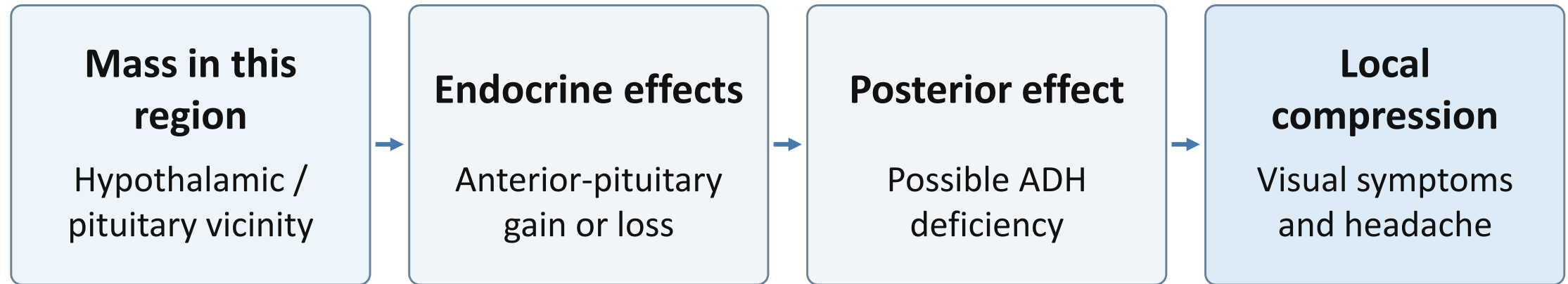
- Localize sellar versus suprasellar effects on the pituitary–hypothalamic axis.
- Distinguish adamantinomatous and papillary craniopharyngioma morphologically.
- Connect CTNNB1/Wnt and BRAF alterations with their respective variants.
- Integrate gross morphology, microscopic findings, and clinical presentation.

The sellar–suprasellar region concentrates vital structures

- Hypothalamus lies immediately above the pituitary axis.
- Optic chiasm and pituitary stalk are vulnerable to nearby expanding lesions.
- A relatively slow-growing lesion can still produce major functional disturbance.



Suprasellar tumors can disturb multiple systems



Two pituitary compartments respond differently

Anterior pituitary

- Hypothalamic factors regulate trophic hormone release.
- Dysfunction can involve GH, ACTH, TSH, gonadotropins, or prolactin.
- Loss can reflect mass-related damage or altered hypothalamic control.

Posterior pituitary

- Hypothalamic axons transport ADH to posterior lobe.
- Impairment can produce central diabetes insipidus.
- Manifestations center on water conservation and diuresis.

Endocrine abnormalities may reflect loss or excess

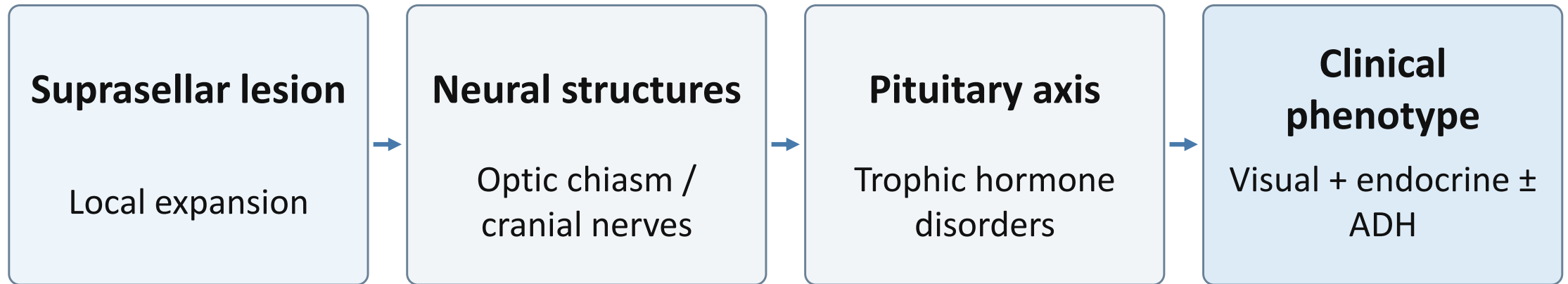
Hypofunction

- Compression or interruption may reduce pituitary output.
- The resulting phenotype depends on affected hormones.
- Children may show growth retardation due to GH deficiency.

Hyperfunction

- The source explicitly allows anterior-pituitary hyperfunction.
- Hyperfunction is not a defining feature of craniopharyngioma.
- Interpret hormone excess separately from mass localization.

Mass effects and endocrine effects must both be evaluated



Optic-pathway proximity explains visual symptoms

- Sellar-region expansion can compress crossing optic fibers.
- Bitemporal visual-field loss is the classic chiasmal compression pattern in the adjacent Robbins section.
- Visual disturbance may accompany headache in craniopharyngioma.
- The specific visual deficit depends on structures affected.

Headache may signal an expanding intracranial mass

- Craniopharyngioma often presents with headache and visual disturbance.
- The lesion may grow toward the third ventricle or base of brain.
- Anatomical location can make a slow-growing lesion clinically consequential.
- Headache is not specific enough to identify tumor histotype.

Two neoplasms dominate the Robbins suprasellar category

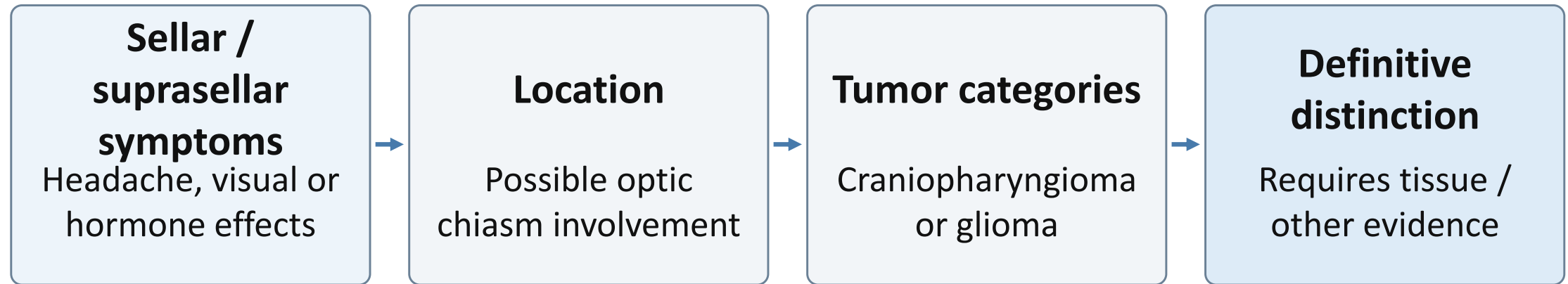
Craniopharyngioma

- Slow-growing epithelial neoplasm arising near the sella.
- Considerable gross and histologic diversity across two variants.
- Main focus of the source section.

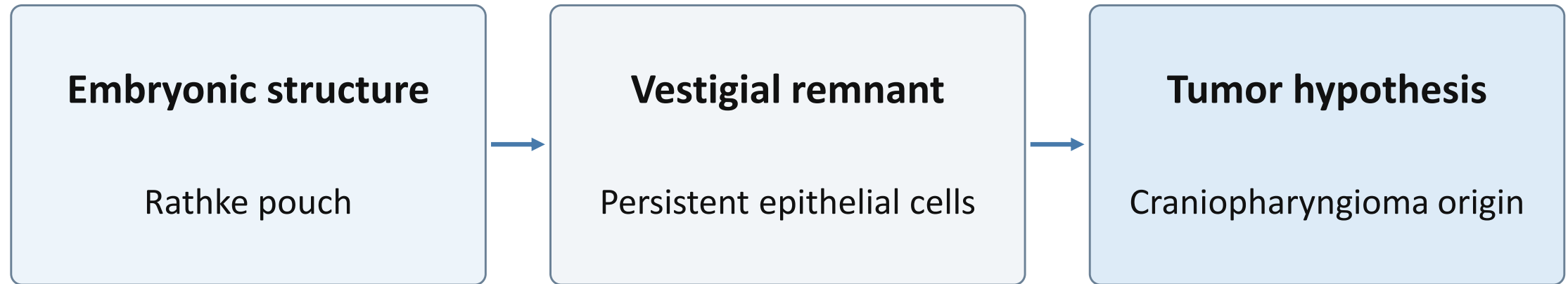
Glioma

- May occur in the hypothalamic / optic pathway region.
- Sometimes arises in the optic chiasm.
- Robbins directs detailed glioma pathology to Chapter 28.

