

Tumors of Sex Cord–Gonadal Stroma

Testicular Leydig cell and Sertoli cell neoplasms

Morphology · Endocrine manifestations · Associated syndromes · Malignancy-associated features

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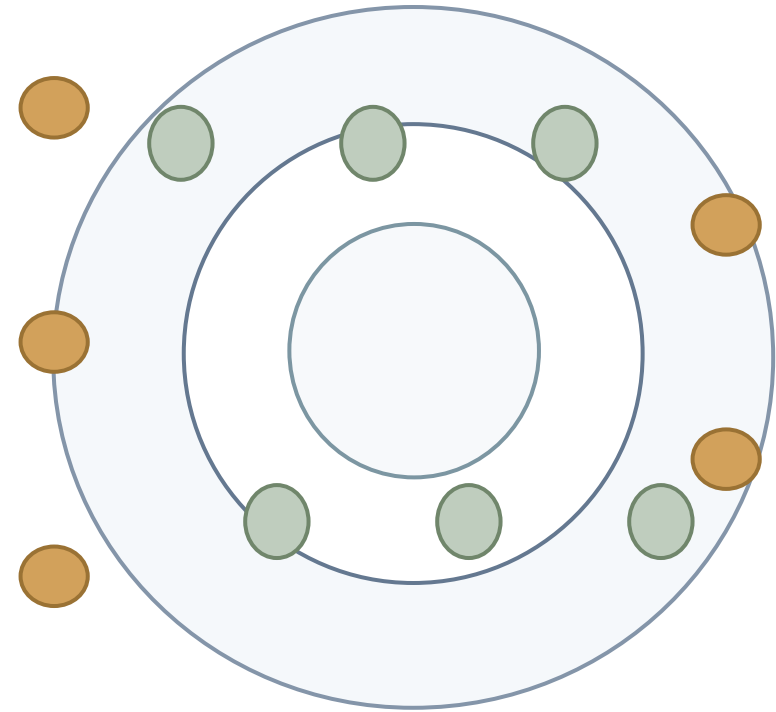
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Learning objectives

- Distinguish sex cord–gonadal stromal tumors from germ cell tumors.
- Recognize the clinical and hormonal presentations of Leydig and Sertoli cell tumors.
- Describe the gross and microscopic features of each tumor.
- Identify the histopathologic features correlated with malignant behavior.
- Apply morphology and clinicopathologic context to realistic diagnostic problems.

Two normal cellular compartments explain the tumor types

- Leydig cells are the interstitial steroid-producing population.
- Sertoli cells are the supporting population within seminiferous tubules.
- Neoplasms retain features of their presumed lineages.

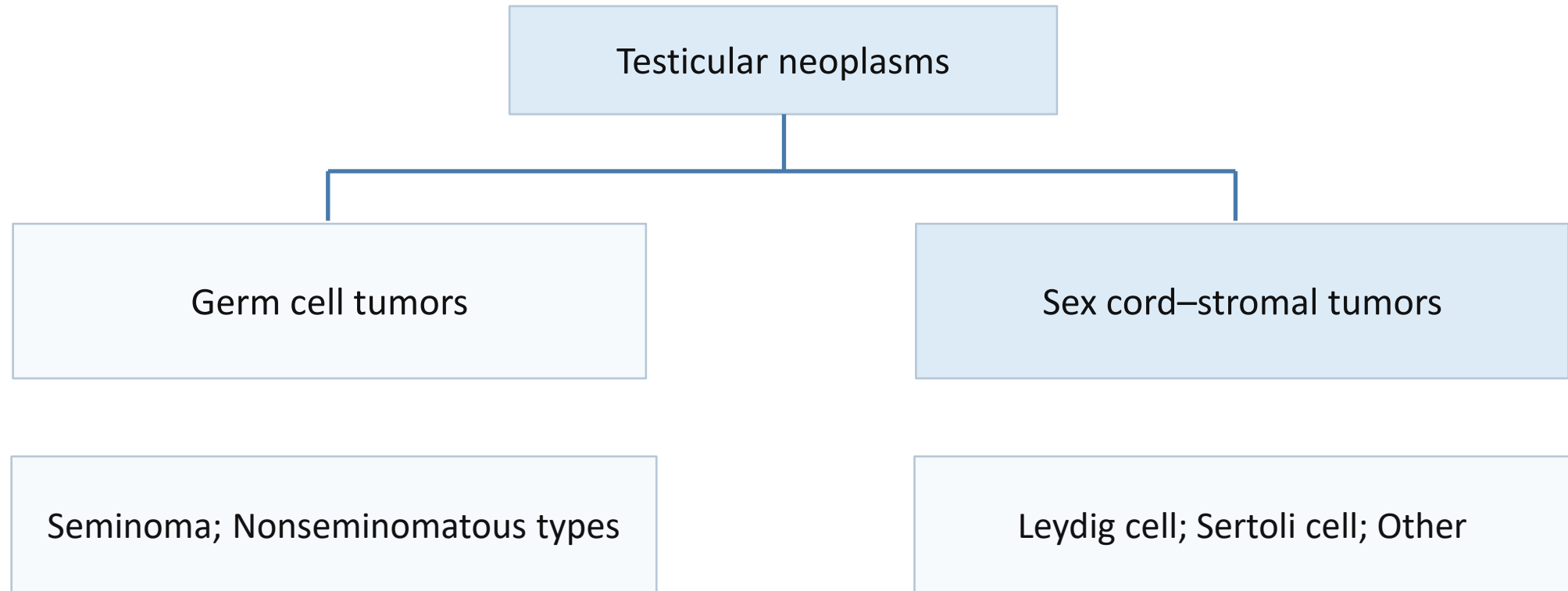


Tubular compartment

Interstitial cells

Schematic — not tissue micrograph

The broader testicular tumor classification



The present lecture addresses the right-hand branch, not a new germ cell tumor subtype.

Differentiation, not clinical symptoms, defines the classification

Tumor lineage

Categories follow the presumed histogenesis and differentiation of the neoplastic cells.

Morphology

Leydig tumors resemble interstitial Leydig cells; Sertoli tumors form cord-like and tubular patterns.

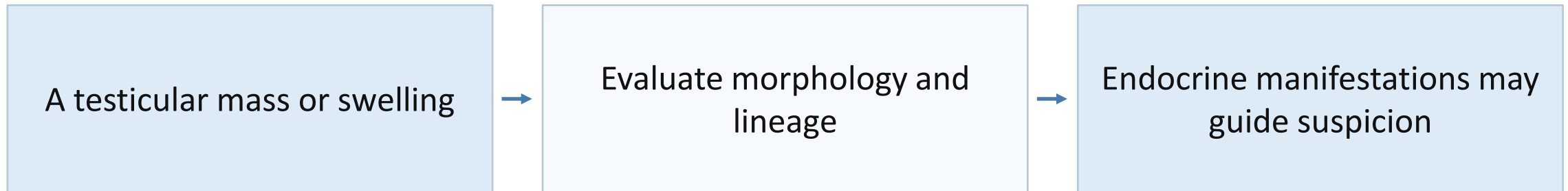
Function

Hormonal activity varies. It supplements recognition but does not replace morphologic classification.

