

Embryonal rhabdomyosarcoma

Vaginal botryoid presentation

Morphology • diagnostic integration • clinical implications

Pathology teaching lecture

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Learning objectives

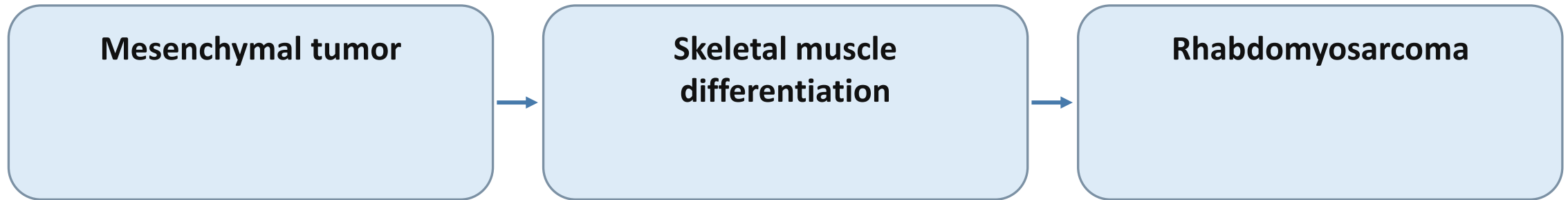
Recognize the vaginal botryoid phenotype and its clinical setting

Explain cambium-layer histology and rhabdomyoblastic differentiation

Use morphology, myogenic markers and molecular context appropriately

Explain local hazards and principles of risk-adapted therapy

Rhabdomyosarcoma is a malignant myogenic sarcoma

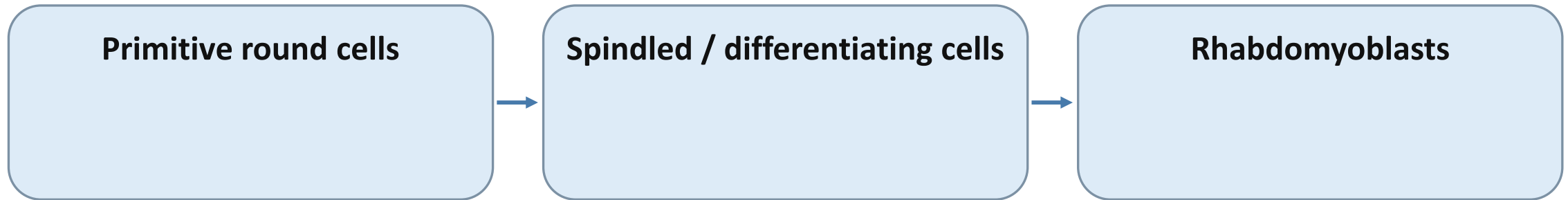


Malignant mesenchymal neoplasm with skeletal muscle differentiation

The defining lineage is rhabdomyoblastic, not epithelial

Tumor site does not need to contain mature skeletal muscle

Embryonal histology reflects immature muscle differentiation



Primitive cells coexist with more recognizable rhabdomyoblasts

Cellular appearance varies with the degree of myogenic maturation

Interpret the whole morphologic spectrum—not a single cell type

The genitourinary tract is a characteristic pediatric site

Anatomic site

Vagina

Bladder

Other genitourinary sites

Histologic type

Embryonal rhabdomyosarcoma

Botryoid growth pattern in luminal sites

Skeletal muscle need not be present at the tumor site

Pediatric rhabdomyosarcoma may occur where normal skeletal muscle is sparse

This distribution to support origin from mesenchymal progenitors

The tumor phenotype reflects differentiation—not necessarily cell of origin

Vaginal rhabdomyosarcoma is uncommon

Typical pediatric context

Embryonal rhabdomyosarcoma
Mesenchymal, myogenic lineage

Adult vaginal cancer context

Squamous carcinoma predominates
Epithelial malignant lineage

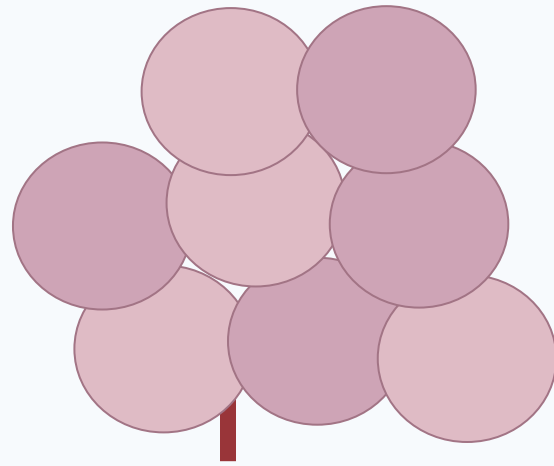
The highest-yield age clue is early childhood

Vaginal embryonal rhabdomyosarcoma is most frequently found in infants

Most affected children in the Robbins description are younger than five

Age is suggestive, not an independently diagnostic criterion

Botryoid denotes a gross growth pattern



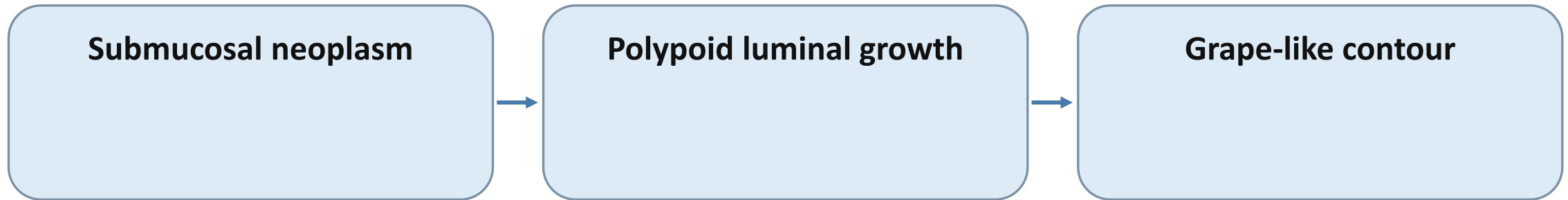
Schematic: Multiple mucosal polypoid lobules