A chiasmal glioma is a localization alternative



Craniopharyngioma is linked to Rathke pouch remnants



Most craniopharyngiomas are suprasellar

Typical localization

- Above the sella turcica.
- Intrasellar extension may be present.
- Relationship to the chiasm shapes symptoms.

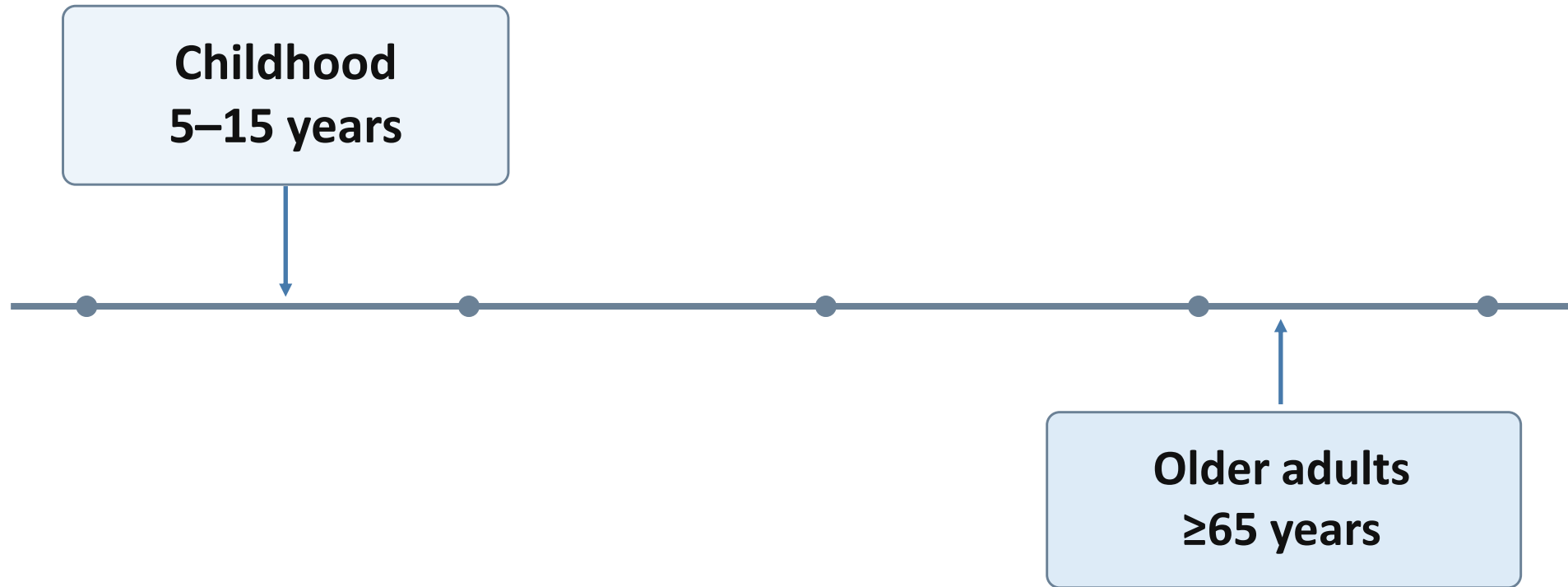
Less common localization

- A small minority occurs wholly within the sella.
- Purely sellar location does not preclude craniopharyngioma.
- Location alone cannot assign histologic subtype.

Craniopharyngioma is an uncommon intracranial neoplasm

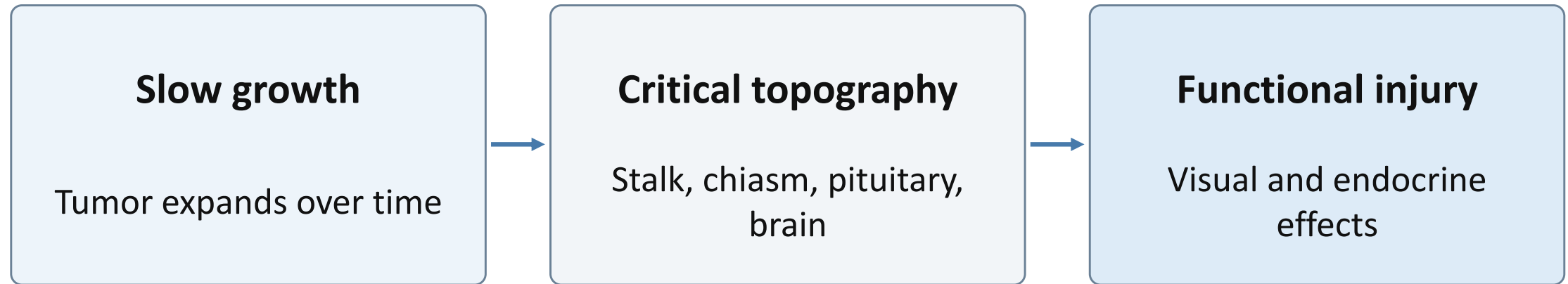
- The textbook attributes approximately 1%–5% of intracranial tumors to craniopharyngioma.
- Its importance is disproportionate to frequency because of the functional anatomy.
- Common presentations arise from mass effect and endocrine disturbance.
- Avoid extrapolating this proportion to other denominators.

The age distribution is bimodal



Age is supportive—not a substitute for morphology.

Slow growth can coexist with destructive local effects



Presentation reflects a combined neurologic–endocrine phenotype

CLINICAL DOMAINS

Use the combined pattern; No isolated feature is a complete diagnosis.