Two principal entities have different dominant phenotypes

Feature	Leydig cell tumor	Sertoli cell tumor
Functional tendency	Often elaborates androgens; Other steroids possible	Most are hormonally silent
Characteristic architecture	Large polygonal eosinophilic cells	Trabeculae, cords and tubules
Common clinical entry point	Testicular swelling $\pm$ endocrine symptoms	Testicular mass

The clinical presentation can be mass-driven or hormone-driven



Interpretive principle

- Some Leydig tumors present through endocrine changes.
- Most Sertoli tumors present as hormonally silent masses.

Features correlated with malignant behavior

Tumor extent

Large size (>5 cm),
infiltrative border,
extratesticular extension

Cellular activity

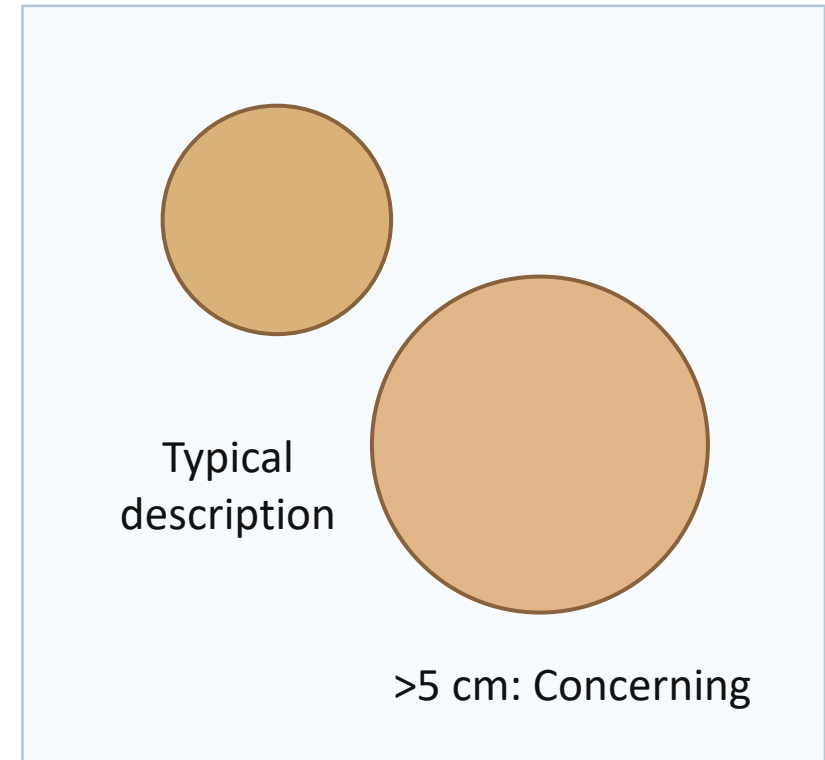
Anaplasia and mitotic
activity

Destruction or access

Necrosis and vascular–
lymphatic invasion

Size is a warning feature—not a stand-alone diagnosis

- A size greater than 5 cm correlates with malignant behavior.
- Leydig cell tumors are usually less than 5 cm at gross examination.
- The typical size and the concerning size threshold serve different purposes.



Schematic; Not drawn to scale

Margins and necrosis assess destructive growth

Infiltrative border

- A poorly confined edge suggests invasion of the surrounding testicular tissue.
- This is listed among malignancy-associated features.

Necrosis

- Tumor necrosis is another adverse histopathologic feature.
- Interpret in the setting of tumor type and other features.

Anaplasia and mitoses assess cell-level aggressiveness

Anaplasia

Pronounced cytologic atypia is a malignancy-associated feature in this group.

Mitotic activity

Increased proliferation is another feature associated with adverse behavior.

The source provides no numeric mitotic cutoff or grading algorithm.

Vascular invasion and extratesticular extension

Vascular–lymphatic invasion

Tumor within a vascular or lymphatic channel is one concerning observation.

Extratesticular extension

Tumor spreading beyond the testicular confines is a separate adverse observation.

Both correlate with malignancy; The source does not define them as a sequential pathway.

Integrate malignancy-associated features, do not invent a score

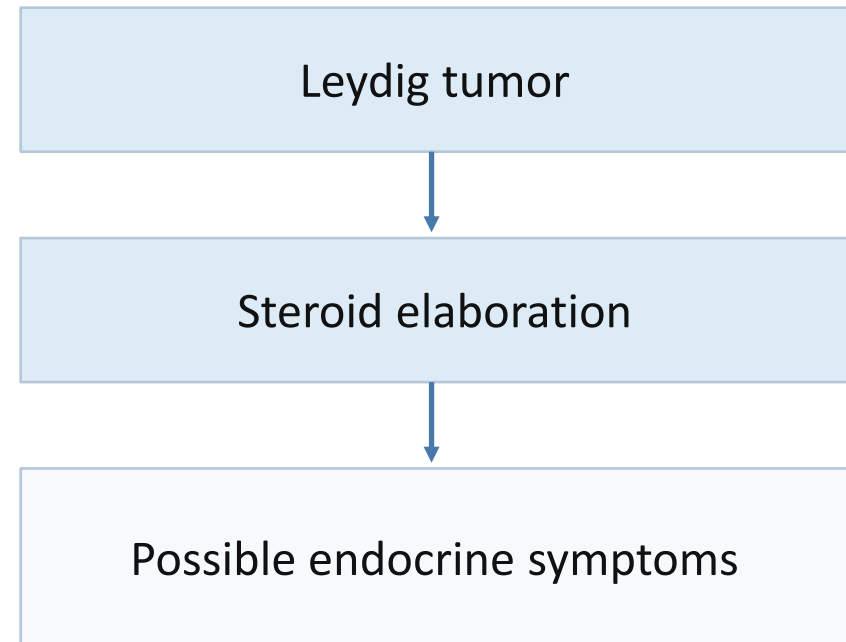
Domain	Features to document
Size	Greatest dimension; Specifically note whether >5 cm
Growth pattern	Infiltrative margins; Extratesticular extension
Tumor biology	Necrosis, anaplasia, mitotic activity
Vascular spread	Vascular–lymphatic invasion

Morphologic risk does not equal an established stage

- Correlations with malignant behavior, not a validated points-based prediction score.
- A tumor may display endocrine activity without having established malignant behavior.
- Conversely, a hormonally silent tumor can have aggressive pathologic features.
- Distinguish the tumor's lineage, its functional phenotype and its behavior.

Leydig cell tumors: Steroid-producing differentiation

- The cells resemble the normal Leydig endocrine population.
- Androgen production is common; Estrogens and corticosteroids are also possible.
- Secretory function explains why the first symptom need not be a palpable mass.