“Sarcoma botryoides” is the historical descriptive name

Botryoid refers to grape-cluster–like polypoid tumor protrusions

The recognized underlying lineage is embryonal rhabdomyosarcoma

Botryoid growth favors a mucosa-lined lumen



Botryoid lesions in hollow visceral walls

Vagina and urinary bladder are prototypical sites

Luminal growth explains why masses may be visible as polyps

Polypoid protrusion is a presentation—not a diagnosis

Gross impression

Rounded

Polypoid

Grape-like

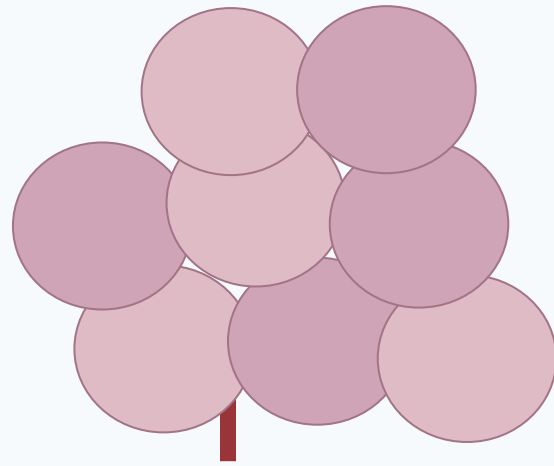
Decisive evidence

Microscopic malignant cells

Myogenic differentiation

Cambium-layer pattern

Why the mass looks like a bunch of grapes



Schematic: Multiple mucosal polypoid lobules

Several rounded polypoid projections
create a lobulated surface

Each protrusion is part of a neoplasm
arising beneath mucosal epithelium

Gross architecture provides a clue; It is
not a specific histologic test

Deep embryonal tumors may be soft and gray

Surface

Exophytic / polypoid

Botryoid configuration

Deeper component

Soft gray tissue

Infiltrative behavior

A deceptively benign appearance is a central pitfall

Robbins specifically warns of confusion with benign inflammatory polyps

Loose edema and inflammatory cells can obscure malignant cellularity

Recognition requires examining the epithelium–stroma interface

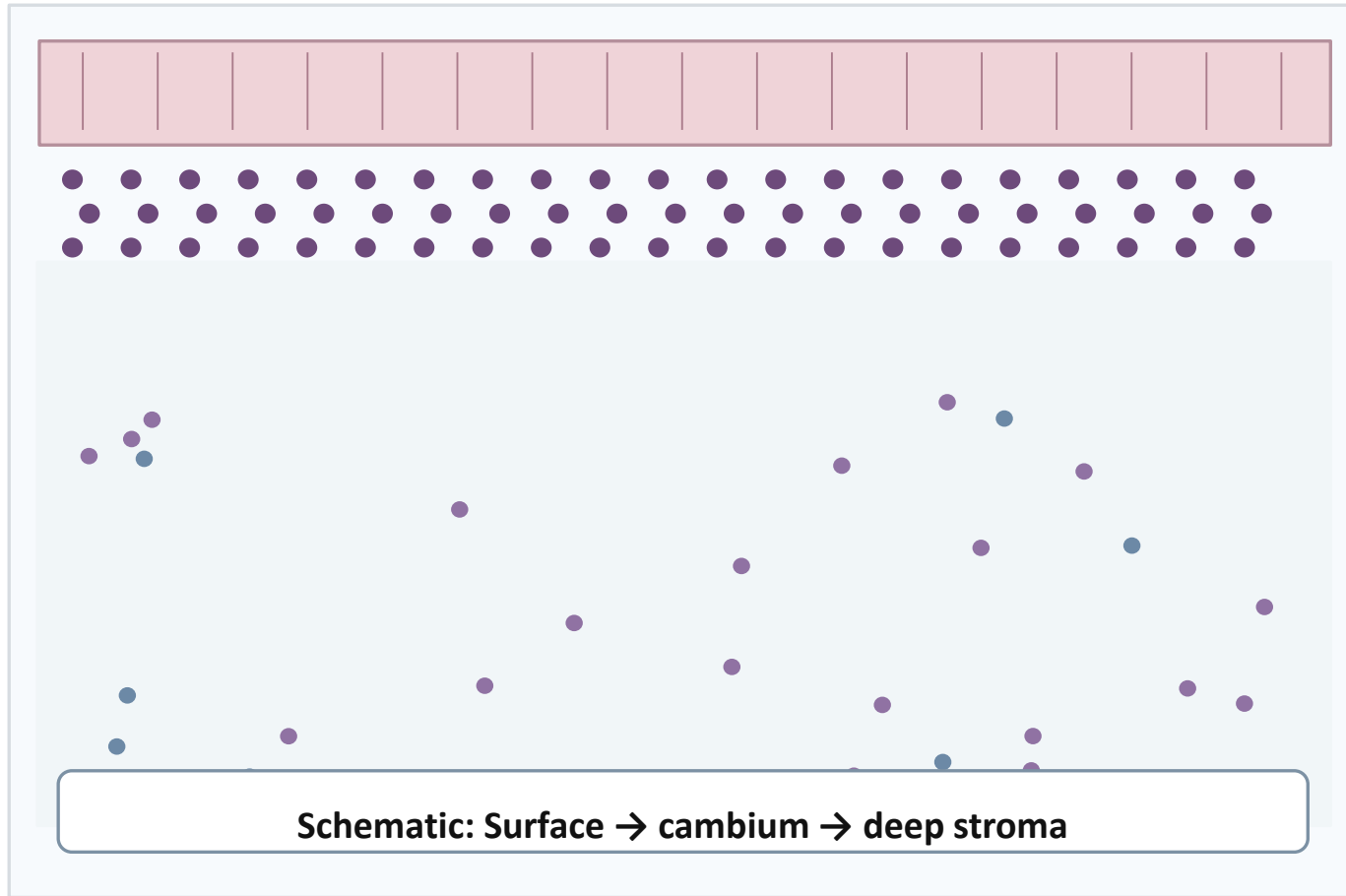
Clinical warning signs require tissue evaluation