Headache

Intracranial mass effect

Visual symptoms

Optic apparatus compression

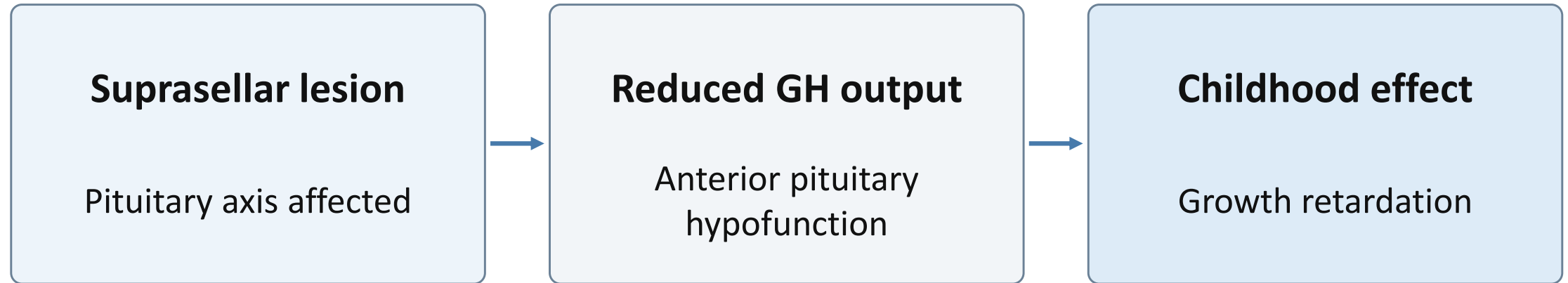
Anterior pituitary

Hypofunction or occasional hyperfunction

Posterior axis

Diabetes insipidus may occur

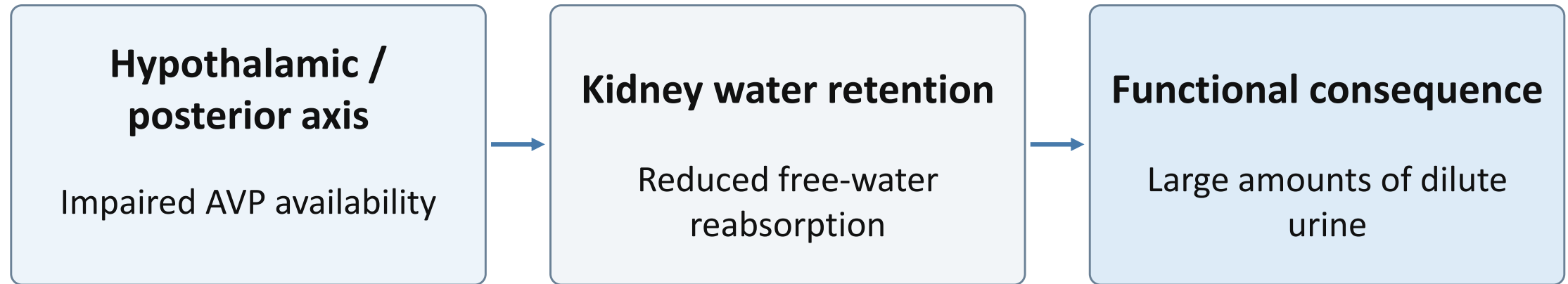
Growth retardation may dominate pediatric presentation



Anterior hormone loss produces axis-specific effects

GH	Growth failure in children
LH / FSH	Reduced gonadal function and fertility
TSH	Secondary hypothyroid manifestations
ACTH	Secondary adrenal insufficiency
Prolactin	Postpartum lactation failure

ADH deficiency results in central diabetes insipidus



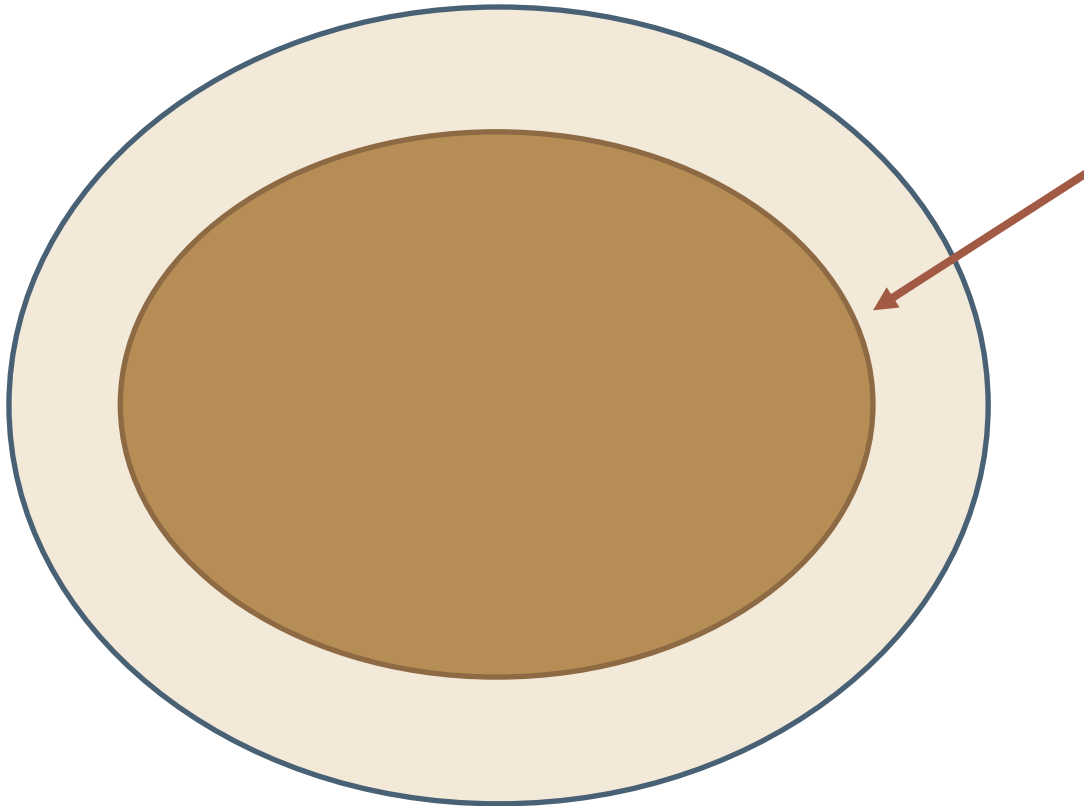
Central diabetes insipidus has a recognizable phenotype

- Arginine vasopressin deficiency (AVP-D) is a contemporary term used.
- Polyuria results from inability to conserve water.
- Thirst and polydipsia commonly compensate for water loss.
- Restricted water access can cause severe dehydration.

Gross size and configuration should be described

- The average craniopharyngioma diameter is approximately 3–4 cm.
- Tumors may be encapsulated and solid.
- Cystic architecture is more common; Multiple locules may be present.
- Gross description should report cystic, solid, and loculated components.

Cystic and multiloculated architecture is characteristic



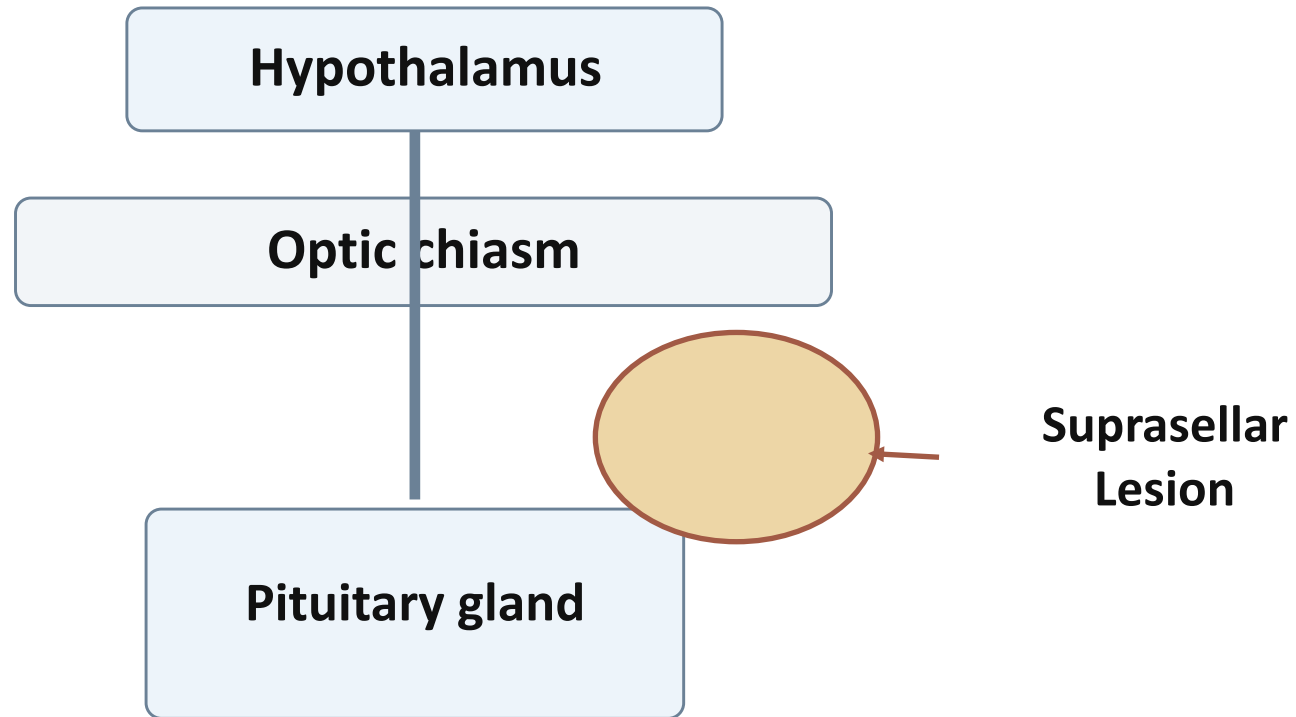
Cystic component

- A complex cystic lesion is compatible with craniopharyngioma.
- The wall and intracystic contents offer distinct diagnostic clues.
- Exact diagnosis requires microscopic correlation.