Leydig cell tumors arise in children and adults

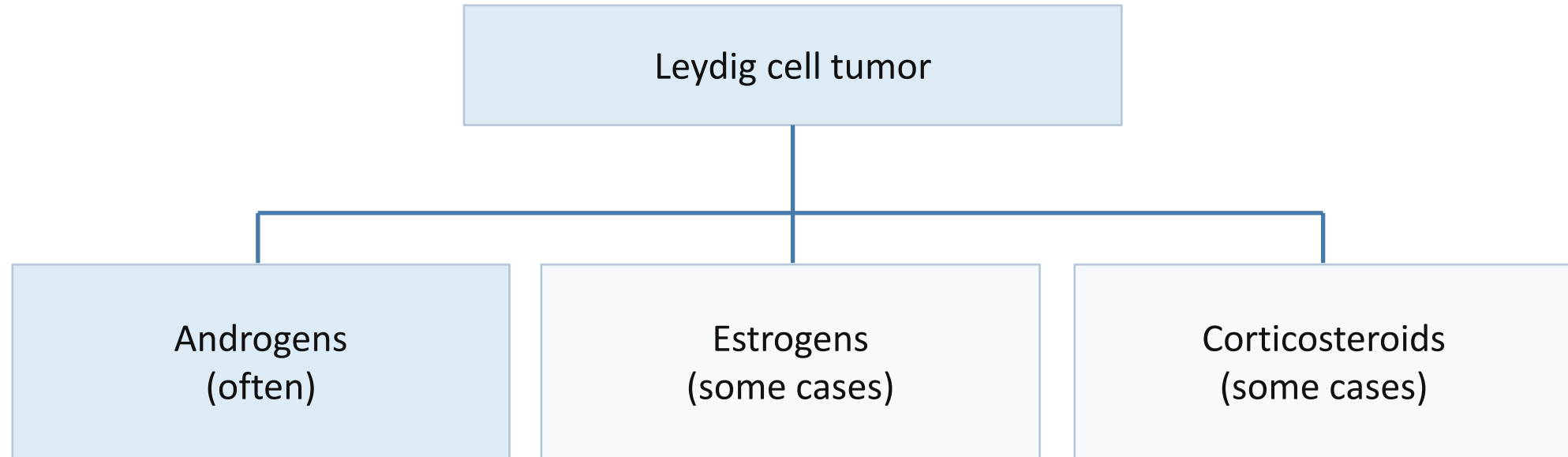
Children

The entity is not confined to adulthood;
Precocious puberty can bring it to clinical
attention.

Adults

Presentation may include swelling,
gynecomastia, decreased libido or other
endocrine symptoms.

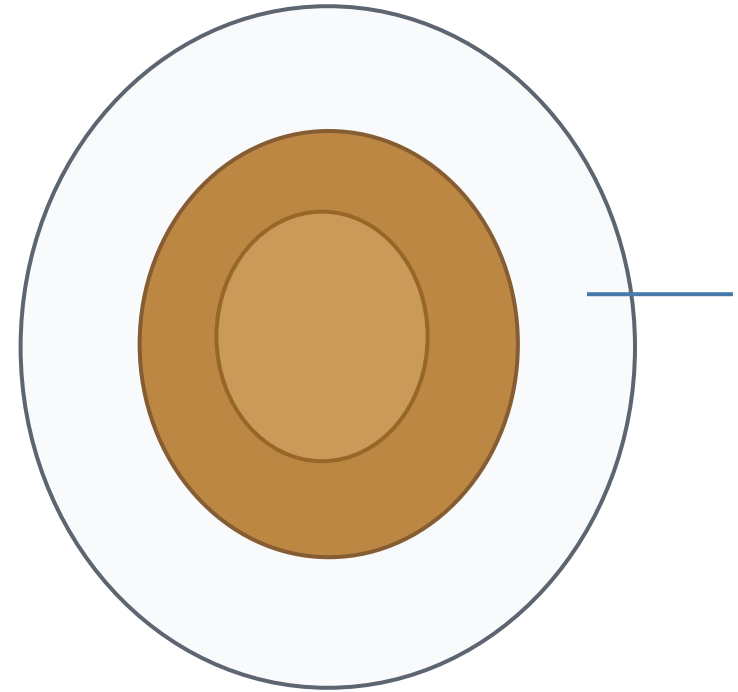
Leydig cell tumors produce a spectrum of steroid hormones



These are products reported; The figure is not a quantitative secretion profile.

Testicular swelling is the most common Leydig presentation

- A mass or swelling can be the first clinical observation.
- An endocrine presentation should not distract from evaluation of the testicular lesion.
- The presentation overlaps with other testicular tumors: Morphology remains essential.



Circumscribed intratesticular nodule

Schematic — not a gross specimen

Gynecomastia may be the clue to a Leydig tumor

Observable symptom

Gynecomastia can bring an otherwise unsuspected testicular lesion to attention.

Why it matters

Leydig cell neoplasms may elaborate estrogenic as well as androgenic products.

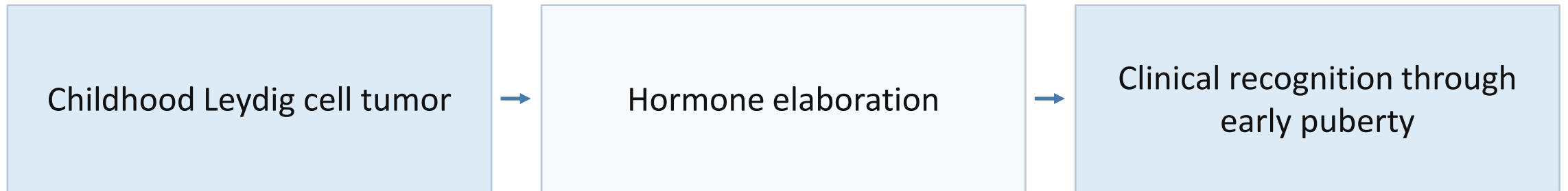
Interpretation

An endocrine symptom supports clinical suspicion; It is not diagnostic by itself.

Decreased libido can accompany a Leydig tumor

- Decreased libido is an explicitly reported presenting feature.
- The tumor may have functional endocrine effects even when testicular swelling is subtle.
- The source does not supply a specific serum-hormone pattern for this presentation.
- Interpret the symptom in the broader clinicopathologic setting.

Precocious puberty is a pediatric presentation



This presentation links endocrine differentiation to patient age; It does not define malignancy.

The same tumor can enter care by different clinical routes

Presentation	Source-based clinical implication
Testicular swelling	Mass-driven detection; Occurs most commonly
Gynecomastia	Endocrine manifestation can trigger examination
Decreased libido	Functional symptoms may accompany a tumor
Precocious puberty	A pediatric clue to steroid-producing tumor

Reported associations with Leydig cell tumors

Gonadal setting

Klinefelter syndrome and
cryptorchidism

Inherited predisposition

Hereditary
leiomyomatosis and renal
cell carcinoma syndrome

Molecular association

Germline alteration in
fumarate hydratase (FH) in
the inherited syndrome

Klinefelter syndrome and cryptorchidism

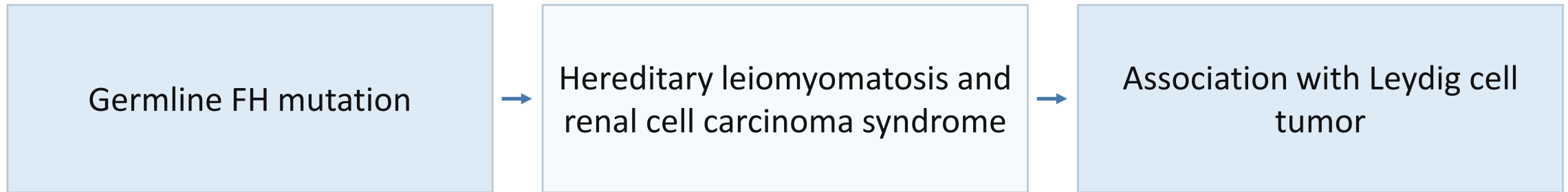
Klinefelter syndrome

- Reported association with Leydig cell tumors.
- An association does not establish the mechanism for an individual tumor.