A growing vaginal polypoid mass in an infant merits assessment

Bleeding and protrusion are documented presentations in published cases

Symptoms and gross appearance cannot replace histopathology

Read the lesion from surface to depth

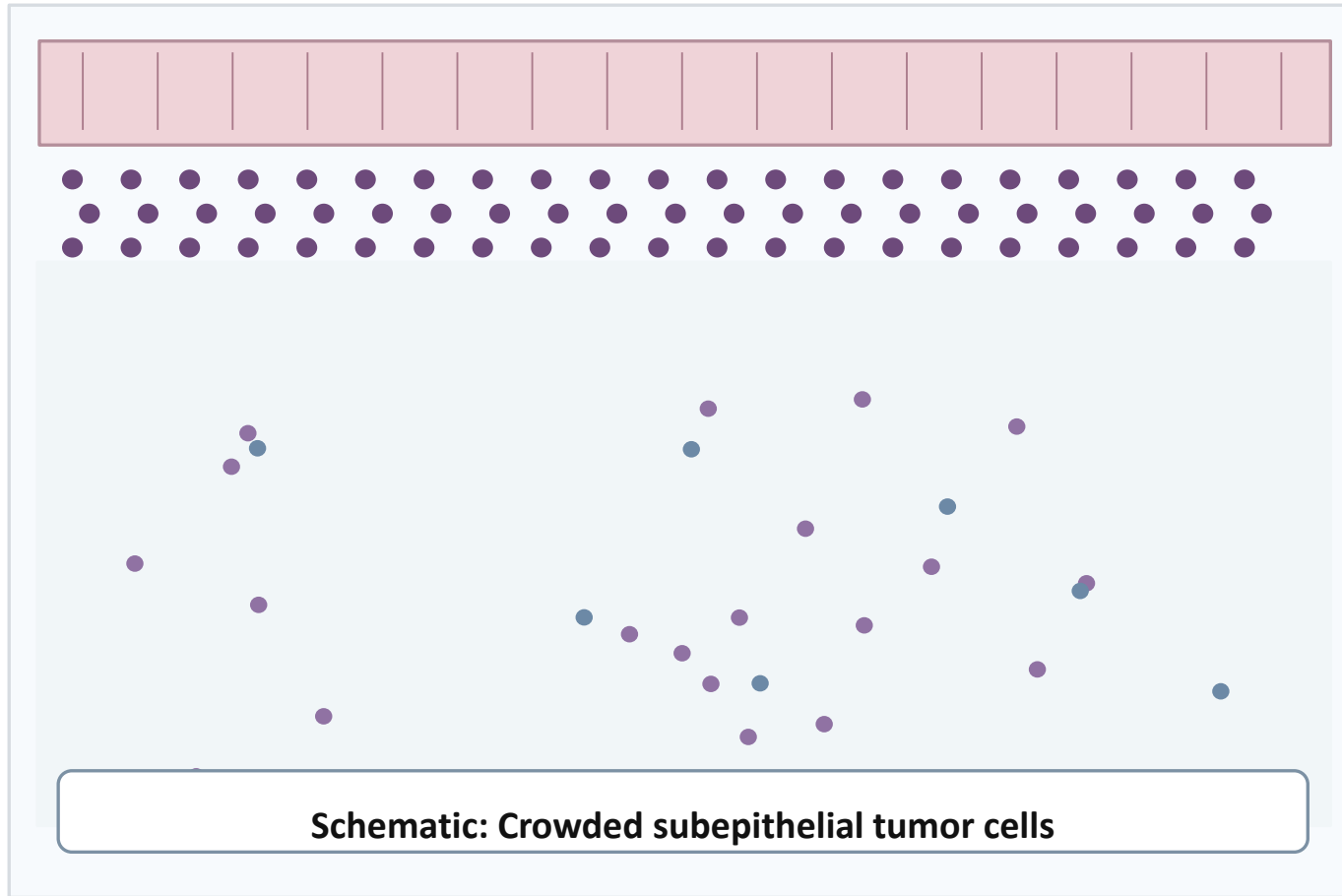


A mucosal epithelial covering overlies the tumor

A dense subepithelial neoplastic cambium layer is present

Deeper stroma is loose, edematous and less cellular

Cambium layer: The diagnostic architectural clue

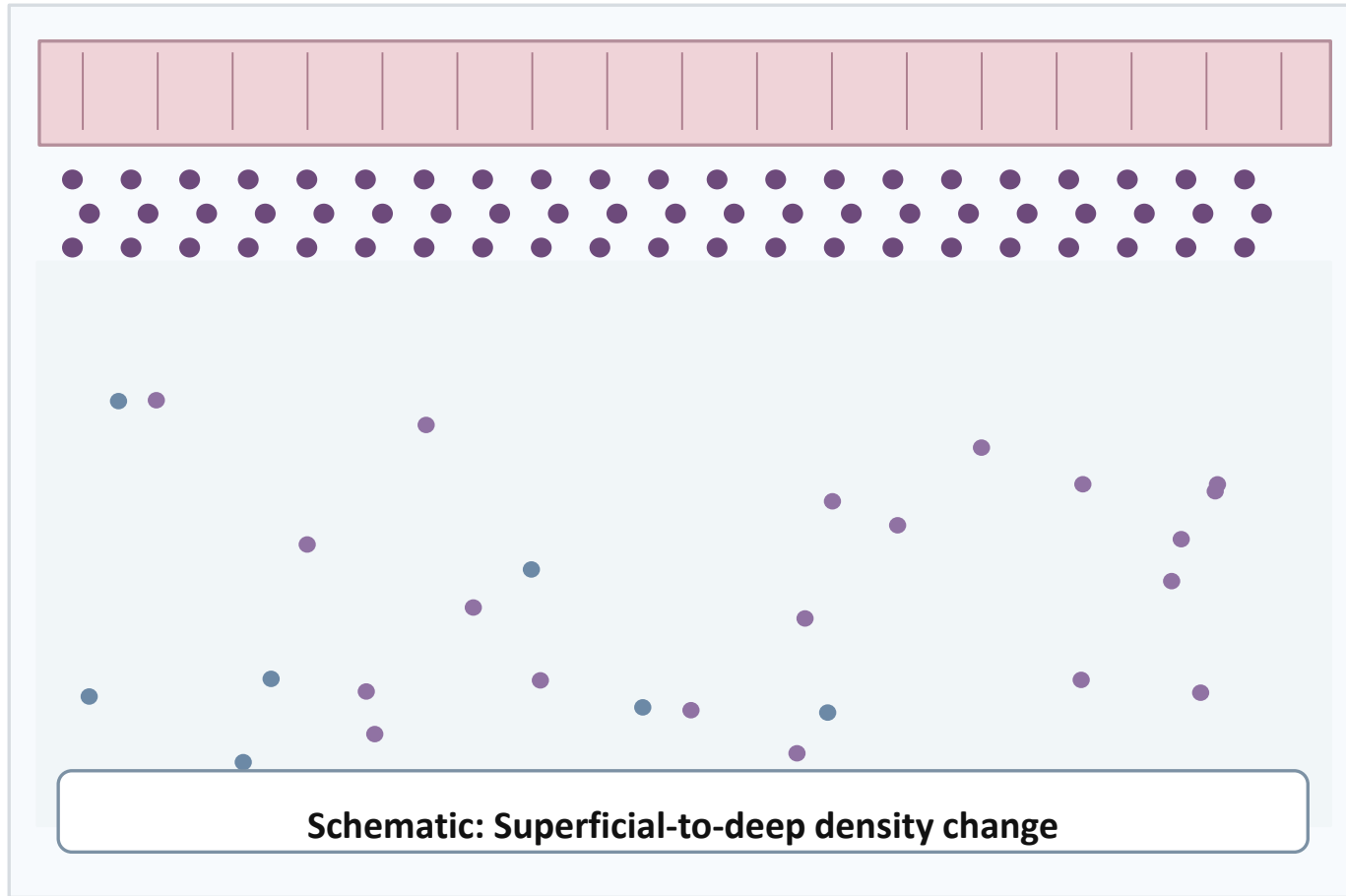


An immediately subepithelial band of crowded malignant cells

Located under the vaginal epithelial surface, not inside epithelium

The name describes an arrangement of cells rather than a distinct cell type

The cambium layer creates a cellularity gradient

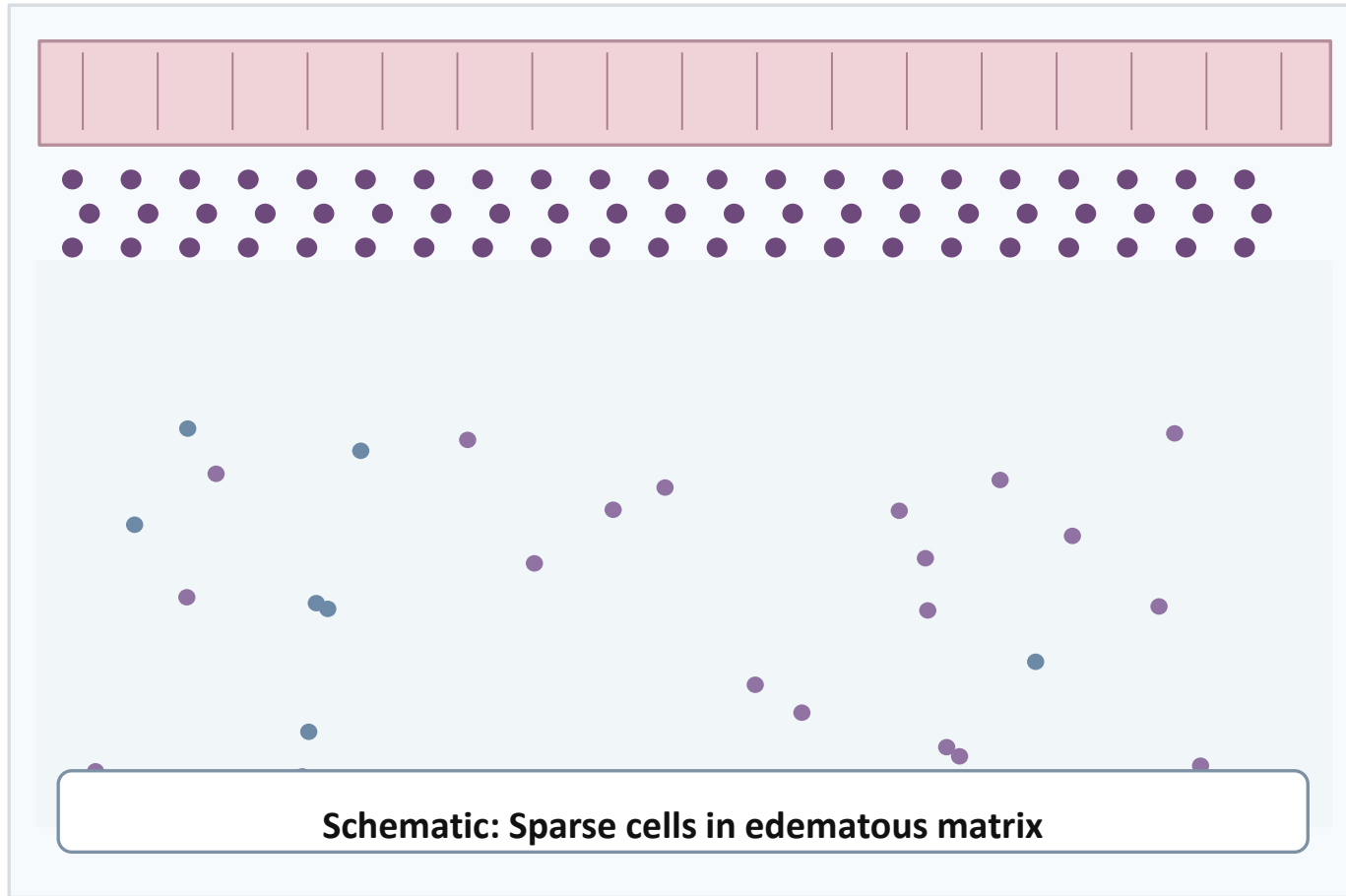


Subepithelial tumor-cell density is relatively high

Cellular density decreases in the deeper myxoid region

Both zones belong to the same malignant process

Deeper tissue may be markedly edematous

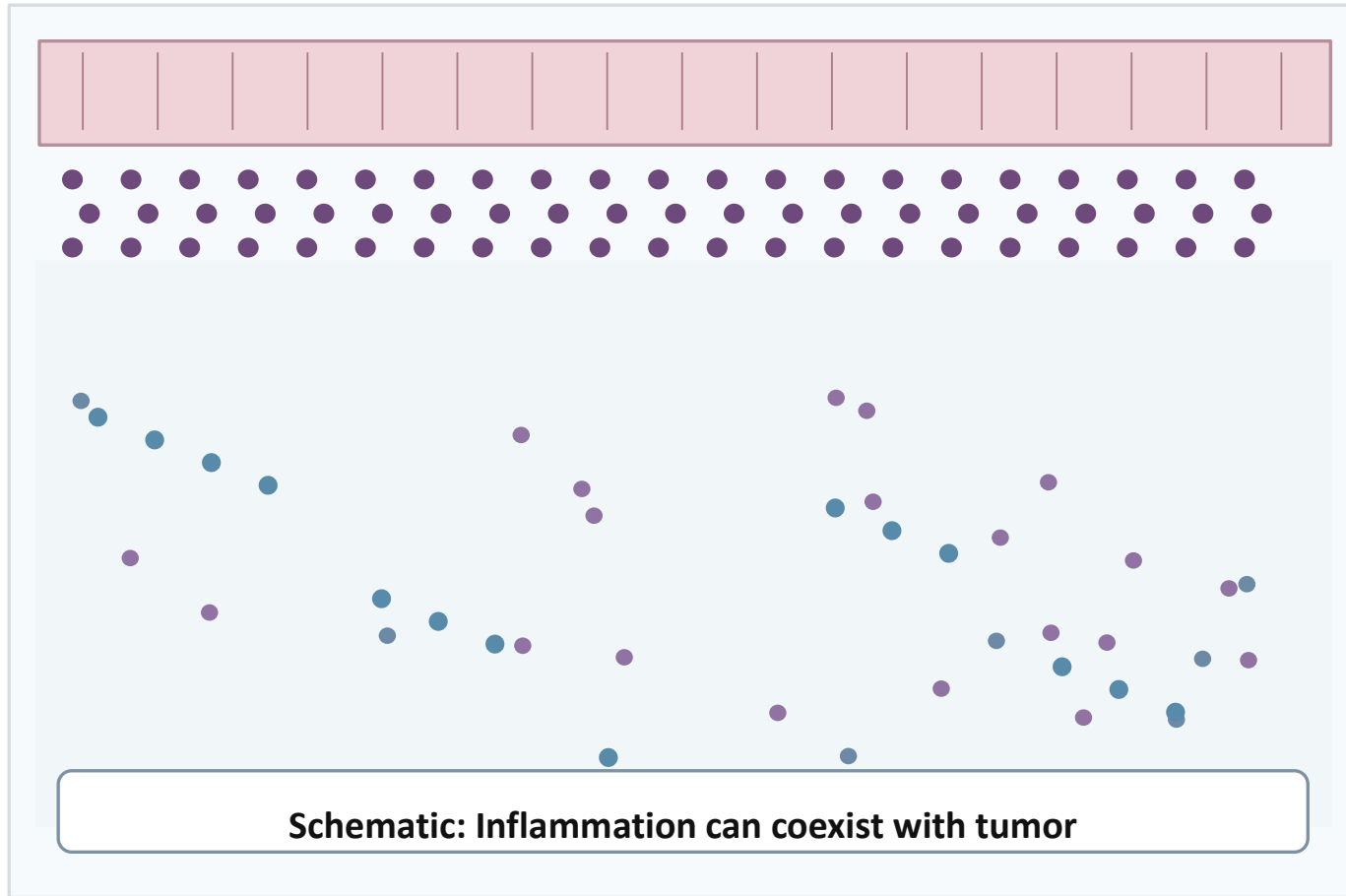


The deep tumor compartment contains loose fibromyxomatous tissue

