

Metastatic Tumors

Metastases involving the central nervous system

Neuropathology • mechanisms, morphology and clinical correlation

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning objectives

- Identify the major primary sites responsible for metastatic CNS tumors.
- Explain the major steps of dissemination and cerebral colonization.
- Distinguish parenchymal masses from meningeal carcinomatosis.
- Correlate morphology, anatomic site and clinical effects.
- Apply the role and limitations of tissue morphology and immunohistochemistry.

A metastatic tumor is a discontinuous deposit

CORE CONCEPT

- Metastasis denotes spread of a primary cancer to a physically separate site.
- An intracranial metastasis is a secondary neoplasm, not a primary brain tumor.
- Metastatic capacity is a defining feature of malignant behavior.
- The histologic origin remains the parent tumor, even in a different organ.

CNS metastases are a major part of intracranial tumor practice

EPIDEMIOLOGIC FRAMING

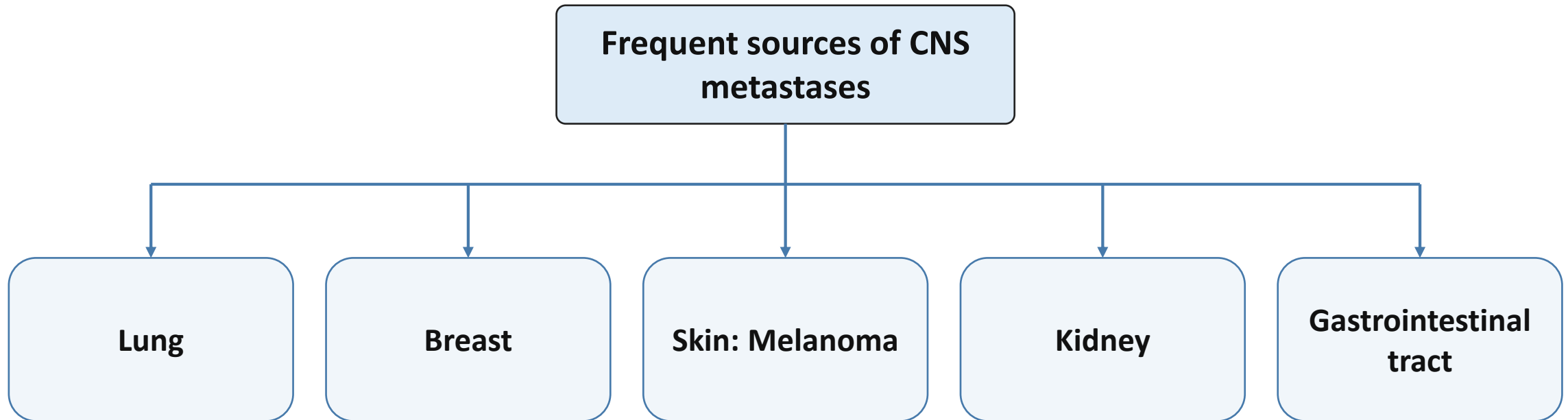
- In hospitalized patient series, metastatic lesions account for approximately one-quarter to one-half of intracranial tumors.
- This proportion describes an institutional case mix; It is not a population-wide incidence rate.
- The category includes metastatic carcinomas and other systemic malignancies.

Most CNS metastases are carcinomas

TUMOR IDENTITY

- Metastatic intracranial lesions as predominantly carcinomas.
- A known history of an epithelial malignancy changes the prior probability of a new brain mass.
- Histologic differentiation may persist in the deposit, supporting assignment to an extracranial primary.

The five most common primary sites



Together these sites contribute approximately 80% of metastases in the cited textbook series.

The “80%” observation is a combined category

INTERPRETING FREQUENCIES

- The five frequent primary sites collectively account for about 80% of brain metastases in the Robbins account.
- This is not a per-site distribution: The five contributions are not specified individually.
- Avoid converting that combined fraction into invented tumor-specific percentages.

Frequency and metastatic propensity are different concepts

RISK INTERPRETATION

- A primary may be common yet uncommonly seed the brain.
- Conversely, an uncommon primary may have a strong tendency for cerebral spread.
- Observed metastatic case frequency reflects both the number of primary cancers and their propensity to metastasize.