Cryptorchidism

- Reported association with Leydig cell tumors.
- This background is also encountered in broader testicular pathology.

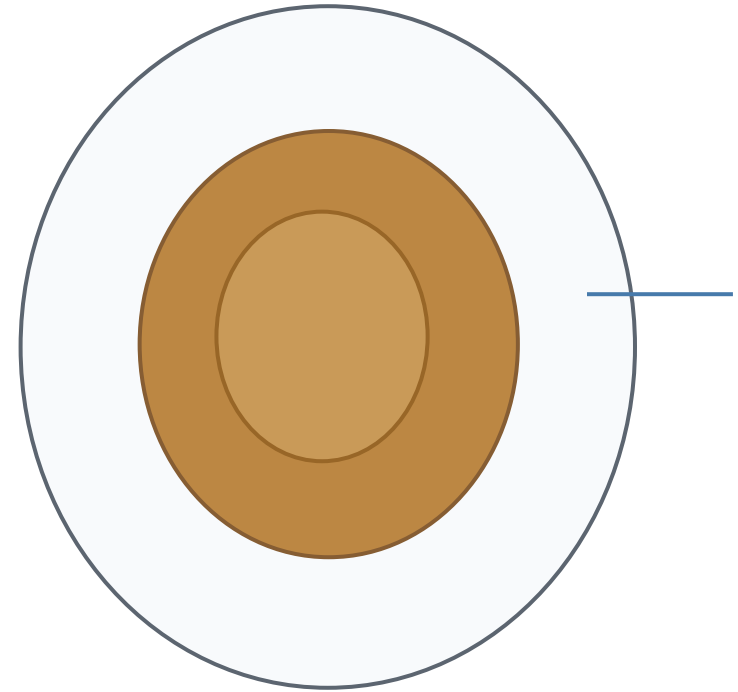
Fumarate hydratase links an inherited syndrome to Leydig tumors



The supplied text identifies the inherited association, not its tumor-specific biochemical mechanism.

The Leydig gross specimen: A sharply defined brown nodule

- Typically circumscribed and nodular.
- Golden-brown, homogeneous cut surface is characteristic.
- The gross appearance reflects a recognizable tumor phenotype but does not alone establish behavior.



Circumscribed intratesticular nodule

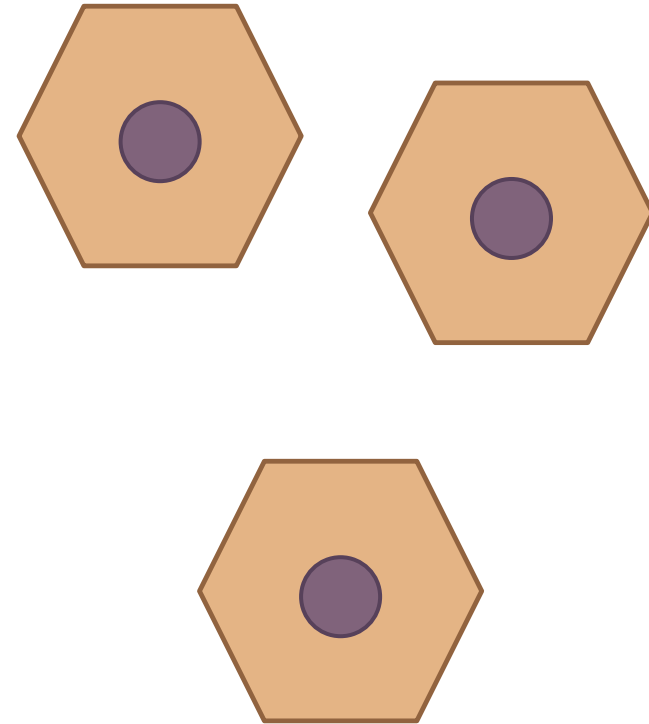
Schematic — not a gross specimen

Most Leydig nodules are smaller than 5 cm

Descriptive observation	Interpretive boundary
Usually <5 cm	Common gross morphology of Leydig cell tumors
>5 cm	One malignancy-associated feature for sex cord–stromal tumors
Size alone	Not presented as a definitive diagnosis of malignancy

Leydig cytology: Polygonal cells with ample cytoplasm

- Large tumor cells resemble normal Leydig cells.
- Cell outlines are round to polygonal.
- Abundant cytoplasm is a defining visual feature.

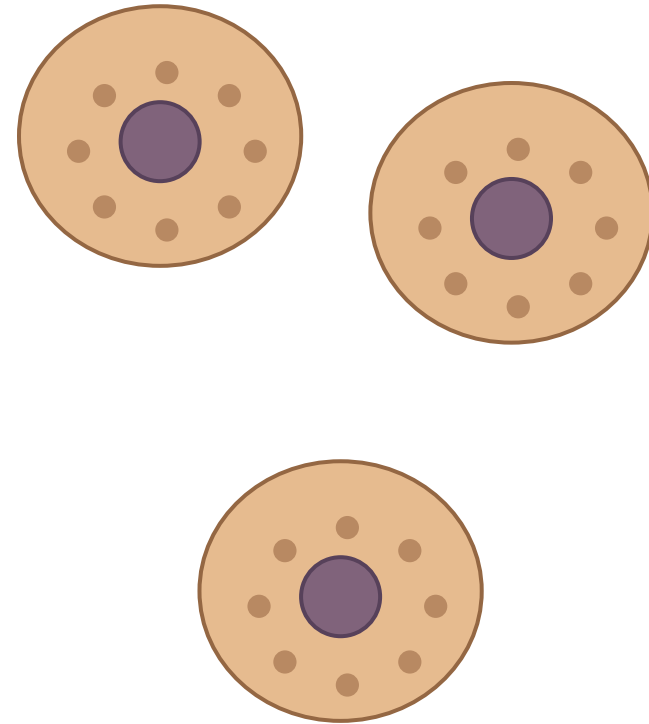


Polygonal cell outline

Schematic — not an H&E specimen

Granular eosinophilic cytoplasm is a major histologic clue

- The cytoplasm is abundant, granular and eosinophilic.
- This cytoplasmic phenotype helps identify Leydig differentiation.
- Interpret cytology together with gross findings and other microscopic details.

