

Tumors and Tumor-Like Lesions of Infancy and Childhood

Pediatric pathology: developmental lesions, benign neoplasms and childhood malignancies

Classification • morphology • clinicopathologic reasoning

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Learning goals for the pediatric mass

- Classify heterotopia, hamartoma and neoplasm without assuming that every mass is malignant.
- Explain why mature, bland tissue can produce clinically important complications.
- Recognize characteristic benign childhood tumor groups and the embryonal malignant phenotype.
- Integrate location, morphology, molecular findings and developmental context in diagnosis.

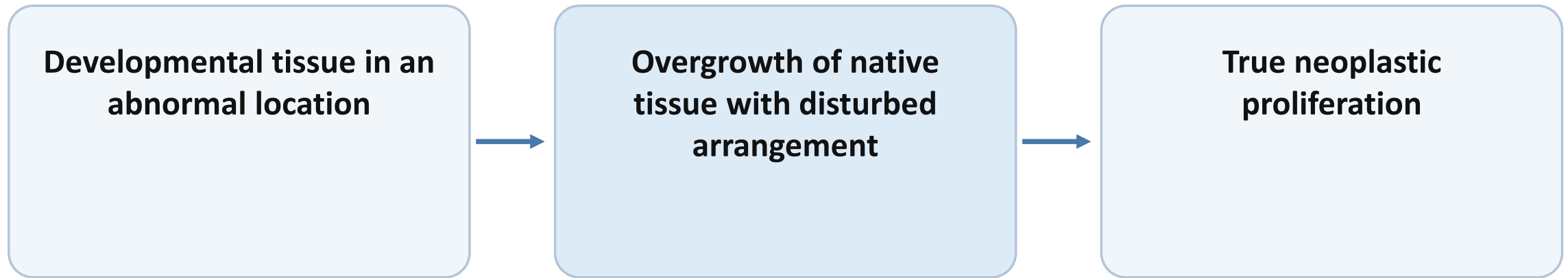
Why childhood masses require a distinct framework

- Benign lesions outnumber malignancies in infancy and childhood.
- Developmental abnormalities can mimic true neoplasia.
- Lesion size and location may determine morbidity despite benign histology.
- Pediatric malignancies differ from adult cancers in histogenesis and natural history.

Childhood cancers: Uncommon but consequential

- Only about 2% of malignant tumors occur during infancy or childhood.
- Its cited U.S. Mortality context identifies cancer, including leukemia, as a major cause of death at ages 5–14 years.
- These textbook figures describe epidemiologic context, not contemporary surveillance estimates.

The first diagnostic fork is lesion type



Ask whether the tissue belongs here, whether its architecture is normal, and whether the lesion represents a neoplasm.

The word “tumor” does not establish neoplasia

Mass-forming process

- A clinically visible or palpable lesion
- May represent a developmental process
- May have entirely mature cells

Neoplastic process

- A proliferative lesion with neoplastic biology
- Can be benign or malignant
- Morphology and clinical context determine interpretation

Architecture, location and behavior are separate axes

Location

Native site or ectopic site?

Architecture

Organized like normal tissue or disordered?

Behavior

Stable, enlarging, involuting, locally aggressive or metastatic?

One axis cannot safely substitute for the others.

Heterotopia means normal tissue in an abnormal site

- Heterotopia is synonymous with choristoma in this textbook context.
- The cells and tissues are microscopically normal but anatomically misplaced.
- A heterotopic focus may resemble a tumor during examination or imaging.
- Most heterotopic rests have little clinical significance.

Heterotopia: Site, not cytologic atypia, is abnormal

Microscopic identity

Mature tissue retains its recognizable differentiation.

Anatomic relation

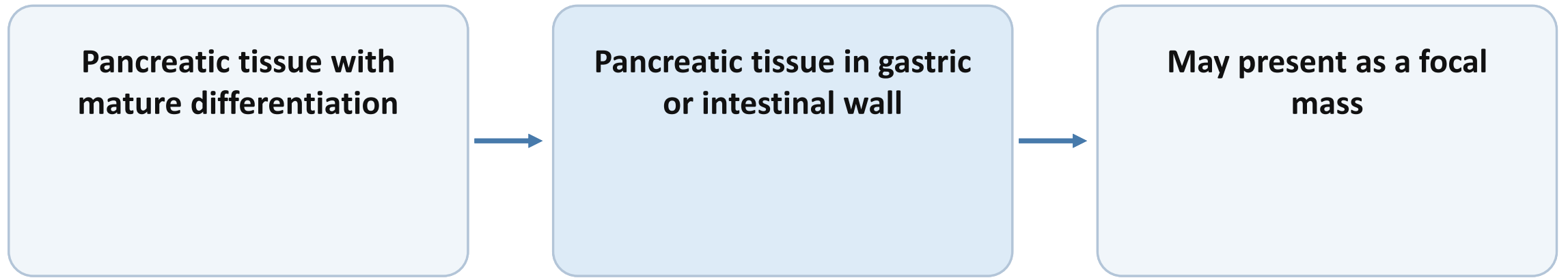
The tissue is located outside its usual organ.

Interpretation

The mass is usually developmental rather than a primary malignancy.

Conceptual schematic: These boxes do not depict real histology.