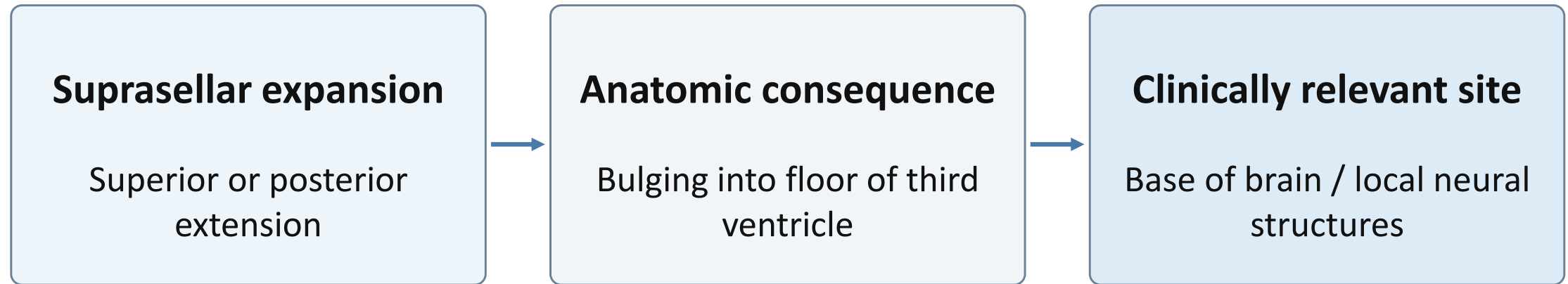
Schematic — cyst outline and fill are illustrative

Encroachment on optic structures explains visual impairment

- Tumor often encroaches on optic chiasm or cranial nerves.
- Local compression explains visual disturbances.
- The same lesion may distort nearby pituitary structures.



Extension toward the third ventricle is important



Two craniopharyngioma variants must be separated

Adamantinomatous

- More often observed in children.
- Frequent calcification, cysts, wet keratin, palisading.
- Recurrent CTNNB1 alterations and Wnt activation.

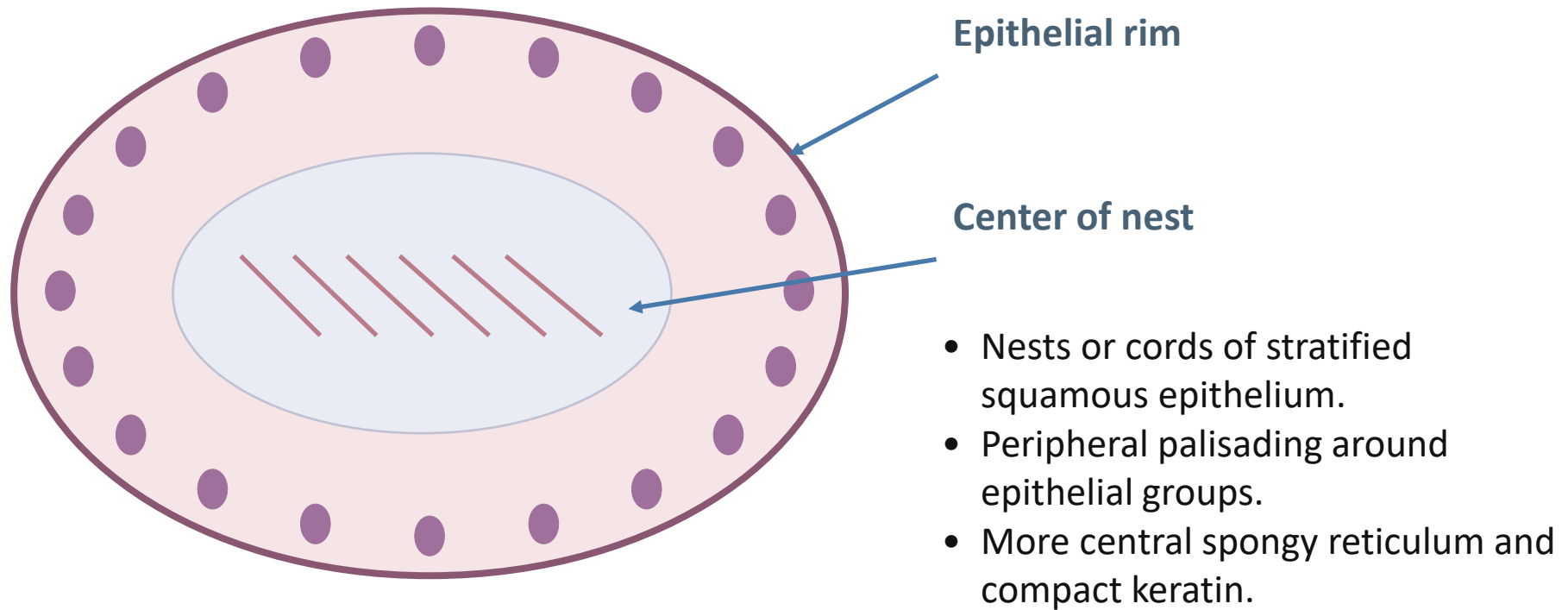
Papillary

- More often observed in adults.
- Squamous-lined papillae and solid sheets.
- Activating BRAF mutations in >90%.

Adamantinomatous type is classically pediatric

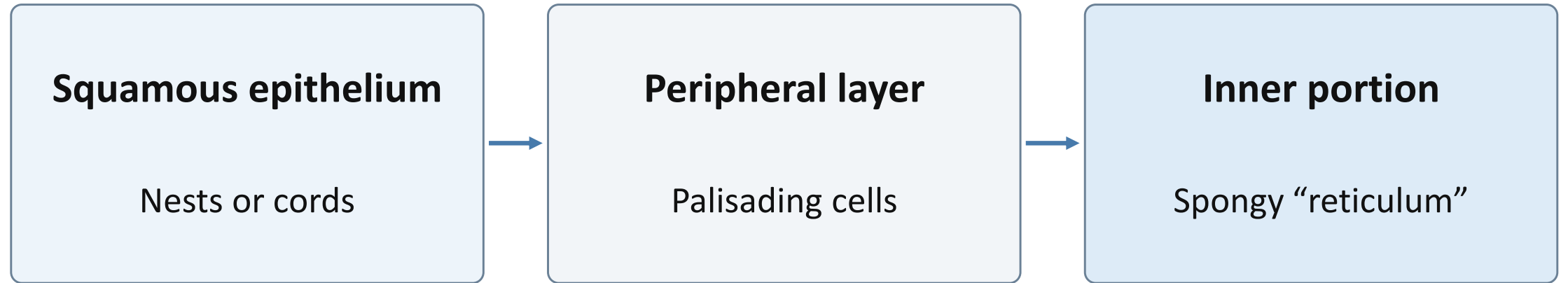
- Most often observed in children, though age alone is not diagnostic.
- Recognizable architecture combines epithelial nests or cords with palisading.
- Cysts, calcifications, and wet keratin reinforce the pattern.
- Molecularly linked to CTNNB1/Wnt pathway activation.