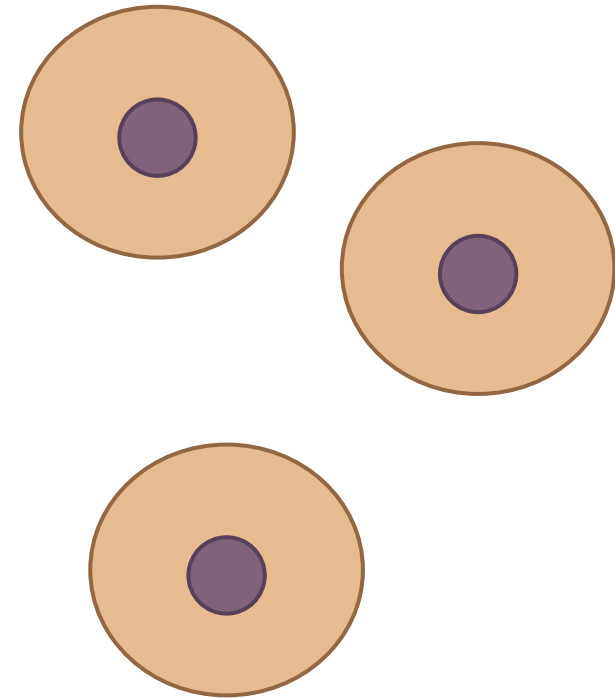


Granular eosinophilic cytoplasm

Schematic — not an H&E specimen

The Leydig cell nucleus is usually central and round

- Histologic description emphasizes a round, centrally placed nucleus.
- This nuclear appearance sits within a large polygonal cell.
- Anaplasia, when present, must be distinguished from the ordinary tumor phenotype.

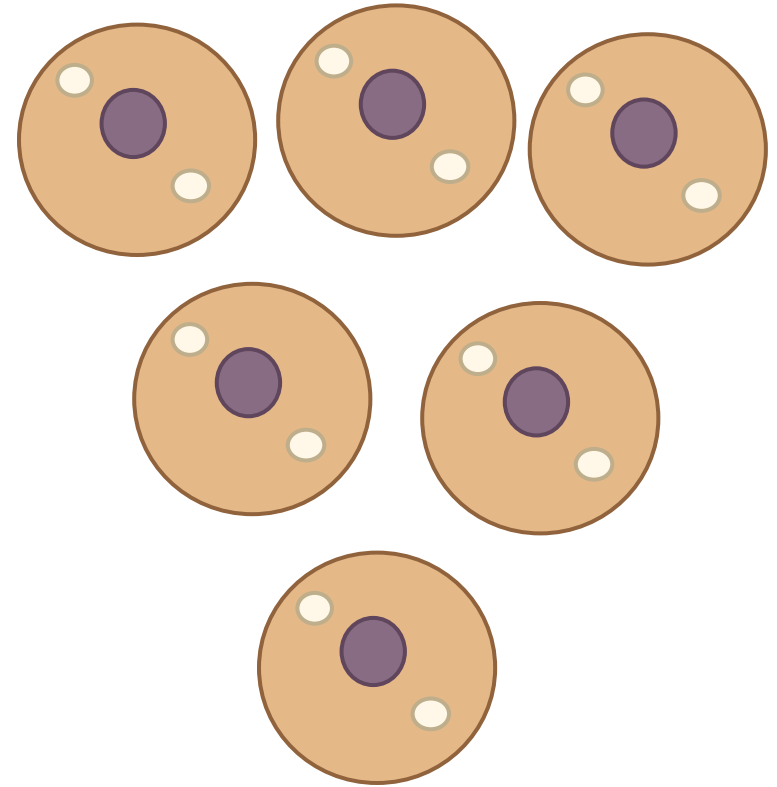


Round, centrally located nucleus

Schematic — not an H&E specimen

Lipid droplets and cytoplasmic vacuoles are common

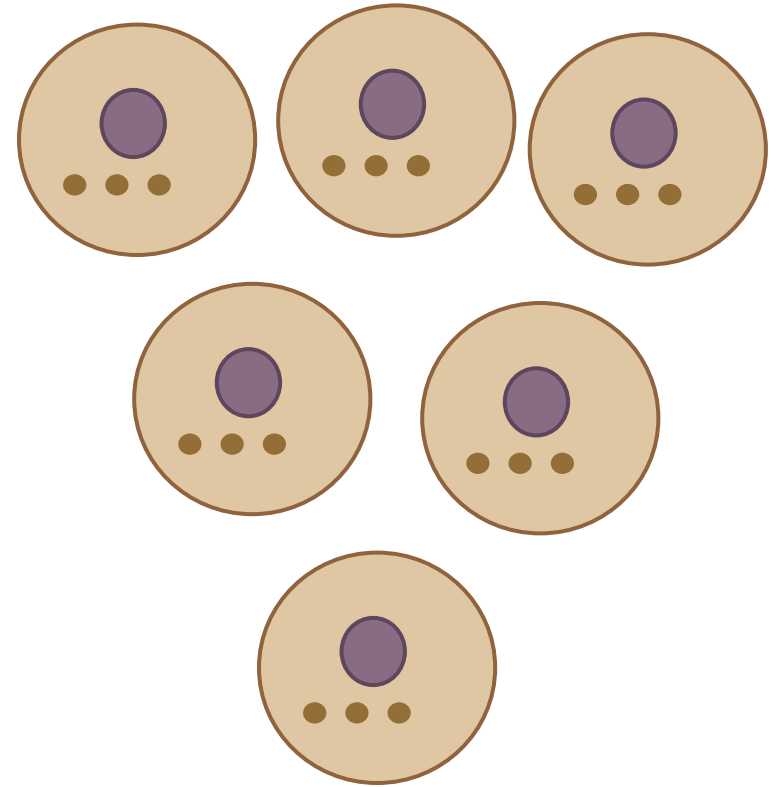
- Leydig tumor cells frequently contain lipid droplets or vacuoles.
- These are additional cytoplasmic clues to endocrine cell differentiation.
- Neither feature is presented as individually pathognomonic.