Ectopic pancreatic tissue as a heterotopia

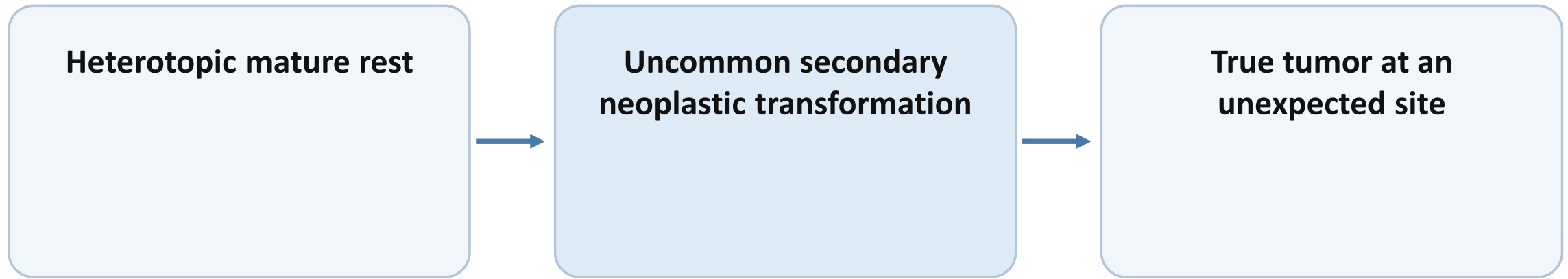


Pancreatic rests in stomach or small intestine as examples of heterotopia.

Ectopic adrenal tissue as a diagnostic trap

- Adrenal rests may occur in kidney, lung or ovary.
- A mass composed of adrenal tissue in the ovary is not automatically an ovarian primary tumor.
- Cell identity and anatomic setting must both be evaluated.
- The rare possibility of a true neoplasm arising in an ectopic adrenal rest.

Heterotopia and neoplasia are not mutually exclusive



The textbook example is an adrenal cortical carcinoma arising in ovarian ectopic adrenal tissue.

Heterotopia: Practical diagnostic questions

- Is the tissue identical to a mature tissue normally found elsewhere?
- Is its location truly ectopic rather than an extension of the native organ?
- Is there convincing neoplastic cytology, invasion or destructive growth?
- Can the clinical and anatomic findings be explained by a developmental rest?

Hamartoma is disorganized overgrowth at a native site

- A hamartoma is a focal, excessive growth of tissue native to the affected organ.
- Its cellular elements are mature and recognizable.
- Normal tissue proportions or architecture are not faithfully reproduced.
- Maturity does not guarantee that the lesion is harmless.

The defining hamartoma problem is tissue arrangement

Cell identity

Mature, native tissue components.

Growth

Excessive local development or proliferation.

Architecture

Disordered relationships rather than normal organ pattern.

Simplified conceptual distinction; Not a photomicrograph.

Why hamartomas are not simply normal tissue

Normal organ

- Expected cell proportions and spatial relationships
- Integrated organ architecture
- No discrete expansile overgrowth

Hamartoma

- Localized excess of native elements
- Disrupted tissue organization
- Can form a clinically significant mass

Hamartoma versus benign neoplasm: A blurred boundary

- The textbook cautions that both lesions may be clonal.
- Clonality alone does not settle whether a lesion should be named hamartoma or benign neoplasm.
- Clinical behavior, tissue organization and established entity definitions remain relevant.

Entities variably called hamartomas

Vascular / muscular

- Hemangiomas
- Lymphangiomas
- Cardiac rhabdomyomas

Glandular / cystic

- Hepatic adenomas
- Developmental cysts of kidney
- Developmental cysts of lung or pancreas

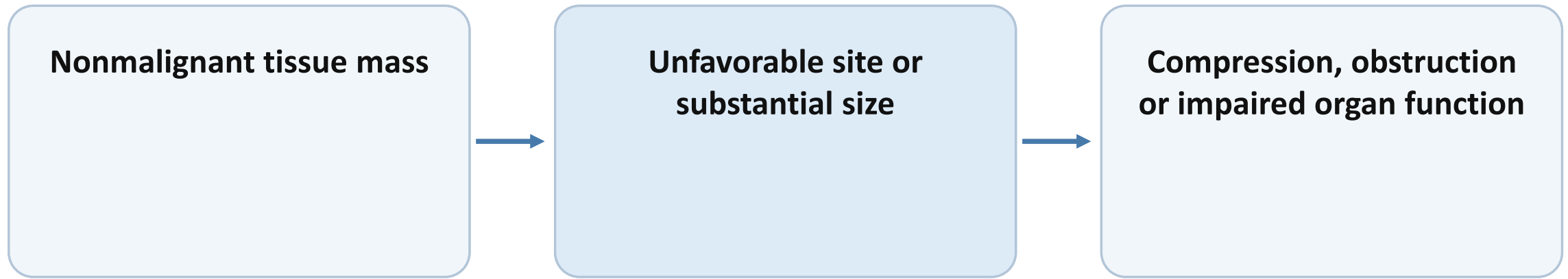
Cardiac rhabdomyoma illustrates organ-specific risk

- Cardiac rhabdomyoma among lesions variably regarded as hamartomas or neoplasms.
- The same bland histology can matter differently depending on location.
- An intracardiac mass deserves assessment for functional effects rather than classification alone.