Contrasting examples of brain metastatic propensity

ILLUSTRATIVE PRIMARY TUMORS

Primary malignancy	Textbook characterization
Choriocarcinoma	Rare tumor, but high likelihood of cerebral metastasis
Prostatic adenocarcinoma	Common cancer, but brain metastases are exceptional
Lung carcinoma	One of the five most frequent sources of CNS metastasis

Why organ preference cannot be inferred from prevalence

TISSUE TROPISM

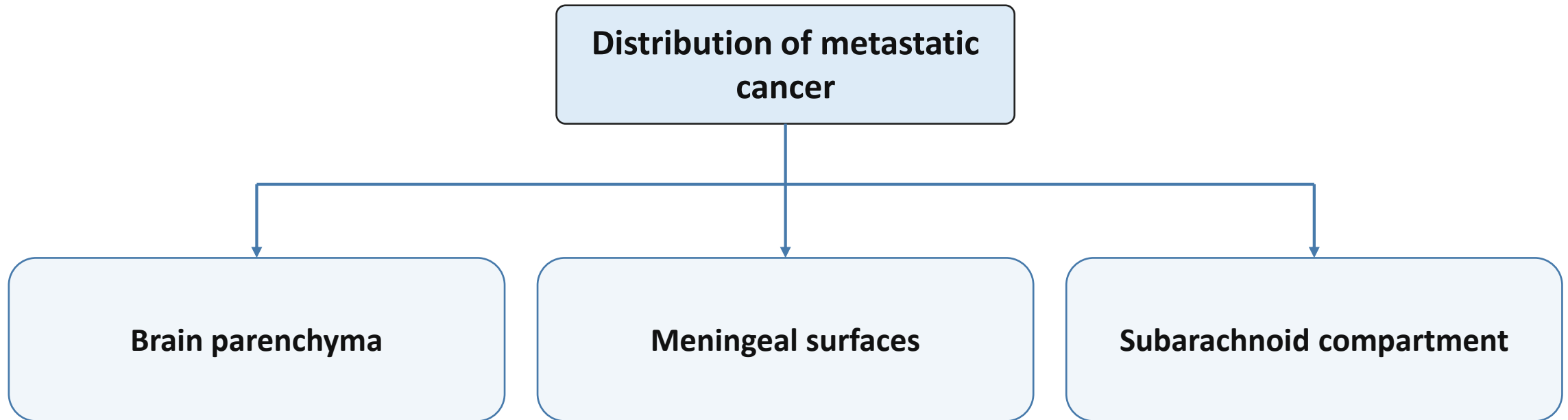
- The anatomy of vascular drainage affects where disseminated tumor cells travel.
- Tumor cell properties and the environment of the distant organ affect colonization.
- Consequently, brain metastatic propensity must not be inferred from the primary tumor's population frequency alone.

Metastasis and local invasion are not equivalent

MALIGNANT BEHAVIOR

- Locally invasive malignant neoplasms do not invariably establish distant deposits.
- CNS gliomas as an example: They invade locally but rarely metastasize outside the CNS.
- A secondary CNS deposit therefore cannot be diagnosed simply by observing infiltrative growth.

CNS involvement occupies distinct compartments



The clinical and pathologic manifestations depend on the anatomic pattern.

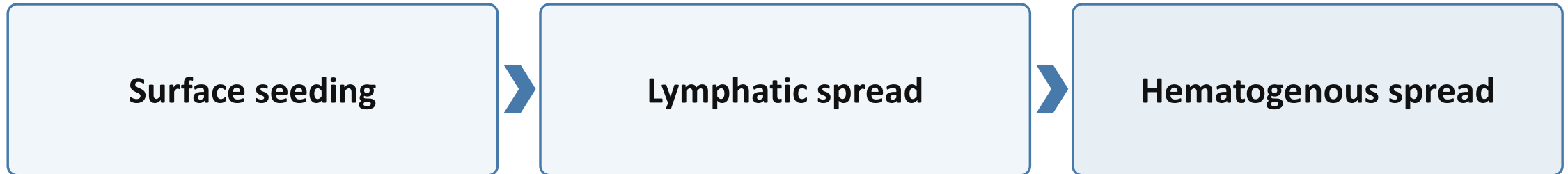
Parenchymal and meningeal involvement are distinct

ANATOMIC FRAMEWORK

Feature	Parenchymal deposit	Meningeal spread
Dominant pattern	Intraparenchymal mass	Surface nodules or diffuse subarachnoid involvement
Usual interface	Gray–white junction is common	Brain, cord and intradural nerve-root surfaces
Major effect	Mass lesion and edema	Neuropathies from nerve-root involvement

Three major pathways of cancer dissemination

CHAPTER 7 FRAMEWORK



- Cavitory surfaces include the meninges.
- Carcinomas commonly use lymphatics for initial dissemination.
- Blood-borne dissemination is an important route for distant organ deposits.