Schematic — not an H&E specimen

Lipofuscin pigment adds another cytoplasmic clue

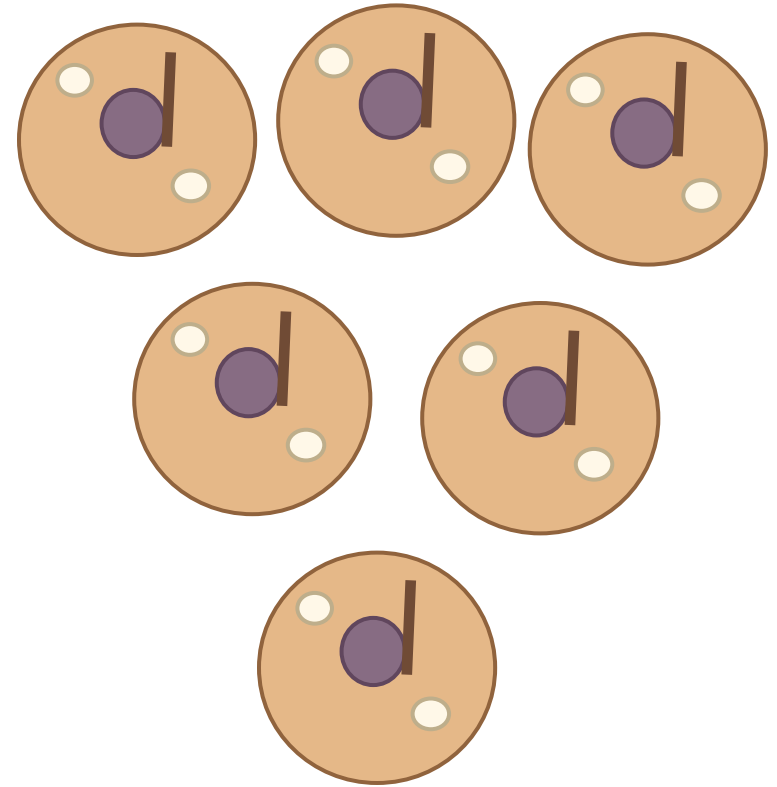
- Intracytoplasmic lipofuscin pigment is described in these neoplasms.
- It may coexist with eosinophilic granular cytoplasm and lipid-related spaces.
- A combination of findings supports recognition more than a single feature.



Schematic — not an H&E specimen

Reinke crystalloids are distinctive but not universal

- Characteristic rod-shaped structures may be seen in the tumor cytoplasm.
- They are called crystalloids of Reinke.
- Them in about 25% of Leydig cell tumors.



Schematic — not an H&E specimen

A negative search for Reinke crystalloids does not exclude the tumor

Positive finding

Reinke crystalloids are highly characteristic when encountered.

Frequency

The reported frequency is about one quarter of Leydig cell tumors.

Diagnostic restraint

Most tumors will not demonstrate them; Use the overall morphology.

Combine the gross and histologic Leydig signatures

Level	Signature
Gross	Circumscribed, homogeneous golden-brown nodule
Cell architecture	Large round-to-polygonal cells
Cytoplasm	Abundant granular eosinophilic material; Lipid/vacuoles; Lipofuscin
Occasional clue	Rod-shaped crystalloids of Reinke (~25%)

A minority of adult Leydig cell tumors behave malignantly

Behavior estimate

Approximately 10% of Leydig cell tumors in adults are malignant.

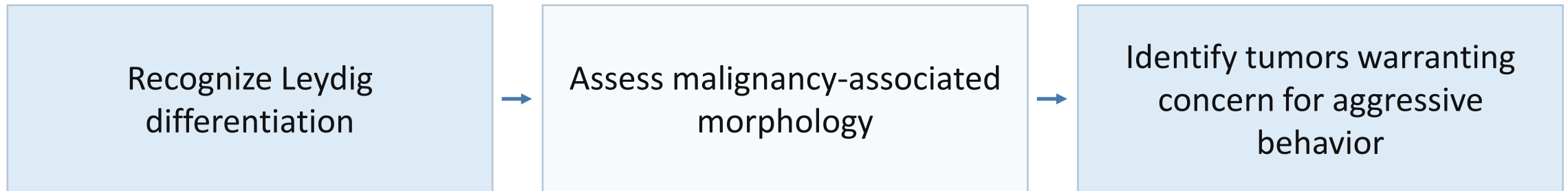
Consequences

Malignant Leydig cell tumors can produce metastases.

Pathology review

Examine size, necrosis, growth pattern, cytology and vascular invasion.

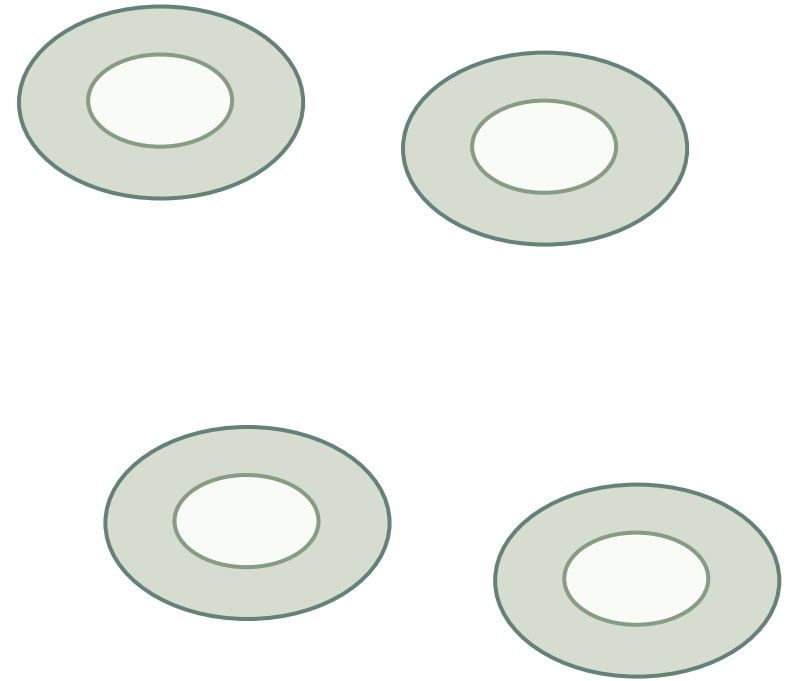
Metastatic capability makes behavior assessment essential



A hormonal presentation does not substitute for assessment of malignant features.

Sertoli cell tumors: Characteristic architectural differentiation

- Most Sertoli tumors are hormonally silent.
- They commonly present as a testicular mass.
- Microscopy emphasizes trabeculae, cords and tubules rather than a Leydig-like sheet of polygonal cells.



Schematic — not histologic evidence

Hormonal silence explains the usual Sertoli presentation

Hormone activity

Most Sertoli cell tumors are described as hormonally silent.

Presentation

The usual clinical entry point is a testicular mass.

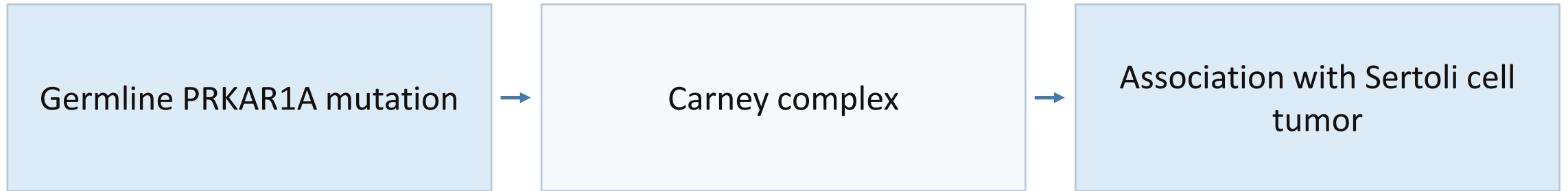
Diagnostic emphasis

Morphology and associated clinical context are central to recognition.