Developmental cysts belong in the mass differential

- Developmental cysts of kidney, lung and pancreas are listed among hamartoma-like lesions.
- A cystic mass should not be presumed neoplastic solely because it distorts the organ.
- Architecture, organ of origin and clinical impact guide interpretation.

Why benign histology may still be dangerous



Biologic benignity and clinical harmlessness are different propositions.

Risk assessment is not equivalent to malignancy grading

Histology

Does the lesion show malignant features?

Anatomy

Does it threaten vital structures?

Course

Is it growing, stable or involuting?

A bland lesion may still require careful clinical evaluation.

Heterotopia, hamartoma and neoplasm compared

Feature	Heterotopia	Hamartoma	Neoplasm
Tissue location	Ectopic	Native organ	Variable
Cell differentiation	Usually normal/mature	Mature/native	Variable
Architecture	Often organ-like rest	Focally disordered	Entity-dependent
Key question	Why is it here?	Why is it overgrown?	What is its biologic behavior?

Case: An ovarian mass containing adrenal tissue

CLINICOPATHOLOGIC APPLICATION

- A young child has a small ovarian lesion composed of recognizable mature adrenal cortical cells.
- Which diagnostic category should be considered before assuming an ovarian neoplasm?
- What additional findings would suggest a true neoplasm in the ectopic rest?

Benign childhood tumors have a different tissue spectrum

- Pediatric solid tumors commonly arise from mesenchymal tissue.
- The textbook contrasts this pattern with the predominance of epithelial tumors in adults.
- Hemangiomas, fibrous lesions and teratomas receive special attention in infancy and childhood.

Mesenchymal predominance: Practical implications

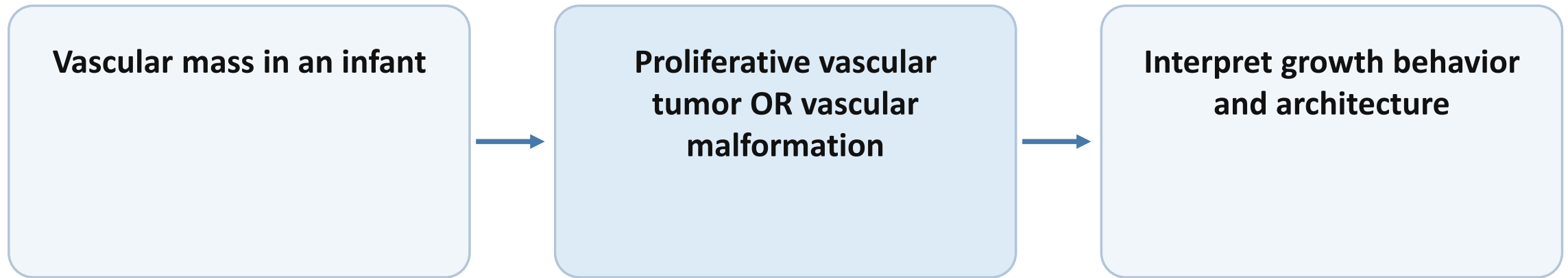
Childhood emphasis

- Vascular proliferations
- Fibroblastic/myofibroblastic lesions
- Embryonal and germ-cell neoplasms

Adult contrast

- Epithelial tumors are prominent
- Organ-specific epithelial primaries dominate many common cancer sites
- Age changes the prior diagnostic probability

Vascular lesions are not a single biological group



The term “hemangioma” has historically been used inconsistently for some malformations.

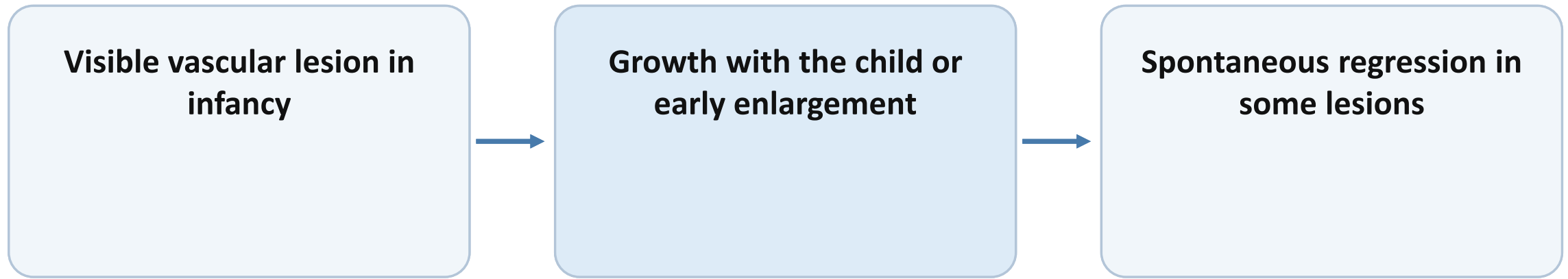
Vascular tumor versus vascular malformation

Concept	Proliferative vascular tumor	Vascular malformation
Defining issue	Vascular cellular proliferation	Structural vascular anomaly
Terminology	Hemangioma used for many benign tumors	May also be mislabeled “hemangioma”
Diagnostic caution	Identify proliferation	Avoid deciding solely by surface appearance

Where infantile vascular masses are encountered

- Most arise in skin, especially head and neck regions.
- They may form flat or raised red-blue masses.
- The category includes lesions clinically described as port-wine stains.
- A superficial color pattern is not sufficient to determine underlying biological type.