Abundant pale matrix can separate neoplastic cells widely

Low cellularity in a field does not imply a reactive lesion

Inflammation is compatible with malignancy

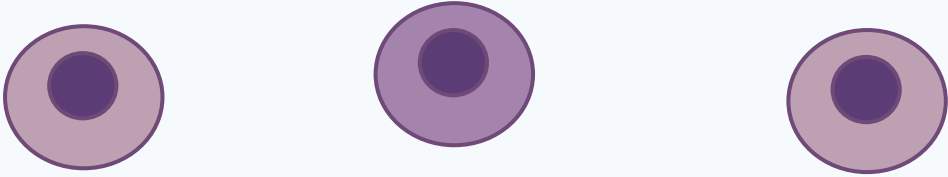


Many inflammatory cells may populate the stroma

Inflammation should not be treated as proof of a benign polyp

Search carefully for subepithelial atypical neoplastic cells

Tumor cells may be small and oval



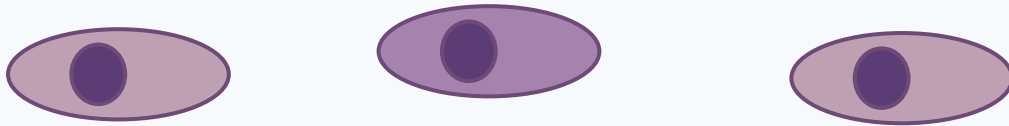
Schematic: Primitive small cells

Primitive malignant cells have small, oval nuclei

Their appearance can be less conspicuously myogenic than mature forms

Architecture and sampling context are important

Primitive cells can be round or spindle-shaped



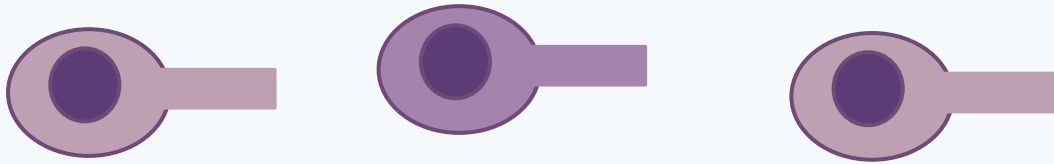
Schematic: Round–spindled spectrum

Chapter 26 describes primitive round and spindled cells

They can form sheets in a myxoid stromal background

Variation within one tumor is characteristic of embryonal morphology

A protruding cytoplasmic tail suggests myogenic differentiation



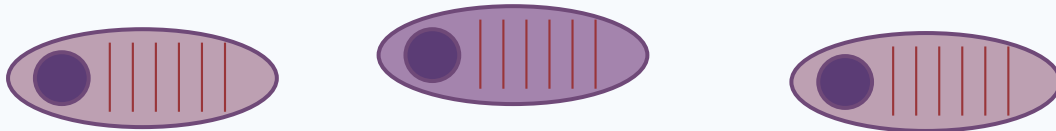
Schematic: One-sided cytoplasmic projection