Several inherited syndromes are linked to Sertoli cell tumors

Associated syndrome	Specific point supported by Robbins
Carney complex	PRKAR1A germline mutation association
Peutz–Jeghers syndrome	Reported tumor association
Familial adenomatous polyposis	Reported tumor association

Carney complex involves PRKAR1A



Carney complex with germline PRKAR1A mutation and cAMP-dependent protein kinase signaling.

Peutz–Jeghers and familial adenomatous polyposis

Peutz–Jeghers syndrome

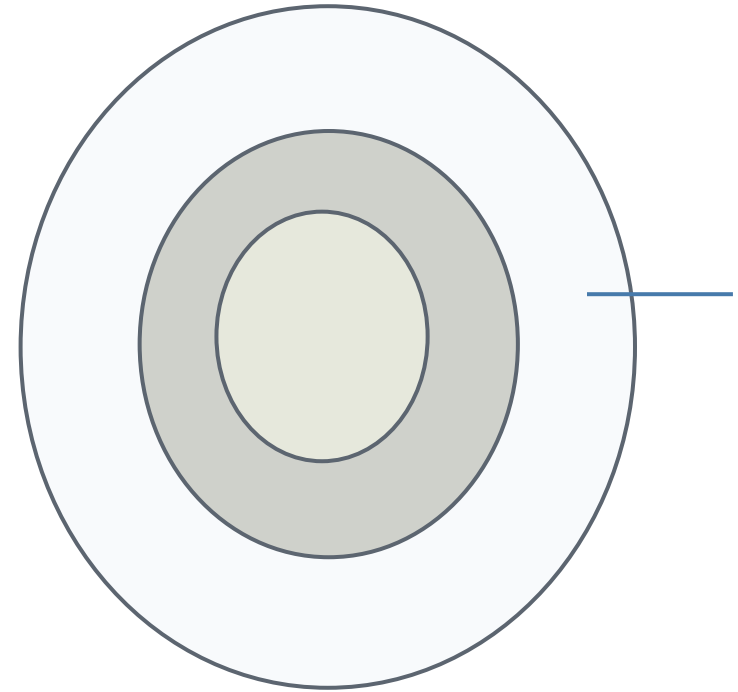
- An association with Sertoli cell tumors.
- A precise genotype-specific tumor risk is not provided in the source.

Familial adenomatous polyposis

- Also included among reported associations.
- Do not infer a specific molecular pathway from this excerpt alone.

The Sertoli gross specimen: Firm and gray-white to yellow

- Typically a small, firm, circumscribed nodule.
- The cut surface is homogeneous.
- The color is described as gray-white to yellow.

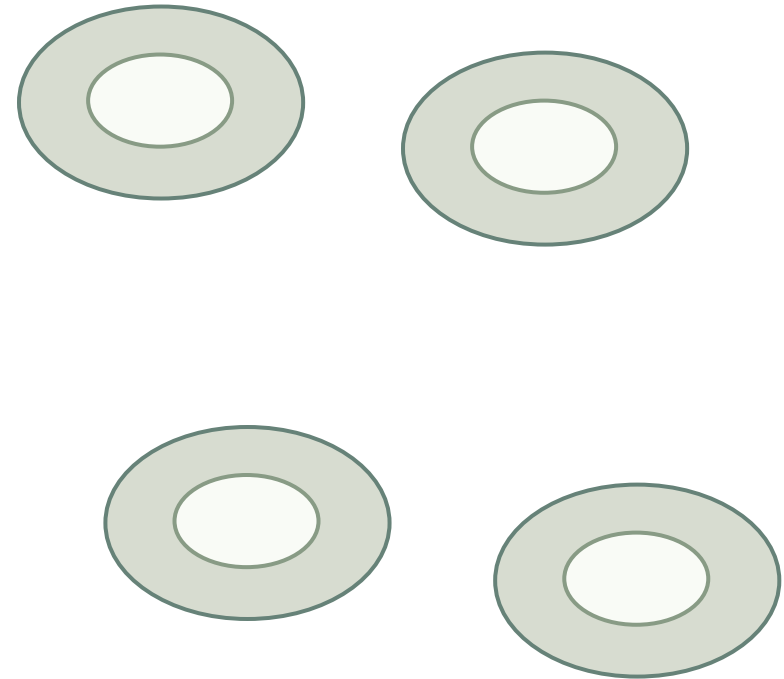


Circumscribed intratesticular nodule

Schematic — not a gross specimen

Sertoli tumors organize into trabeculae and tubules

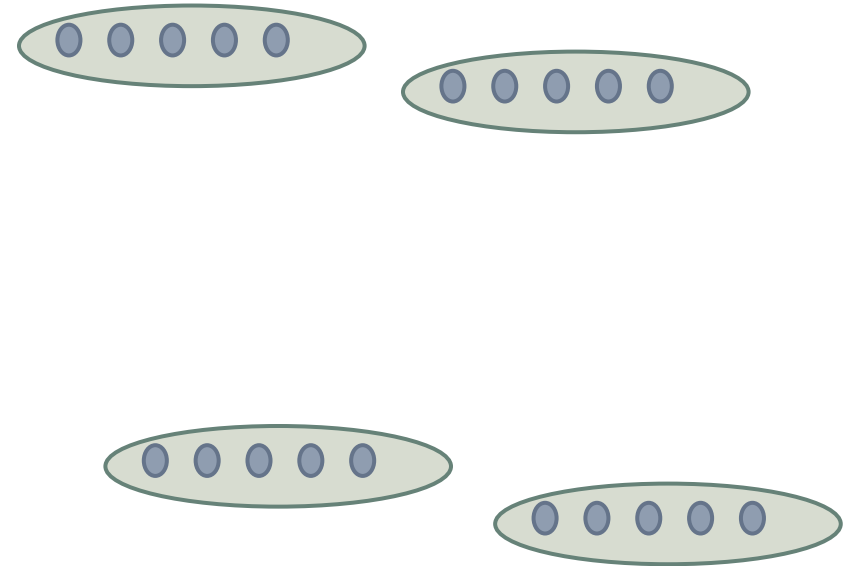
- Histology commonly shows distinctive trabeculae.
- Trabeculae may give rise to cord-like structures.
- Tubular structures are another characteristic pattern.



Schematic — not histologic evidence

Cord-like architecture is a key Sertoli pattern

- The neoplastic cells form elongated cords and trabeculae.
- Cord-like structures are not simply a color or cytoplasmic characteristic.
- Identify the architecture before relying on individual cell features.



Schematic — not histologic evidence

Cellular morphology and architecture distinguish the types

Diagnostic axis	Leydig	Sertoli
Principal visual clue	Large polygonal cells	Trabecular, cord-like and tubular pattern
Cytoplasm	Granular eosinophilic; Possible vacuoles/pigment	Not specifically characterized in this excerpt
Distinctive finding	Reinke crystalloids in a subset	Architectural tubules and cords

Most Sertoli tumors are benign; Some are malignant

Common behavior

The majority of Sertoli cell tumors follow a benign course.

Malignant minority

Approximately 10% are reported to pursue a malignant course.

Assessment

The general sex cord–stromal adverse morphology list remains relevant.