Some vascular lesions enlarge then regress



Variability; Involution is not a universal feature of vascular anomalies.

Familial vascular malformations: A molecular example

- A subset of CNS cavernous vascular malformations occurs in familial settings.
- KRIT1, CCM2 and PDCD10 as implicated genes.
- This illustrates that vascular anomalies may reflect inherited developmental signaling defects.

Fibrous childhood lesions form a biologic spectrum

Fibromatosis

- Sparsely cellular spindle-cell proliferation
- Fibroblastic or myofibroblastic lineage
- Behavior must be judged in context

Infantile fibrosarcoma

- Cellular lesion resembling adult fibrosarcoma
- Molecularly distinctive in many cases
- Generally favorable prognosis relative to adult counterpart

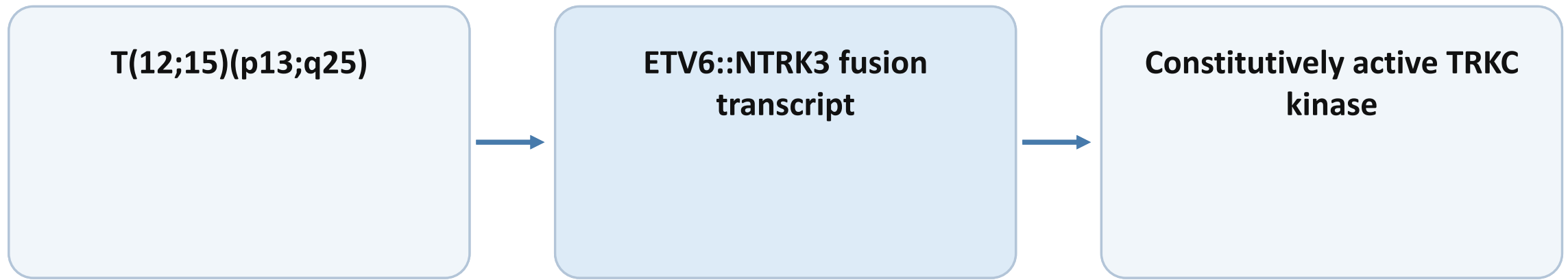
Fibromatosis: A spindle-cell pattern

- Relatively sparsely cellular proliferations of spindle-shaped cells.
- A spindle-cell appearance is a morphologic description, not a stand-alone risk category.
- Anatomic extent and clinicopathologic context remain necessary.

Infantile fibrosarcoma: Morphology can mislead

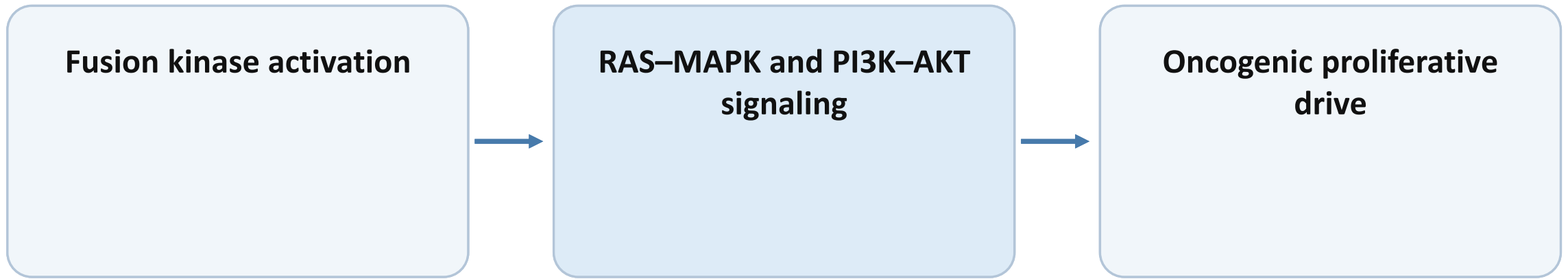
- Histology may closely resemble adult fibrosarcoma.
- Despite this resemblance, infantile fibrosarcoma generally has an excellent prognosis.
- The distinction highlights why age and specific molecular alterations matter in pediatric pathology.

ETV6::NTRK3 is a characteristic oncogenic fusion



The fusion is especially useful diagnostically among soft-tissue tumors account.

How ETV6::NTRK3 produces a growth signal



A mechanistic rationale for targeted inhibition, rather than a generic histology label.

Molecular classification can change treatment options

- Infantile fibrosarcomas with ETV6::NTRK3 fusion may respond to selective NTRK inhibition.
- Robbins specifically describes marked responses in previously unresectable fusion-positive lesions.
- Treatment selection requires actual molecular characterization; Morphologic resemblance is insufficient.