Adamantinomatous architecture is epithelial

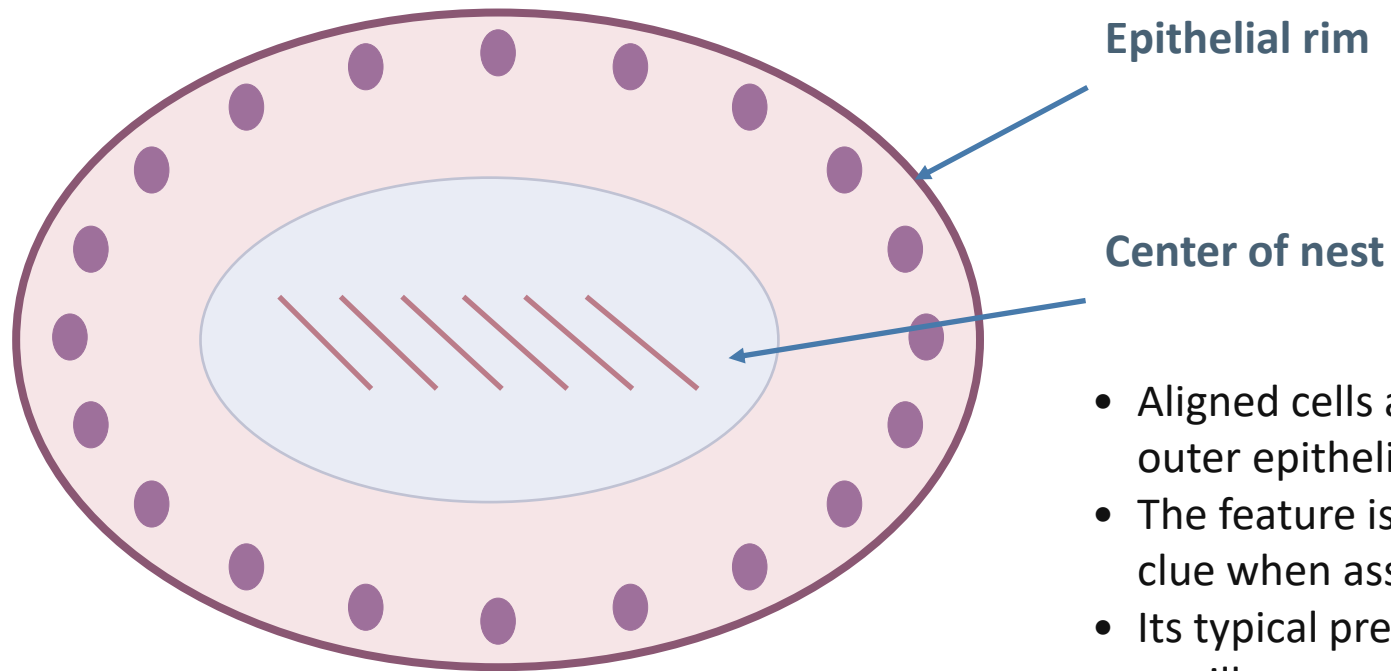


Schematic — not a histologic specimen

Nests and cords are the structural starting point



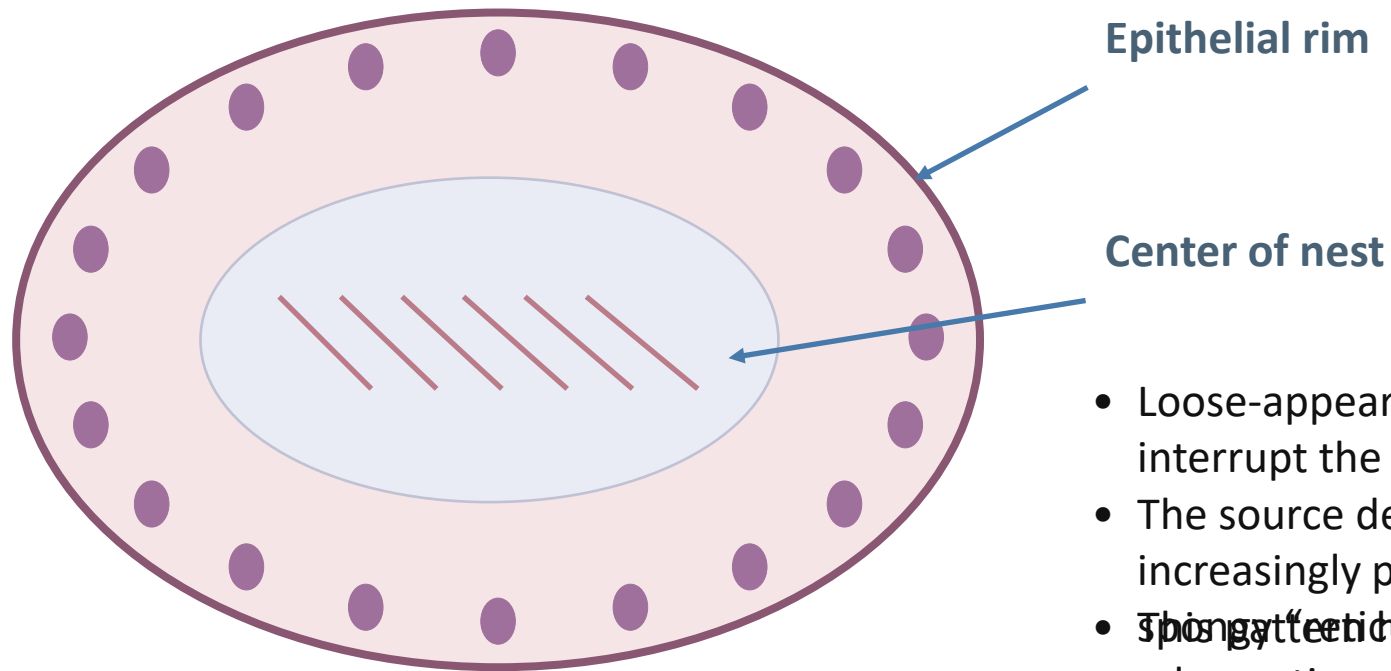
Peripheral palisading localizes to the epithelial rim



- Aligned cells appear along the outer epithelial boundary.
- The feature is a useful architectural clue when assessed with others.
- Its typical presence contrasts with papillary craniopharyngioma.