Some rhabdomyoblasts have cytoplasm extending from one end

The resulting “tennis-racket” silhouette is

Morphology is supportive but not sufficiently sensitive alone

Cross-striations are specific but often difficult to find



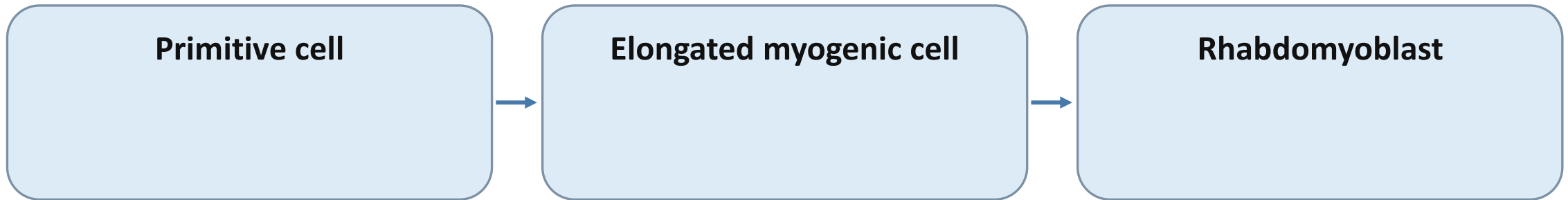
Schematic: Rare cross-striations

Cross-striations indicate skeletal muscle differentiation

They are described as rare in the vaginal embryonal tumor

Do not rule out rhabdomyosarcoma because striations are absent

Different maturational stages coexist

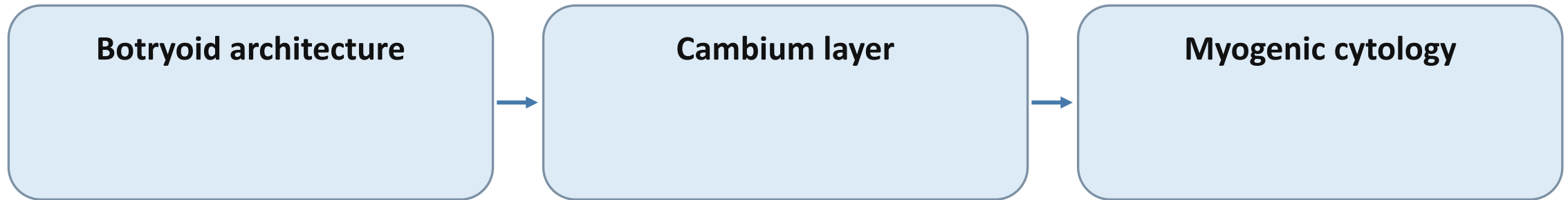


A field may contain undifferentiated small cells and eosinophilic rhabdomyoblasts