Teratomas illustrate differentiation versus behavior

- Teratomas can contain tissue differentiated along germ-layer lineages.
- The textbook separates mature, immature and overtly malignant forms.
- A high degree of histologic maturation does not automatically settle clinical risk in every setting.

Three germ layers underpin teratomatous tissues

Ectoderm

Examples include neural or squamous epithelial differentiation.

Mesoderm

Examples include muscle or connective tissue differentiation.

Endoderm

Examples include glandular epithelial differentiation.

Conceptual lineage map; These are examples of tissue differentiation, not a diagnostic micrograph.

Teratoma categories differ in biological potential

Category	Core histologic pattern	Interpretation
Mature	Well-differentiated tissue types	Often benign; May be cystic
Immature	Immature tissue, commonly neuroepithelium	Potential correlated with immature tissue extent
Malignant	Unequivocal malignancy, often another germ-cell component	Requires identification of malignant component

Sacrococcygeal teratoma is a characteristic pediatric site

- Sacrococcygeal tumors as the most common childhood teratomas.
- They are frequently congenital and may attain considerable size.
- The anatomic setting creates a distinct clinical problem even before histologic classification.

Teratomas can accompany congenital anomalies

- Associations with hindgut and cloacal anomalies and midline defects.
- Examples include meningocele and spina bifida.
- The text does not attribute these anomalies simply to mass compression by the teratoma.

Mature and immature tissue can coexist

- A teratoma may include several well-differentiated tissue types.
- Immature neuroepithelial elements are particularly relevant when assessing immaturity.
- The search for an associated malignant germ-cell component is a separate diagnostic task.

Benign lesion family: Integrate composition with course

Lesion group	Clue to identity	Important caveat
Heterotopia	Normal tissue outside native site	Unexpected location may simulate neoplasm
Hamartoma	Disorganized native mature tissues	Can be symptomatic despite benign histology
Vascular anomaly	Vascular morphology; Variable course	Tumor and malformation are not synonyms
Fibrous lesion	Fibroblastic spindle-cell pattern	Age/molecular data alter expected behavior
Teratoma	Multiple differentiated tissue types	Maturity and malignant components must be assessed

Childhood malignancies differ from adult carcinomas

- Hematopoietic, neural, soft-tissue, bone and renal sites are prominent in pediatric cancers.
- Developmental pathways and constitutional predisposition play important roles.
- Primitive embryonal histology is common among pediatric solid cancers.
- Spontaneous differentiation or regression is documented in selected tumors.

Anatomic distributions create age-related priors

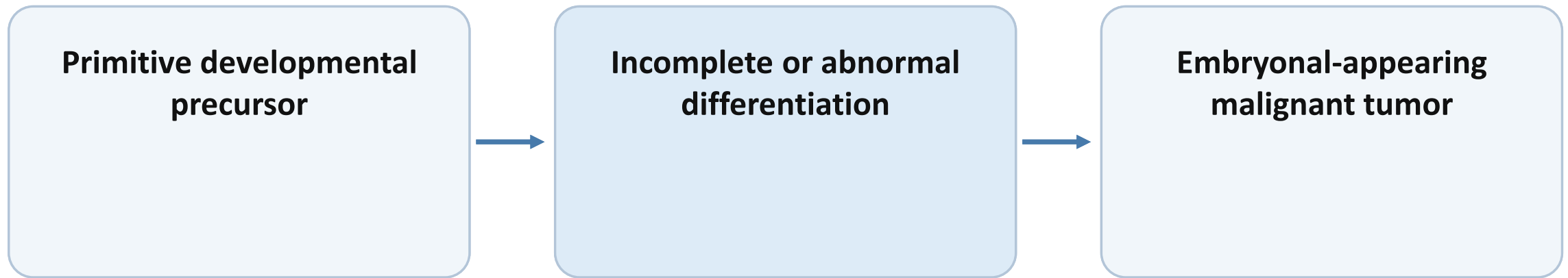
Children

- Hematopoietic system
- Central and sympathetic nervous system
- Soft tissue, bone and kidney

Adults

- Common cancers frequently involve epithelial sites
- Textbook examples: Lung, breast, prostate, colon and skin
- Clinical differential changes with age

Embryonal tumors resemble disrupted organogenesis



Organ-specific differentiation can still suggest the lineage of origin.

Why some pediatric tumors look “small round blue”

- Many malignant pediatric tumors comprise sheets of primitive cells.
- Cells often have scant cytoplasm and small dark nuclei.
- The shared appearance describes a pattern, not a single disease.
- Different origins demand clinicopathologic and ancillary discrimination.