Routes describe general metastatic biology; Specific lesions may involve more than one mechanism.

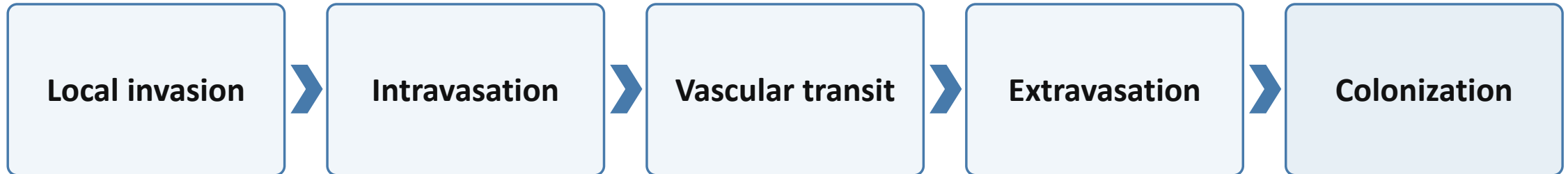
Hematogenous dissemination can deliver tumor cells to the CNS

CNS COLONIZATION

- The metastatic cascade requires entry of tumor cells into circulation.
- Blood-borne cells must survive transport, leave vessels and establish new growth.
- Normal vascular routes alone do not fully determine the observed organ specificity of metastases.

The metastatic cascade has sequential barriers

MECHANISTIC OVERVIEW



- A cell reaching the circulation has not necessarily formed a metastasis.
- Establishment of a growing secondary deposit is the decisive final step.

Reduced cell–cell adhesion facilitates escape

PRIMARY-SITE INVASION

- Tumor cells may alter adhesion molecules that normally maintain epithelial cohesion.
- Reduced cadherin-mediated adhesion is one recognized route toward an invasive phenotype.
- Changes in cellular adhesion must be integrated with matrix remodeling and movement.

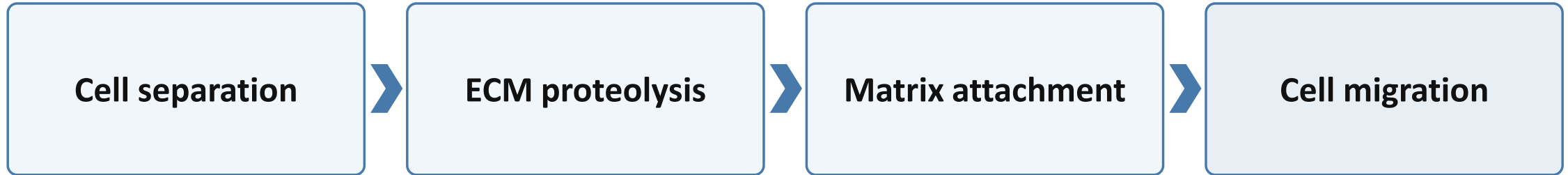
Extracellular matrix degradation permits migration

PRIMARY-SITE INVASION

- Invasion requires passage through basement membranes and interstitial matrix.
- Matrix metalloproteinases and other proteases can participate in degradation and remodeling.
- Tumor–stroma interactions influence the amount and spatial pattern of matrix breakdown.

The invasion sequence is coordinated

PRIMARY-SITE INVASION



- Changes in adhesion, protease activity and motility work as a linked process.
- The steps are conceptual; Actual tumor-cell invasion is not strictly linear.

Cell motility involves the cytoskeleton

PRIMARY-SITE INVASION

- Invasive migration requires attachment at the leading edge and detachment behind the cell.
- Actin cytoskeletal contraction provides the movement needed through remodeled matrix.
- Paracrine and autocrine signals can facilitate migration.