The broader spectrum helps link the primitive component to muscle lineage

Variable recapitulation of skeletal muscle development

Three linked morphological observations support diagnosis

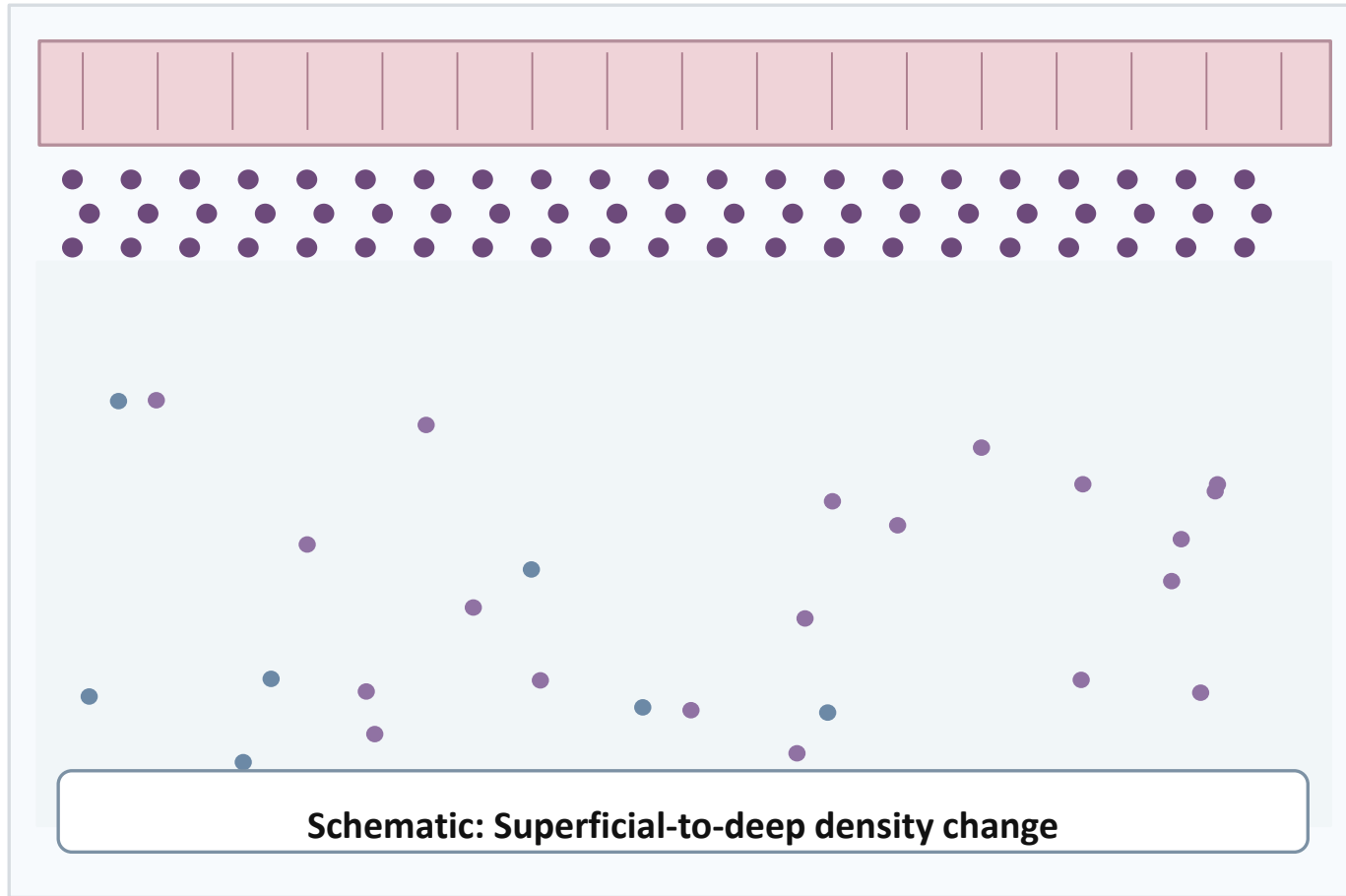


Polypoid mucosa-lined growth

Crowded subepithelial cambium layer

Primitive/rhabdomyoblastic cells in myxoid stroma

Low-power interpretation: Begin with architecture

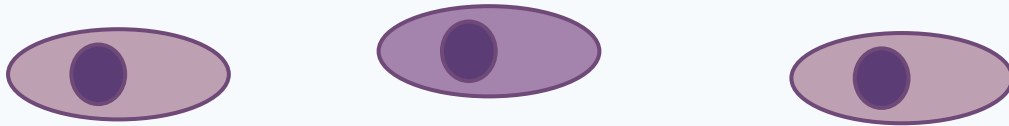


First identify the epithelial surface and any luminal projections

Then look for subepithelial condensation of tumor cells

Finally compare cellularity in deeper stroma

High-power interpretation: Define the neoplastic cells



Schematic: Round–spindled spectrum

Seek small oval or spindle cells within the loose stroma

Examine atypical cells for eosinophilic cytoplasm and elongated forms

Cross-striations, when present, support skeletal muscle differentiation

Sampling only edematous stroma risks under-recognition

Limited sample

Edema

Inflammation

Sparse tumor cells

More representative sample

Epithelium

Cambium layer

Primitive myogenic cells

The malignant cells reside beneath the vaginal epithelium



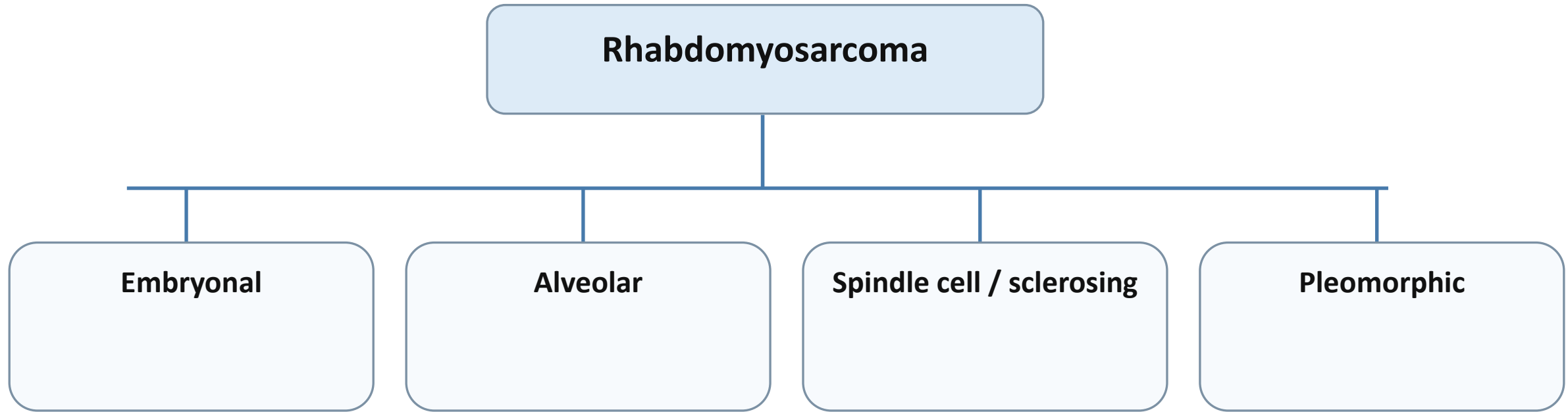
Schematic: Crowded subepithelial tumor cells

The overlying epithelial layer is not the neoplastic lineage

The tumor is a mesenchymal process in the underlying tissue

This relationship differentiates it from a primary epithelial carcinoma

Four broad rhabdomyosarcoma categories



Botryoid is a morphologic pattern within embryonal disease.

Embryonal is the pediatric reference subtype

Common childhood and adolescent rhabdomyosarcoma subtype

Frequently encountered in head/neck and genitourinary sites

Vaginal botryoid growth belongs within the embryonal family

Alveolar morphology is architecturally different

Embryonal / botryoid

Cambium layer near epithelium

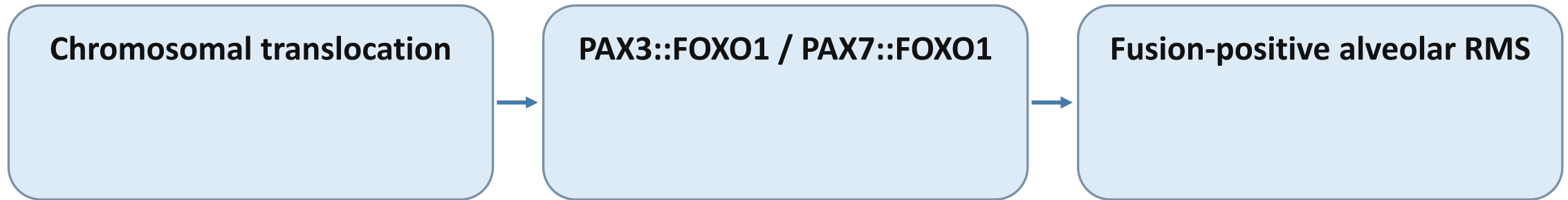
Variable cells in myxoid stroma

Alveolar

Fibrous septa

Discohesive central cells

Alveolar tumors frequently have PAX::FOXO1 fusions



FOXO1 fuses with PAX3 or PAX7 in many alveolar tumors

The fusion reflects a different molecular mechanism from typical embryonal tumors

Morphology and molecular characterization should be integrated

Spindle cell/sclerosing is a separate category

Fusiform tumor cells may form long fascicles or storiform areas

Some tumors show dense sclerotic stroma

A subset has MYOD1 alterations; Do not generalize to every case

Pleomorphic rhabdomyosarcoma usually affects adults

Large, bizarre or multinucleated malignant cells predominate

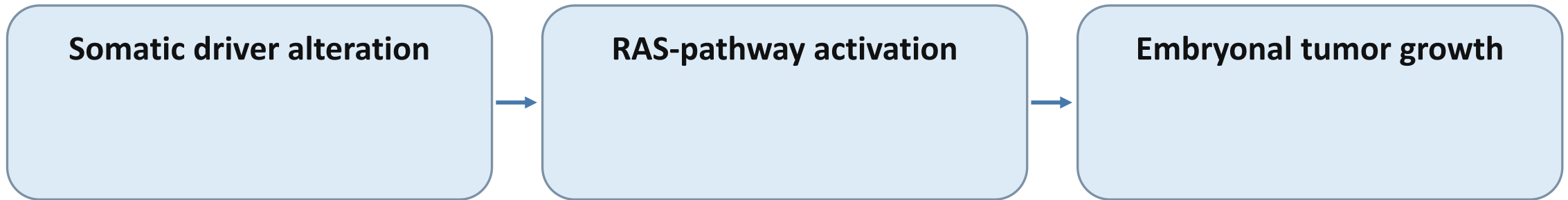
Morphology overlaps with other pleomorphic sarcomas

Myogenic immunostains help support classification

Subtype distinctions: Morphology and genotype

Subtype	Characteristic pattern	Molecular context
Embryonal	Primitive + differentiating cells	Frequent RAS pathway
Alveolar	Septated / discohesive aggregates	Often PAX::FOXO1
Spindle/sclerosing	Fascicular / sclerotic	MYOD1 in a subset
Pleomorphic	Bizarre pleomorphic cells	Genetically heterogeneous

RAS-pathway activation contributes to embryonal disease



Frequent somatic driver mutations activating RAS signaling

This provides molecular context for embryonal histology

A RAS-pathway variant is not required to identify every individual tumor

Embryonal and fusion-positive alveolar disease differ

Embryonal pattern

Commonly RAS-altered

Usually PAX::FOXO1-negative

Fusion-positive alveolar

PAX3::FOXO1 or PAX7::FOXO1

Distinct molecular group

Molecular testing must answer a defined question

Fusion testing is relevant to distinguishing certain rhabdomyosarcoma groups

A negative fusion result cannot independently prove botryoid architecture

Histology, phenotype, and the molecular result answer complementary questions

Myogenin supports skeletal muscle differentiation

Myogenin is a skeletal-muscle-related nuclear transcription factor

Myogenin immunohistochemistry as useful in RMS diagnosis

Interpret expression in morphologically identified tumor cells

A practical myogenic immunohistochemical panel

Marker	Cellular location	Interpretive role
Myogenin	Nucleus	Myogenic differentiation
MYOD1	Nucleus	Myogenic differentiation
Desmin	Cytoplasm	Muscle-associated marker