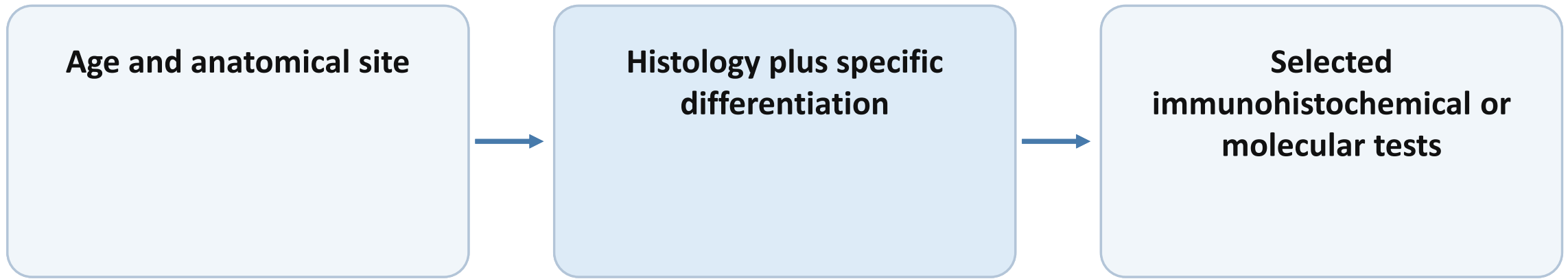
The “-blastoma” suffix signals embryonal differentiation

- Nephroblastoma, neuroblastoma and hepatoblastoma recall developing organ tissues.
- The suffix is a naming clue, not proof of a shared molecular mechanism.
- The anatomical site and observed differentiation constrain the diagnosis.

Small round blue cell tumors: Differential

Category	Examples	Distinguishing context
Neural	Neuroblastoma, medulloblastoma, retinoblastoma	Anatomic site and neural differentiation
Renal	Wilms tumor	Developing renal structures
Hematolymphoid	Lymphoma	Lineage-specific studies
Mesenchymal	Rhabdomyosarcoma, Ewing sarcoma	Lineage morphology and molecular studies

Site-first diagnostic reasoning reduces ambiguity



Location often makes the diagnosis possible, but some cases require ancillary studies.

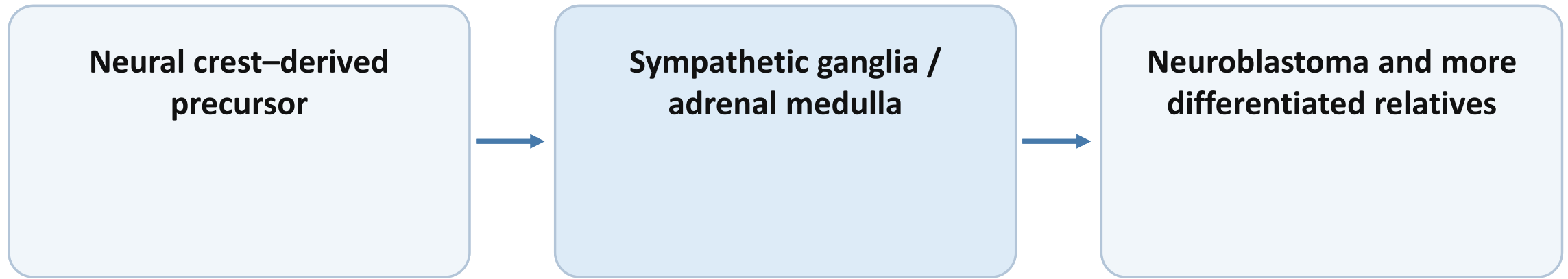
Developmental anomalies can signal tumor predisposition

- A close relationship between teratogenesis and oncogenesis in some childhood cancers.
- Congenital anomalies may identify an underlying tumor-predisposition syndrome.
- Hereditary aberrations are relatively more prominent in some pediatric tumor groups.

Spontaneous regression is a real but selective phenomenon

- Selected fetal and neonatal malignancies may regress or differentiate spontaneously.
- This phenomenon is especially important in some neuroblastic lesions.
- Regression is not a general permission to assume that an undiagnosed pediatric mass is innocuous.

Neuroblastic tumors arise along the sympathetic lineage



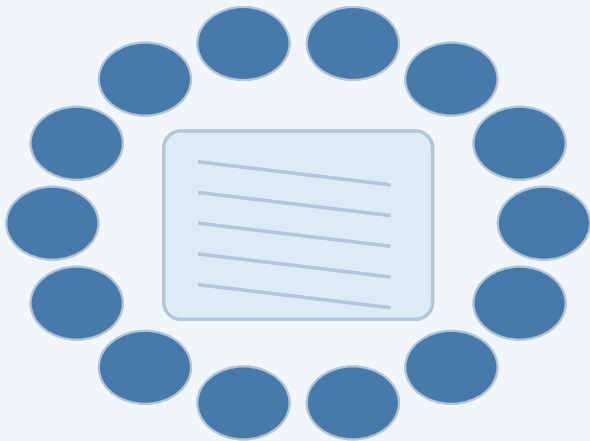
Neuroblastoma is a key pediatric embryonal tumor, discussed in depth in its dedicated series topic.

Where neuroblastoma begins and spreads

- The adrenal medulla is a prominent primary site.
- Other lesions occur along the sympathetic chain, including abdominal paravertebral and posterior mediastinal locations.
- Advanced tumors can involve lymph nodes, liver, bone and bone marrow.