Schematic — not a histologic specimen

Spongy reticulum is prominent within epithelial nests



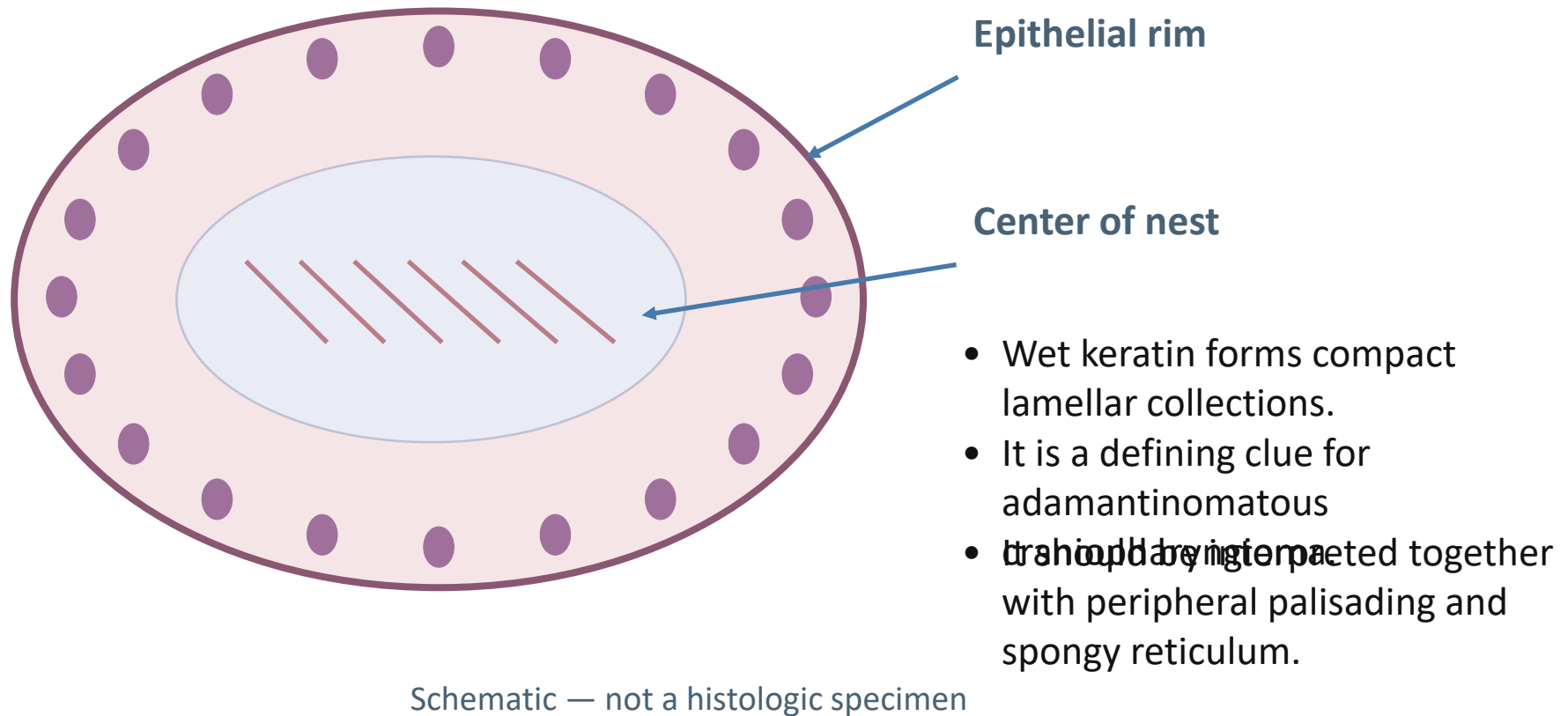
Epithelial rim

Center of nest

- Loose-appearing internal areas interrupt the epithelial cords.
- The source describes an increasingly prominent inner
- Spongy reticulum helps distinguish adamantinomatous from papillary type.

Schematic — not a histologic specimen

Compact lamellar “wet” keratin is diagnostic



Calcification is a frequent adamantinomatous feature

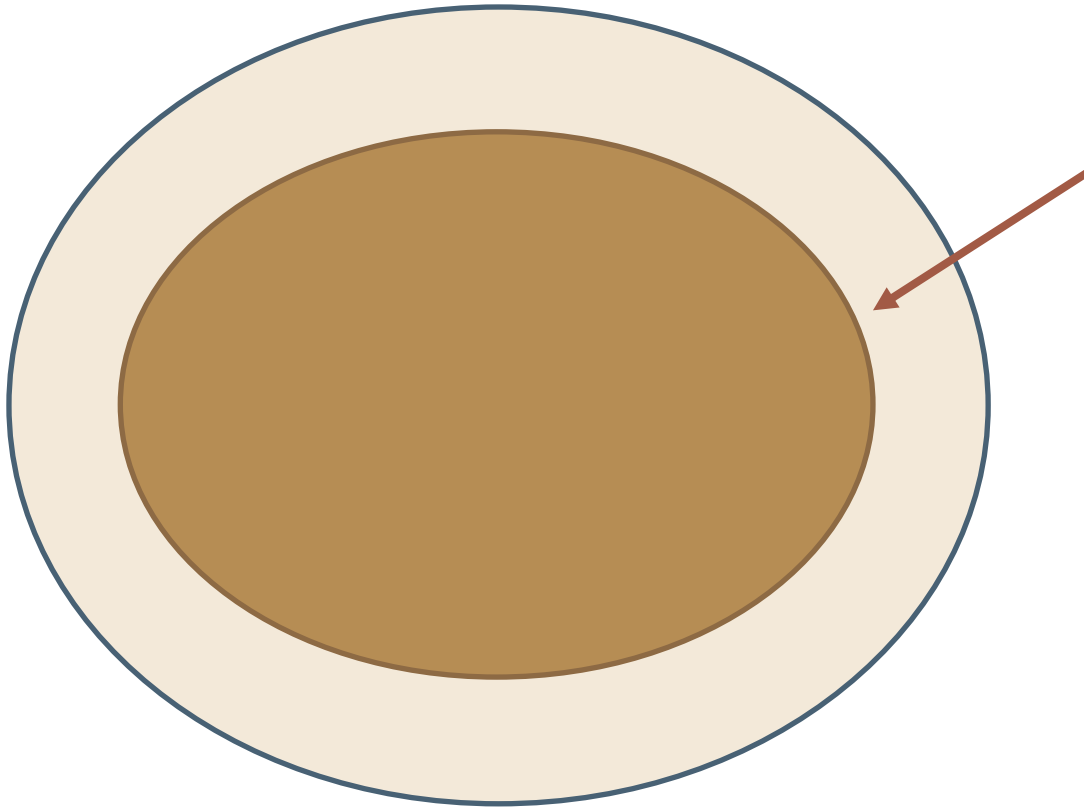
Microscopic tissue finding

- Dystrophic calcification is common.
- Calcification coexists with keratinization and cystic change.
- It is a component of the morphologic pattern.

Radiologic correlation

- Calcifications are frequently demonstrable on imaging.
- Calcification helps favor adamantinomatous type.
- Papillary tumors calcify only rarely.

Cyst contents may resemble “machine oil”



Cystic component

- Characteristic cyst fluid is thick and brownish-yellow.
- Cholesterol-rich contents.
- The descriptive term “machine oil” applies to gross appearance—not histologic diagnosis.

Schematic — cyst outline and fill are illustrative

Fibrosis and chronic inflammation accompany the tumor

ASSOCIATED MICROSCOPIC FINDINGS

Use the combined pattern; No isolated feature is a complete diagnosis.

Fibrosis

Stromal response accompanying epithelial tumor

Chronic inflammation

Inflammatory cells may be present

Cyst formation

Often prominent in adamantinomatous type

Dystrophic calcification

Frequent associated change

Fingerlets of epithelium can extend into brain



Reactive gliosis marks the brain–tumor interface

Epithelial component

- Tumor fingers can interdigitate with adjacent brain.
- The border may be locally irregular rather than smooth.
- This is distinct from the central keratinized epithelium.

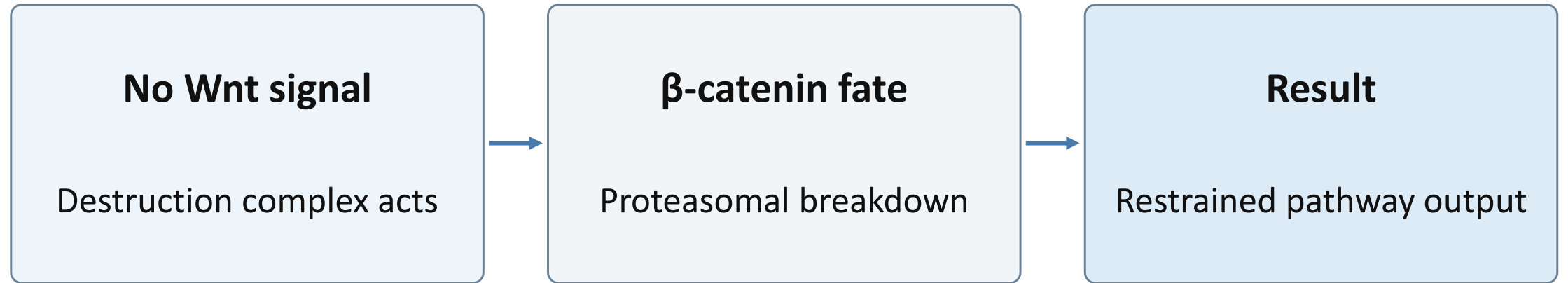
Host tissue response

- Adjacent brain shows a prominent glial reaction.
- The response belongs to brain parenchyma.
- Recognizing both components aids interpretation.

CTNNB1 is associated with adamantinomatous type



Wnt signaling normally controls β -catenin turnover



Aberrant β -catenin signaling supplies the contrast



Adamantinomatous diagnosis is a pattern diagnosis

RECOGNITION MATRIX

Use the combined pattern; No isolated feature is a complete diagnosis.