Nuclear versus cytoplasmic staining is meaningful

Nuclear

Myogenin

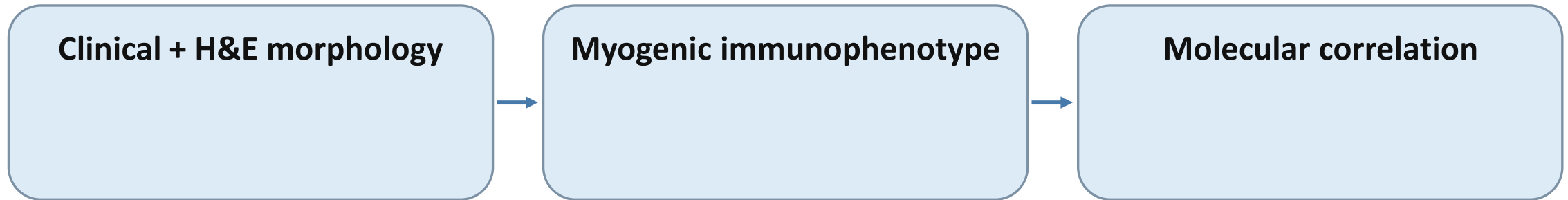
MYOD1

Cytoplasmic

Desmin

Different interpretive role

Diagnosis is an integrated tissue-based conclusion



Clinical setting and anatomy suggest the differential

H&E establishes malignant pattern and myogenic cytology

Immunohistochemistry substantiates lineage; Targeted molecular tests refine subgroup

Avoid single-marker diagnostic shortcuts

A positive myogenic marker does not establish a particular growth pattern

A negative fusion test does not replace a tissue diagnosis

Review morphology when IHC, site and age are discordant

Inflammatory polyp and botryoid RMS can look alike

Inflammatory polyp

Reactive/inflammatory appearance

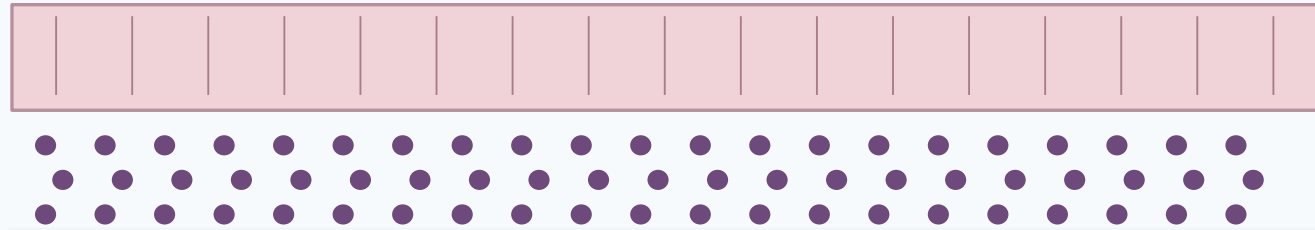
No established malignant myogenic
infiltrate

Botryoid embryonal RMS

Cambium layer

Primitive malignant rhabdomyoblasts

The critical distinction is malignant cellularity



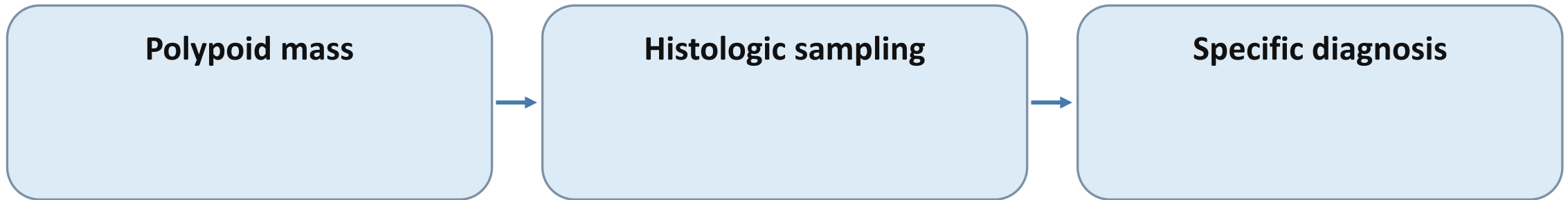
Schematic: Crowded subepithelial tumor cells

A benign label should not rest on edema or inflammation alone

Identify whether primitive atypical cells form a true subepithelial band

Integrate lineage testing if histologic findings warrant it

A vaginal polyp is a descriptive clinical finding



Polyp shape tells you how tissue projects into a lumen

It does not identify lineage or biological behavior

Histologic classification resolves the benign-versus-malignant question

Embryonal and alveolar patterns should not be conflated

Botryoid embryonal

Mucosa

Cambium

Myxoid stroma

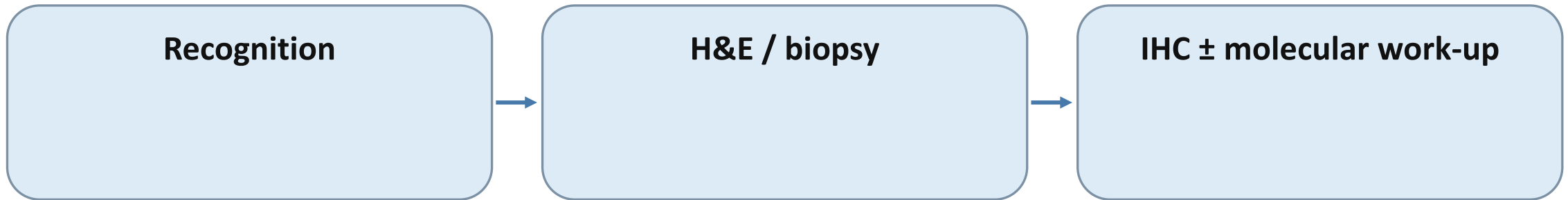
Alveolar

Fibrous septa

Central discohesion

FOXO1 fusion often

A stepwise diagnostic approach



Recognize the characteristic age/site and abnormal polypoid mass

Review low-power architecture and high-power rhabdomyoblasts

Confirm muscle lineage and classify appropriately

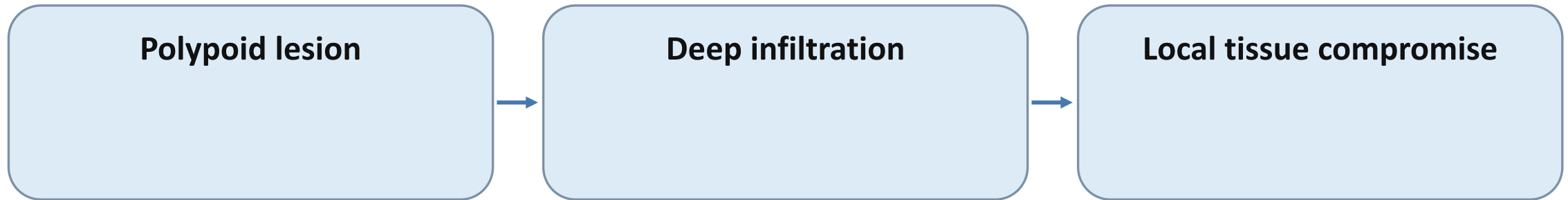
Pathology documentation should preserve the essentials

Record site and specimen type

Describe botryoid growth, differentiation and invasion when evaluable

Distinguish histologic category from margin or extent information

The disease is locally aggressive despite a polypoid surface



A tendency for local invasion

An exophytic component does not exclude deep extension

Anatomic extent influences treatment planning

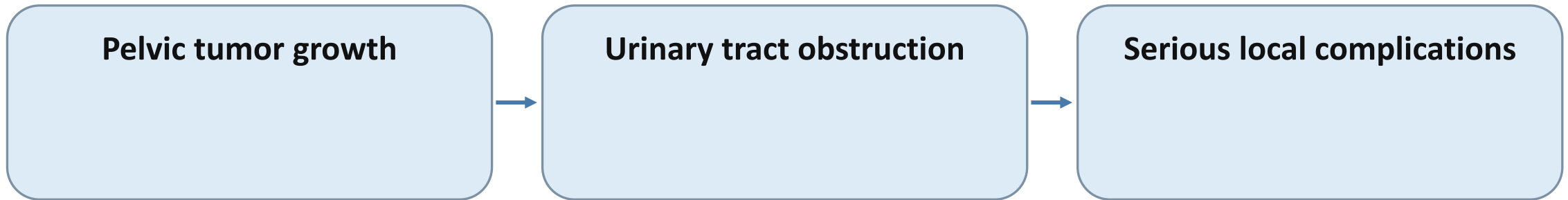
Peritoneal penetration is a severe local hazard