Neuroblastoma has a recognizable primitive histology

Simplified Homer–Wright pseudorosette

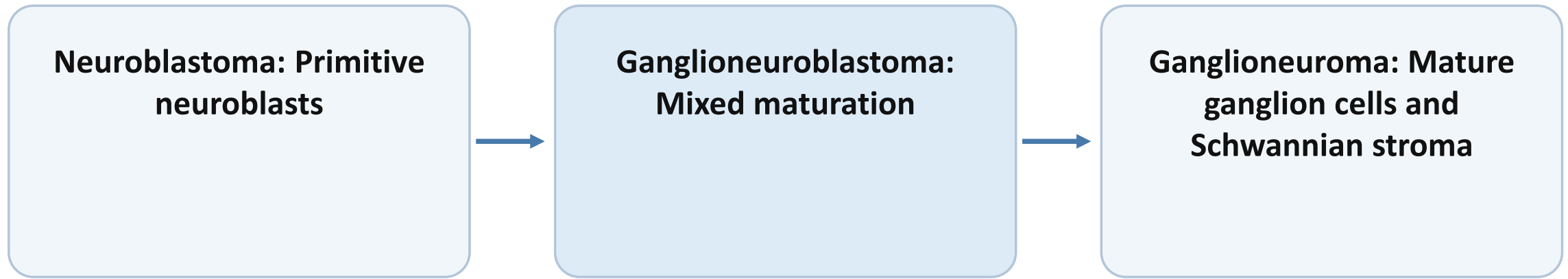


Central neuropil + surrounding primitive neuroblasts

- Sheets of small primitive cells contain dark nuclei and scant cytoplasm.
- Faint eosinophilic fibrillary neuropil reflects neuritic processes.
- Homer–Wright pseudorosettes contain central neuropil surrounded by neuroblasts.
- PHOX2B is a useful immunohistochemical lineage marker.

Original editable schematic — not histology

Neuroblastic tumors show a maturation continuum



These names denote differing degrees of differentiation rather than identical histology.

Neuroblastoma can produce catecholamines

- Most neuroblastomas synthesize catecholamines.
- Elevated urinary vanillylmandelic acid (VMA) and homovanillic acid (HVA) can support diagnosis.
- Catecholamine production does not imply that hypertension is as common as in pheochromocytoma.

Neuroblastoma prognosis is biologically heterogeneous

Clinical stage / age

Pretreatment extent and younger age influence risk.

Tumor differentiation

Schwannian stroma and maturation are favorable features.

MYCN / ploidy

MYCN amplification is adverse; Whole-chromosome gains can be favorable.

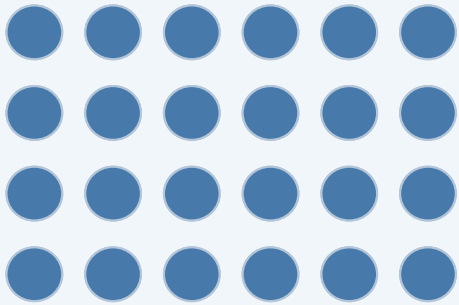
Avoid treating every neuroblastoma as equivalent in expected course.

Wilms tumor recapitulates developing kidney

- Wilms tumor (nephroblastoma) is the most common primary childhood renal neoplasm.
- Its cell populations represent abortive stages of nephrogenesis.
- Congenital malformation syndromes and genetic lesions reveal developmental mechanisms.

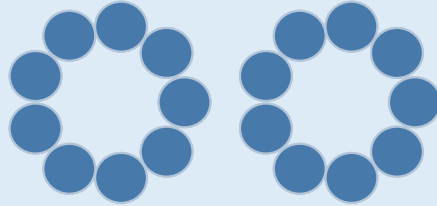
Triphasic Wilms tumor: Three diagnostic compartments