Intravasation opens access to distant organs

VASCULAR ACCESS

- Cancer cells must traverse endothelial barriers to enter blood or lymphatic spaces.
- Vascular invasion is associated with hematogenous dissemination.
- Entry into a vessel is necessary for blood-borne spread but insufficient to establish a brain deposit.

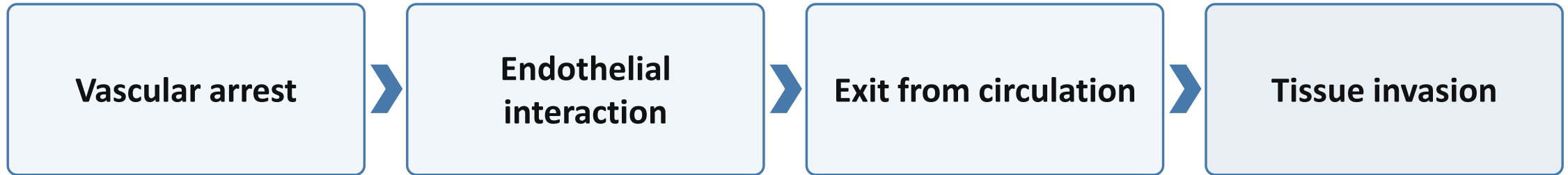
Circulating tumor cells face several threats

CIRCULATORY PHASE

- Mechanical forces, loss of matrix attachment and host immune defenses can eliminate tumor cells.
- Circulating cell clusters and interactions with platelets may favor tumor-cell survival.
- Most disseminating cancer cells do not produce a clinically significant metastasis.

Extravasation reverses key invasion steps

DISTANT-SITE ENTRY



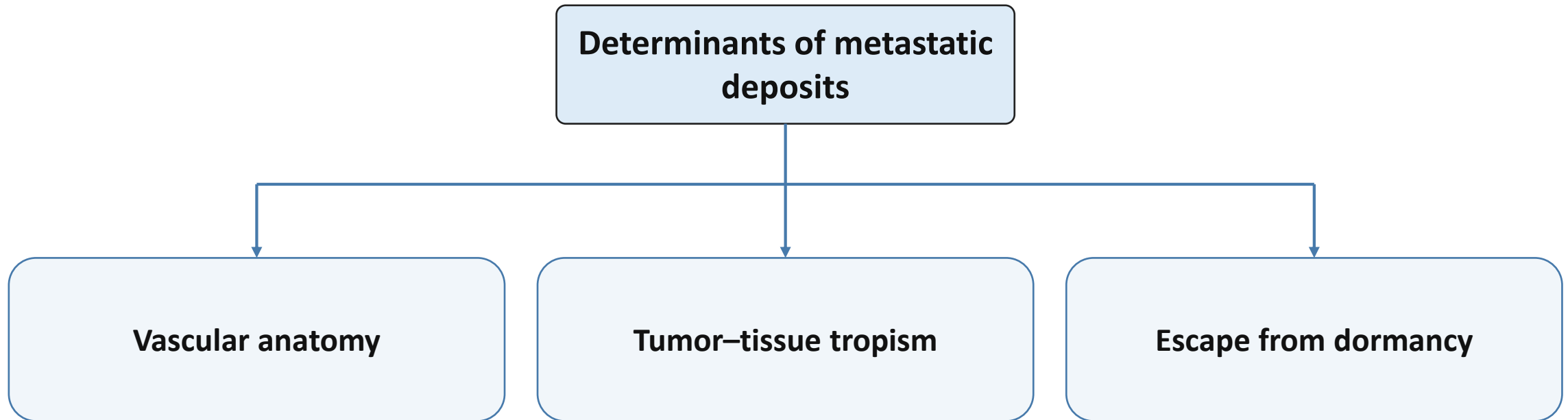
- Successful access to brain tissue still does not guarantee an expanding metastatic tumor.
- Tumor cells must adapt to the local parenchymal environment.

Colonization is the critical bottleneck

DISTANT-SITE GROWTH

- Surviving arrival at a distant site is distinct from sustained growth.
- Cerebral tissue provides a microenvironment different from that of the primary cancer.
- Adaptation, escape from dormancy and expansion determine whether a secondary mass becomes clinically apparent.