Epithelial layout

Stratified squamous nests and cords

Surface organization

Peripheral palisading

Internal architecture

Spongy reticulum

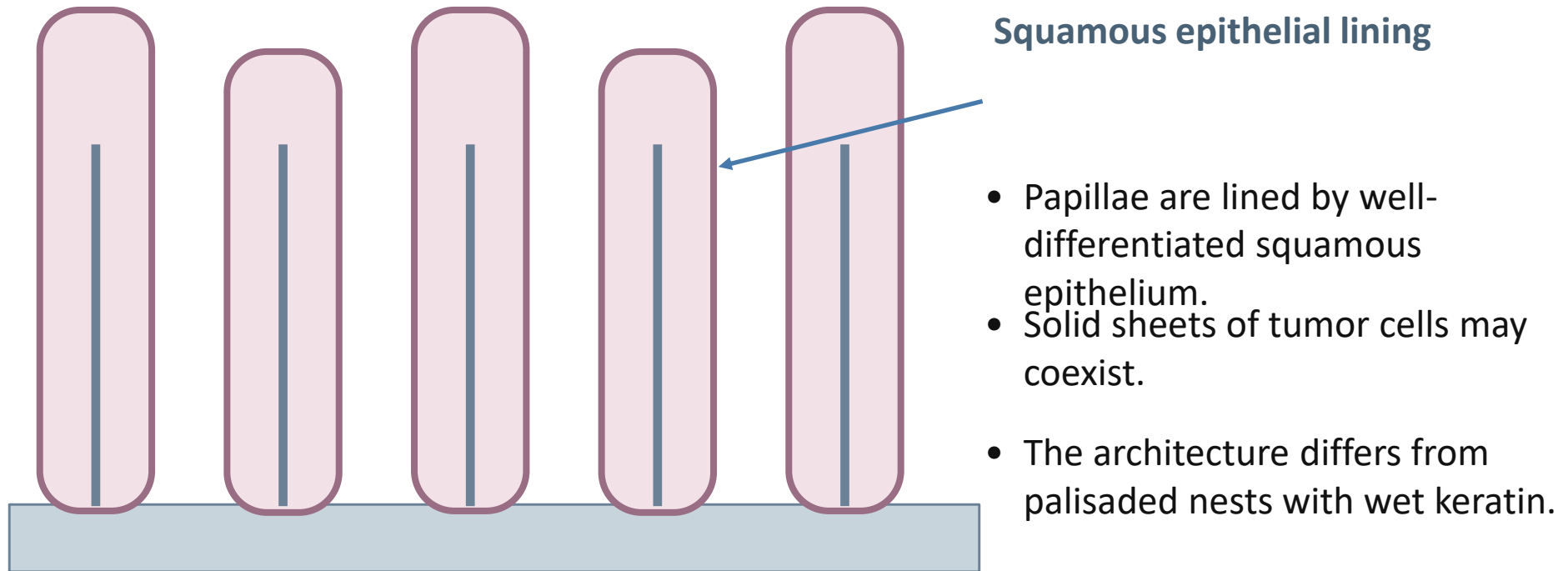
Keratin / associated findings

Wet keratin, cysts and calcification

Papillary craniopharyngioma is predominantly adult

- Most often observed in adults.
- Solid cellular sheets coexist with papillae.
- Papillae are lined by well-differentiated squamous epithelium.
- The typical absence of adamantinomatous hallmarks is diagnostically useful.

Papillary type is organized around squamous-lined papillae



Schematic — not a histologic specimen

Solid sheets coexist with papillary architecture

Papillary structures

- Squamous-lined projections define the name.
- They contribute to the characteristic microscopic architecture.
- Evaluate them alongside other features.

Solid component

- Solid sheets of squamous cells also occur.
- A wholly stereotyped papillary pattern is not required.
- Interpret across representative tissue sections.

Papillary type typically lacks wet keratin

Adamantinomatous

- Characteristic compact lamellar wet keratin.
- Peripheral palisading and spongy reticulum typical.
- Cysts and calcifications frequent.

Papillary

- Wet keratin usually absent.
- Spongy reticulum and palisading usually absent.
- Solid sheets and squamous-lined papillae typical.

Calcifications and cysts are uncommon in papillary type

- Calcification as rare in papillary lesions.
- Prominent cyst formation is generally absent compared with adamantinomatous lesions.
- Negative findings complement positive papillary architecture.
- Avoid treating any single absent feature as an absolute exclusion criterion.

Loss of palisading helps identify papillary tumors

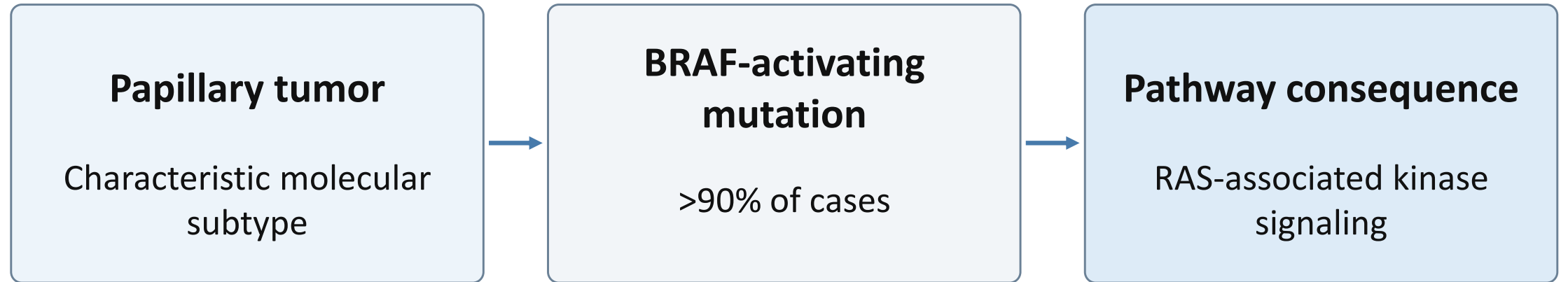
Adamantinomatous edge

- Peripheral squamous cells often display a palisaded pattern.
- The outer cell rim contrasts with spongy inner epithelium.
- Wet keratin supports this subtype.

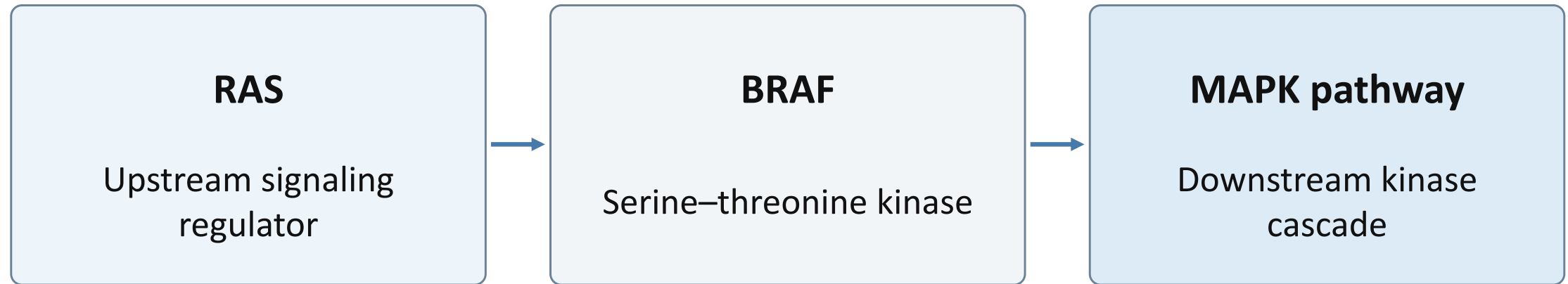
Papillary edge

- The characteristic peripheral palisade is lacking.
- Squamous epithelial lining follows papillary contours.
- Architecture is more decisive than age alone.

BRAF activation is central to papillary tumor biology



BRAF is a serine–threonine kinase downstream of RAS



BRAF inhibitors create a subtype-specific treatment link

Molecular prerequisite

- Papillary histology is strongly associated with BRAF activation.
- Activating BRAF alterations in >90%.
- Testing establishes the molecular target in an individual case.