Blastemal



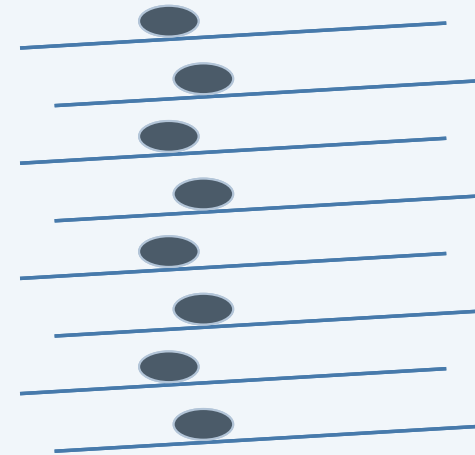
Primitive small blue cells

Epithelial



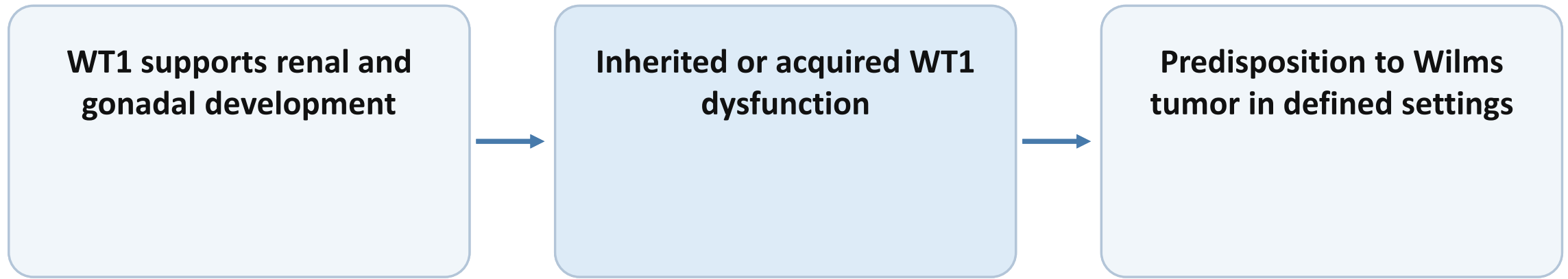
Abortive tubules or
glomeruloid forms

Stromal



Fibroblastic or myxoid
matrix

WT1 is a developmental tumor-suppressor example

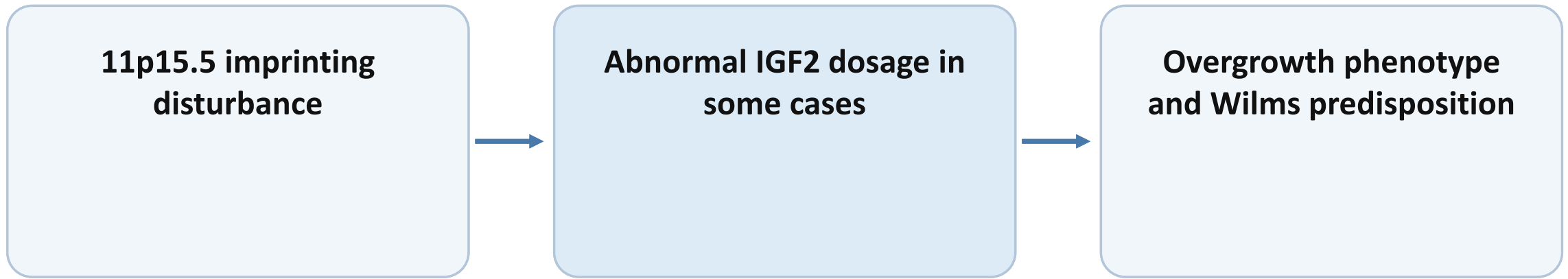


WAGR and Denys–Drash involve distinct WT1 abnormalities.

WAGR and Denys–Drash show different WT1 lesions

Syndrome	Genetic mechanism	Associated features
WAGR	11p13 deletion affecting WT1 and PAX6	Aniridia and genitourinary abnormalities
Denys–Drash	Dominant-negative WT1 DNA-binding-region mutation	Gonadal dysgenesis and early nephropathy

Beckwith–Wiedemann links imprinting to overgrowth



This mechanism is distinct from the WT1 lesions implicated in WAGR or Denys–Drash.

Nephrogenic rests connect malformation and cancer

- Nephrogenic rests are persistent embryonal renal tissue considered precursor lesions.
- They may be found near Wilms tumors and are particularly frequent in bilateral cases.
- Recognition of rests has implications for contralateral renal surveillance.

Anaplasia changes Wilms tumor risk

- Anaplastic areas contain enlarged hyperchromatic, pleomorphic nuclei and atypical mitoses.
- Anaplasia to TP53 alteration, chemotherapy resistance and adverse prognosis.
- Documenting anaplasia is therefore more consequential than merely describing a high mitotic count.

Two abdominal embryonal tumors: Major contrasts

Feature	Neuroblastoma	Wilms tumor
Lineage	Sympathetic neural crest / adrenal medulla	Developing renal tissue
Microscopic clue	Neuropil; Homer–Wright pseudorosettes	Blastema, tubules and stroma
Molecular clue	MYCN status in risk stratification	WT1 / imprinting pathways in predisposition
Clinical clue	Catecholamine metabolites may be elevated	Abdominal renal mass; Congenital associations

Survivorship changes the long-term pathology burden

- Advances in treatment have improved survival for many childhood cancers.
- Late effects of chemotherapy and radiotherapy have become increasingly important.
- Second malignancies can reflect treatment exposure, inherited risk or both.
- Judicious treatment intensity is part of the long-term clinicopathologic perspective.

Case integration: An infant with a spindle-cell mass

CLINICOPATHOLOGIC APPLICATION

- An infant has a rapidly enlarging soft-tissue mass composed of cellular spindle cells.
- Why should adult-type fibrosarcoma prognosis not be transferred automatically?
- Which characteristic molecular finding would be worth investigating?

Case integration: An abdominal embryonal tumor

CLINICOPATHOLOGIC APPLICATION

- A toddler has a large abdominal mass; The biopsy shows sheets of small dark cells.
- What additional anatomic information immediately narrows the differential?
- Which findings favor neuroblastoma versus a Wilms tumor?

A five-question checklist for any pediatric mass

- Is this ectopic normal tissue, disorganized native tissue or a neoplasm?
- Which developmental lineage and organ site are implicated?
- Does histology demonstrate differentiation, invasion or anaplasia?
- Which clinical course and molecular studies are characteristic?
- Could benign histology still conceal substantial local functional risk?

Synthesis: distinguish biology from clinical impact

- Heterotopia: normal tissue located where it does not belong.
- Hamartoma: excessive, disorganized overgrowth of tissues native to the organ.
- A morphologically benign lesion may still be clinically important because of its location or size.
- Childhood malignancies require age-appropriate, developmental and lineage-based interpretation.
- Integrate anatomy, morphology, and targeted molecular evidence rather than relying on the appearance of a mass alone.