Penetration into the peritoneal cavity

The threat reflects invasive extension, not merely surface bulk

Extent assessment is clinically necessary

Urinary tract obstruction is another major danger



Expansion or invasion near pelvic urinary structures can obstruct outflow

Obstruction as a potentially fatal consequence

Assess urinary tract compromise when clinically suspected

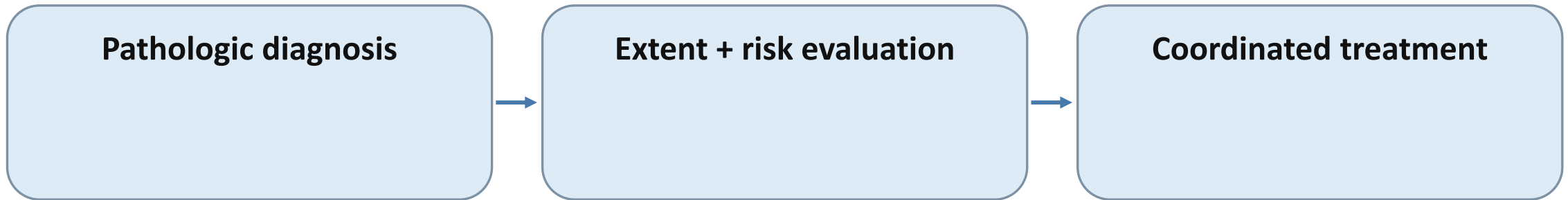
Early recognition creates a chance for organ preservation

Misclassification as benign inflammation may delay oncologic assessment

Robbins favors conservative surgery combined with chemotherapy

Approach should be individualized by disease extent and pediatric oncology review

Rhabdomyosarcoma requires multimodal treatment planning



Surgery and systemic chemotherapy are principal modalities

Radiation may be incorporated in selected risk-/site-dependent settings

Management needs specialist, multidisciplinary assessment

Local control and systemic therapy address different risks

Local control

Conservative surgery when feasible

Anatomic preservation

Systemic control

Chemotherapy

Management of microscopic dissemination
risk

Do not confuse favorable subtype with benign behavior

Botryoid morphology as the most favorable RMS variant overall

This is a relative prognostic comparison across subtypes

Risk also depends on location, extent and treatment response

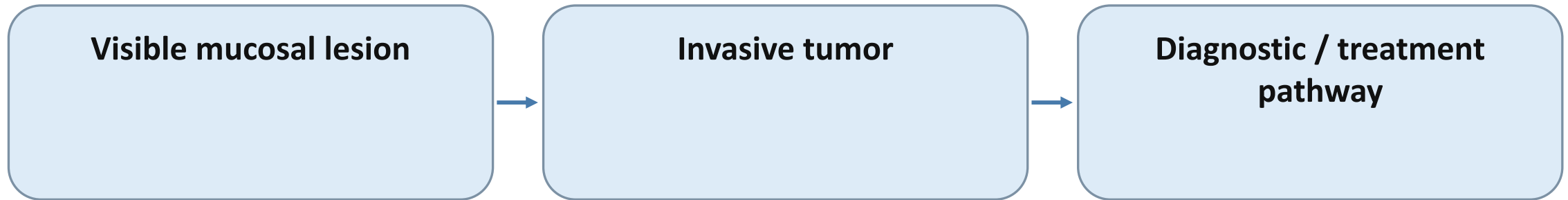
Modern terminology requires a qualification

Botryoid is a recognizable morphologic pattern of embryonal RMS

Current WHO/NCI classification does not treat it as a separate major RMS entity

Historical prognostic differences partly reflect site and risk features

Clinical morphology can be tied to consequences



Surface botryoid growth may prompt recognition

Deep extension makes the lesion clinically dangerous

Timely pathological diagnosis enables staging and multimodal management

Case 1: Grape-like mass in a toddler

Clinicopathologic problem

A 2-year-old has a rapidly enlarging polypoid mass at the vaginal introitus

What malignant diagnosis must be considered despite the polypoid contour?

Which part of the biopsy should be examined especially closely?

Case 1: Explain the finding

Interpretation and reasoning

Consider embryonal rhabdomyosarcoma with botryoid morphology

Assess the epithelial interface for a cambium layer

Look for malignant primitive cells and rhabdomyoblastic differentiation

Case 2: Edematous polyp biopsy

Clinicopathologic problem

A sampled lesion shows loose myxoid stroma and inflammatory cells

A more superficial field shows a crowded band of small oval malignant cells

How should the superficially bland stroma be interpreted?

Case 2: A reassuring stroma can mislead

Interpretation and reasoning

The deep stroma is part of the described botryoid pattern

The subepithelial cambium band is a major diagnostic clue

Inflammation does not negate malignancy

Case 3: An RMS with alveolar architecture

Clinicopathologic problem

Fibrous septa partition discohesive tumor-cell clusters

A PAX3::FOXO1 fusion is identified

Which subtype best matches the composite findings?

Case 3: Distinguish the molecular subgroup

Interpretation and reasoning

These findings support fusion-positive alveolar rhabdomyosarcoma

They do not describe the classic vaginal botryoid pattern

Tumor taxonomy should integrate histology and molecular evidence

Five diagnostic errors worth avoiding

Calling a childhood vaginal polyp inflammatory without checking its cambium zone

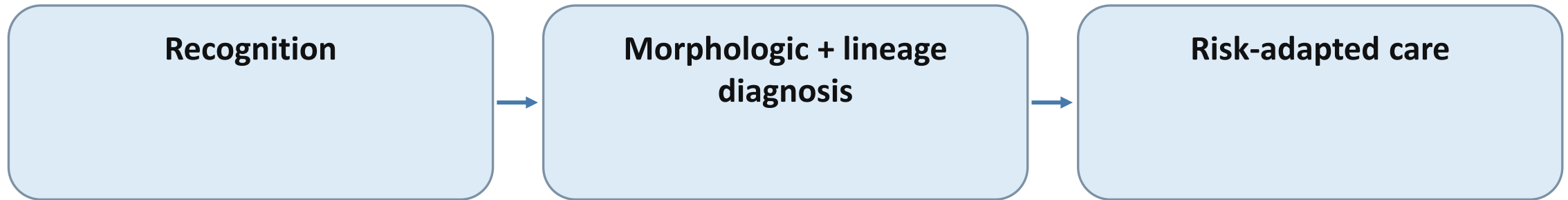
Expecting cross-striations in every case

Using edema as evidence against malignancy

Equating every rhabdomyosarcoma with PAX::FOXO1 positivity

Treating botryoid morphology as evidence of indolence

The clinicopathologic synthesis



A young child with a grape-like vaginal mass raises strong suspicion

Cambium layer + myxoid stroma + primitive/rhabdomyoblastic cells define its morphology

Myogenic IHC confirms differentiation; Extent and risk guide treatment

References and source boundaries

Robbins, Cotran & Kumar, Pathologic Basis of Disease, 11th ed. (2026), Ch. 22, p. 904;
Ch. 26, pp. 1102–1103

NCI PDQ Childhood Rhabdomyosarcoma Treatment (current online professional summary)

NCI PDQ Childhood Cancer Genomics (current online professional summary)

Additional clinical presentations are examples, not statistics or diagnostic criteria