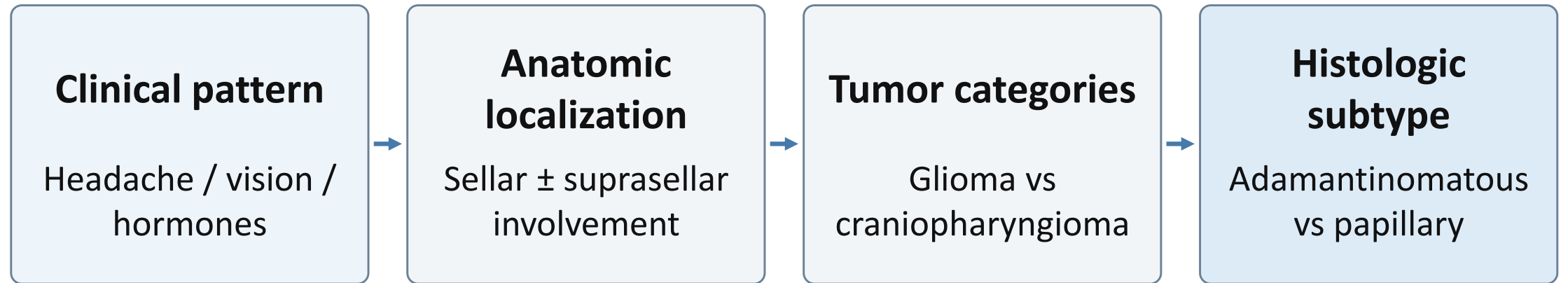
Therapeutic significance

- Most papillary tumors respond well to BRAF inhibitors description.
- This does not establish response for other suprasellar tumors.
- Regimen selection lies beyond this pathology-focused lecture.

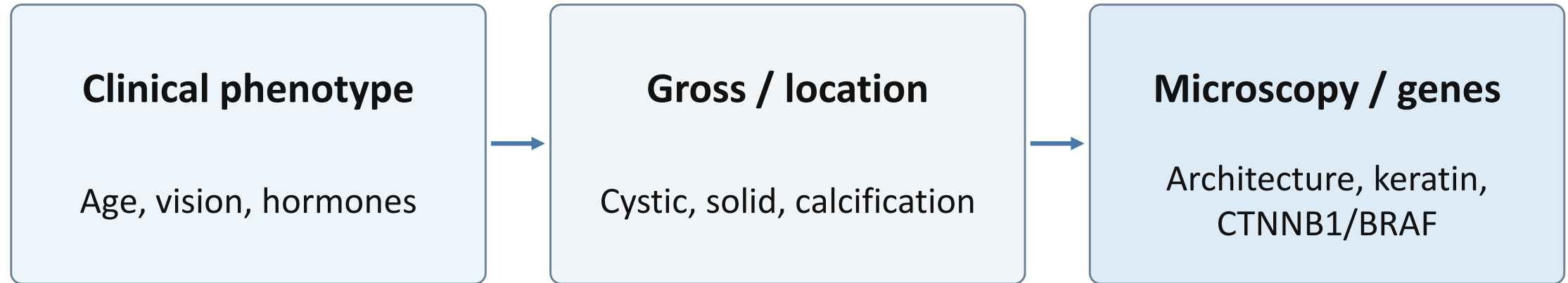
Morphology and molecular biology are concordant

Feature	Adamantinomatous	Papillary
Typical age	Childhood	Adulthood
Architecture	Nests / cords; Palisading	Solid sheets + papillae
Keratin	Wet keratin typical	Wet keratin usually absent
Cysts / calcium	Common	Usually absent / rare
Molecular	CTNNB1 → Wnt	BRAF activation

Localizing a suprasellar mass precedes tissue typing



Clinicopathologic interpretation requires three evidence types



Case application: Child with endocrine and visual symptoms

Clinical stem

A school-age child has growth retardation, headache, and visual disturbance.

Information to integrate

- Growth failure suggests GH-axis effect.
- Suprasellar localization connects findings.
- Calcified cystic lesion is reported.

Diagnostic question

Which craniopharyngioma subtype is most consistent?

Adamantinomatous is favored; Histology is required.

Case application: Palisading with wet keratin

Clinical stem

A tissue specimen contains squamous cords, peripheral palisading, and compact lamellar keratin.

Information to integrate

- Squamous epithelial tumor architecture.
- Peripheral palisading.
- Lamellar “wet” keratin.

Diagnostic question

Identify the characteristic morphologic variant.

Adamantinomatous craniopharyngioma.

Case application: Adult tumor with papillae

Clinical stem

An adult has a suprasellar epithelial tumor with solid squamous sheets and papillae.

Information to integrate

- No diagnostic wet keratin identified.
- No typical palisading pattern.
- Papillary / sheet-like architecture.

Diagnostic question

Which variant is most strongly supported?

Papillary craniopharyngioma.

Case application: A molecular treatment rationale

Clinical stem

A papillary craniopharyngioma shows an activating BRAF alteration.

Information to integrate

- Defined papillary morphology.
- Tumor harbors a targetable kinase alteration.
- Frequent response to BRAF inhibition.

Diagnostic question

Which pathway-related therapeutic idea follows?

BRAF-directed therapy is a biologically coherent option.

Diagnostic pitfalls arise from overusing isolated clues

- Age associations do not substitute for microscopic subtype identification.
- Cysts or calcification alone are not a complete diagnosis.
- Papillary features must be evaluated with absent adamantinomatous hallmarks.
- A molecular alteration should be interpreted in the correct morphologic context.

The core differential is architectural and molecular

PRACTICAL DISCRIMINATORS

Use the combined pattern; No isolated feature is a complete diagnosis.

Typical setting

Childhood ACP versus adult PCP

Positive morphology

Wet keratin / palisading versus papillae / sheets

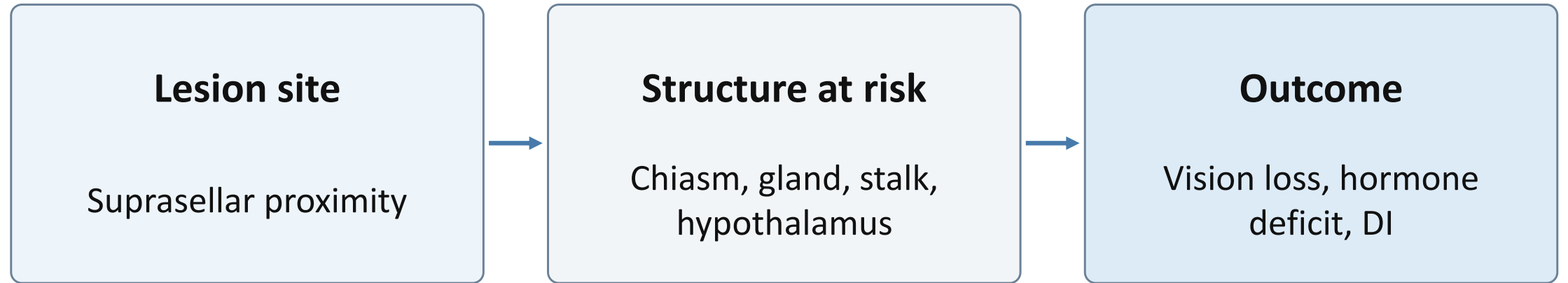
Ancillary changes

Calcified cystic ACP versus typically noncalcified PCP

Pathway

CTNNB1/Wnt versus BRAF

Clinical consequences follow topography, not variant alone



Synthesis: Two histotypes, one critical anatomic site

Adamantinomatous

- Often pediatric; Wet keratin is distinctive.
- Palisading, spongy reticulum, cysts and calcium.
- CTNNB1 and Wnt pathway activation.

Papillary

- Often adult; Papillae and squamous sheets.
- Lacks characteristic adamantinomatous morphology.
- Activating BRAF alterations and therapy relevance.

References and source limitations

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Chapter 24, pp. 971–978; principal section p. 978.
- Robbins Chapter 7: Wnt/ β -catenin and RAS–BRAF signaling used for restricted mechanistic context.
- Text extraction mixed unrelated thyroid passages into this section; these were excluded.
- No original chapter PDF or licensed authentic photomicrograph was supplied; all on-slide morphologic visuals are labeled schematics.