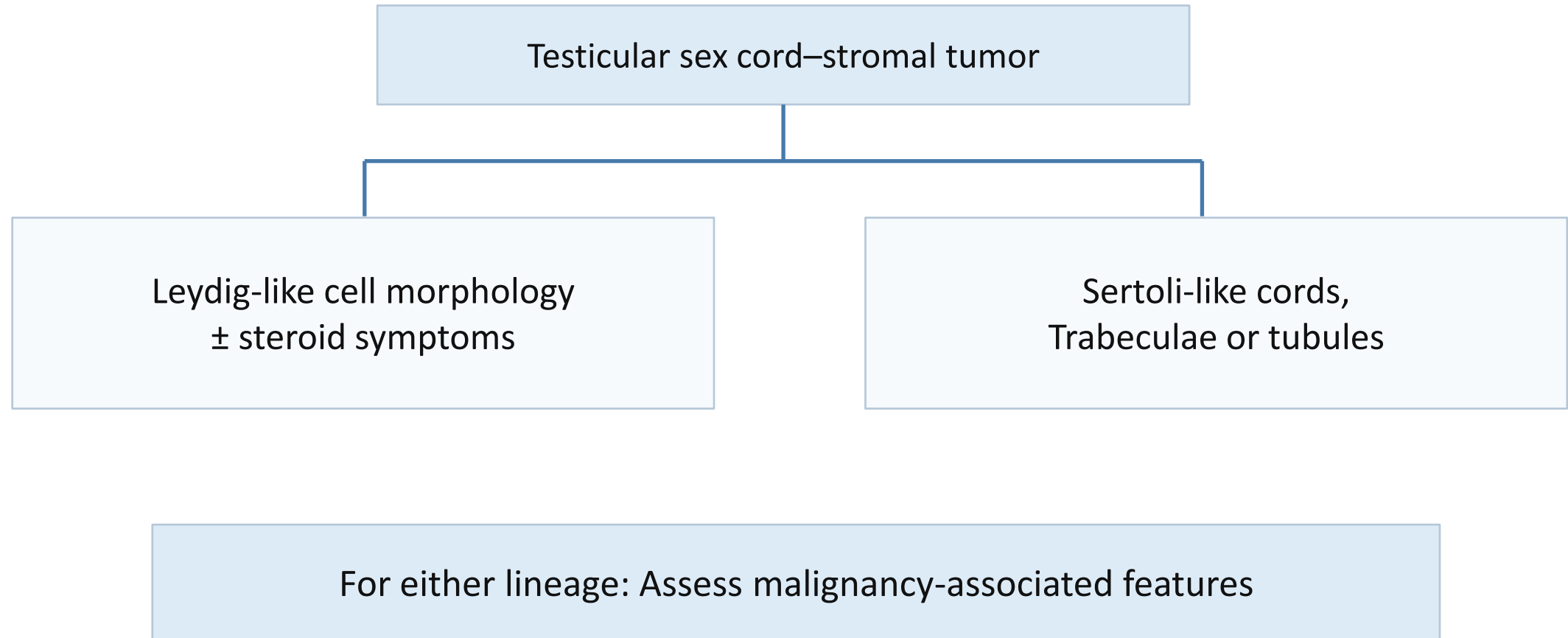
A clinically useful side-by-side tumor profile

Domain	Leydig cell tumor	Sertoli cell tumor
Presentation	Mass ± endocrine effects	Most often a mass
Functional tendency	Often steroid-producing	Most often hormonally silent
Gross	Golden-brown nodule	Gray-white to yellow nodule
Micro	Polygonal eosinophilic cells	Cords, trabeculae, tubules

General malignancy-associated features apply across lineages

Behavior concern	Morphologic observations
Concerning bulk or spread	>5 cm; Extratesticular extension
Invasive growth	Infiltrative border; Vascular–lymphatic invasion
High-grade histology	Anaplasia; Increased mitotic activity; Necrosis

A source-faithful interpretation pathway



Case 1 — identify the probable tumor

A boy develops precocious puberty and a unilateral testicular nodule. The resected mass is circumscribed and golden brown.

Which interpretation is most strongly supported?

A. Leydig cell tumor

B. Sertoli cell tumor

C. Testicular lymphoma

Case 1 — the endocrine and gross clues converge

- Childhood onset is explicitly possible for Leydig cell tumors.
- Precocious puberty is a recognized Leydig presentation.
- The golden-brown, circumscribed nodule matches its classic gross appearance.

Supported interpretation

Leydig cell tumor

Case 2 — interpret the microscopic pattern

An adult has a hormonally silent testicular mass. Histology demonstrates trabeculae with cords and tubular structures.

Which interpretation is most strongly supported?

A. Sertoli cell tumor

B. Leydig cell tumor

C. Hormone secretion proves germ cell origin

Case 2 — the architectural pattern is discriminating

- Most Sertoli tumors are hormonally silent.
- Trabeculae, cords and tubules are the textbook Sertoli pattern.
- A secretory phenotype is not necessary for Sertoli lineage.

Supported interpretation

Sertoli cell tumor

Case 3 — assess behavior

A sex cord–stromal tumor measures 6 cm and has focal necrosis, infiltrative growth and vascular–lymphatic invasion.

Which interpretation is most strongly supported?

A. These are malignant-associated pathologic findings

B. A hormone level is required before interpreting the findings

C. A size of 6 cm excludes malignant potential

Case 3 — several adverse features are present

- Tumor size exceeds the source threshold of >5 cm.
- Necrosis, infiltrative margins and vascular–lymphatic invasion are on the adverse-feature list.
- The findings raise concern; The excerpt supplies no validated numerical scoring rule.

Supported interpretation

Morphology concerning for
malignant behavior

Three recurrent diagnostic errors to avoid

Pitfall	Safer interpretation
“Any Reinke crystals must be present”	They occur in about 25%; Absence does not rule out Leydig tumor
“No hormone symptoms means no stromal tumor”	Most Sertoli tumors are hormonally silent
“Size alone proves malignancy”	Use the overall set of pathology-associated features

What this source does—and does not—establish

Directly supported

- Key clinical presentations and associated syndromes
- Gross and cellular morphology for Leydig and Sertoli tumors
- Listed malignant-associated features and approximate malignant proportions

Not specified in this excerpt

- Immunohistochemistry panels or sensitivity estimates
- Molecular classification beyond stated associations
- Formal scoring, staging or specific treatment algorithms

Core clinicopathologic distinctions

Leydig

Golden-brown circumscribed mass; Eosinophilic polygonal cells; Endocrine manifestations may dominate.

Sertoli

Small firm gray-white/yellow mass; Cords, trabeculae and tubules; Mostly hormonally silent.

Behavior

Inspect size, necrosis, invasion, anaplasia, mitotic activity and extension.

References and source scope

Primary reference

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 21, “The Lower Urinary Tract and Male Genital System,” p. 886: “Tumors of Sex Cord–Gonadal Stroma.”

Parent context

Chapter classification of testicular tumors (Table 21.6) and the surrounding testicular tumor discussion.

Histopathology is illustrated by original native schematics, not reproduced photomicrographs.