Site specificity reflects more than blood flow



These are the three broad factors emphasized, Chapter 7.

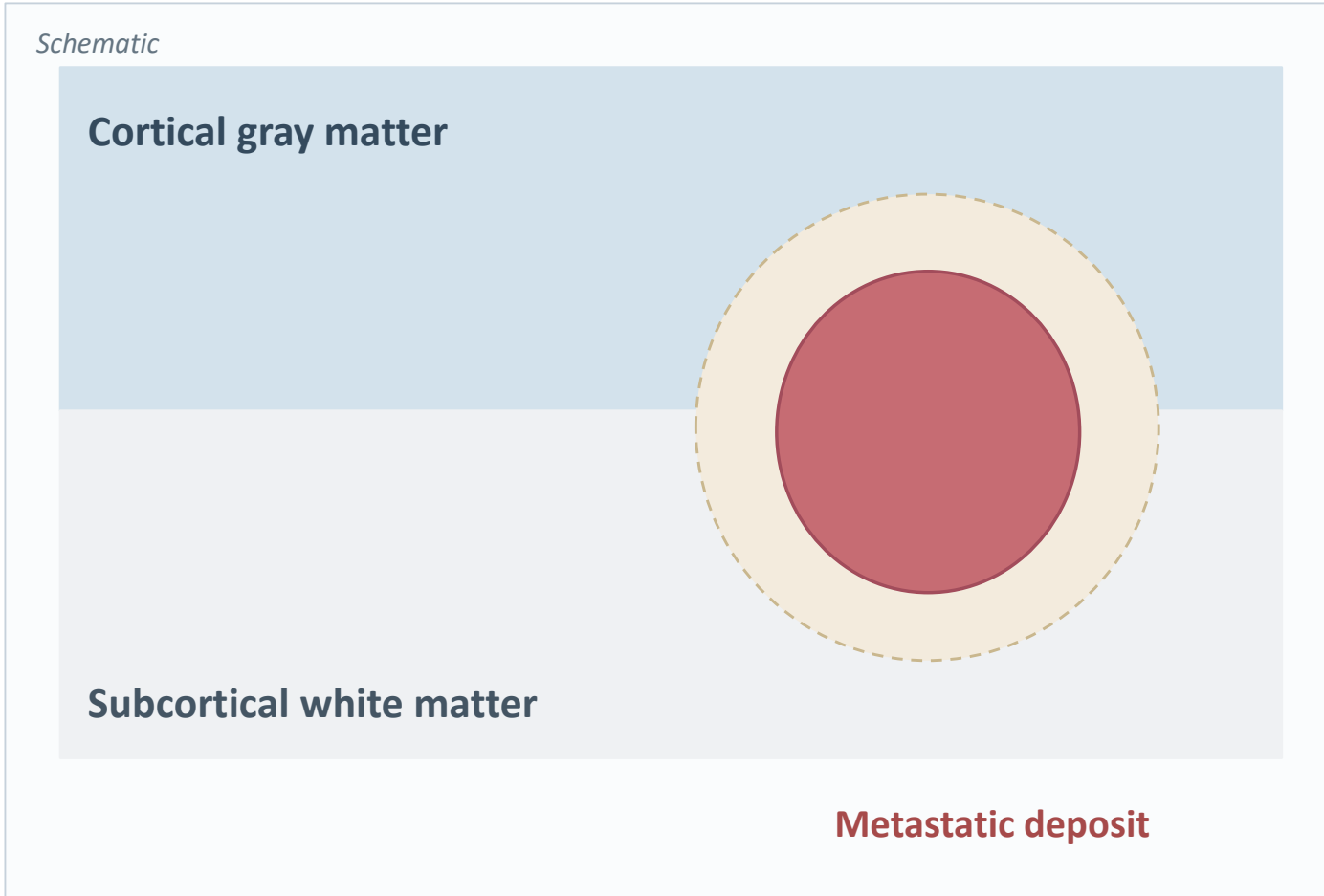
The metastatic cascade is inefficient

BIOLOGICAL SELECTIVITY

- A tumor may release circulating cells without developing identifiable distant disease.
- Each step imposes selective constraints on disseminated cells.
- The presence of a brain metastasis demonstrates successful completion of multiple biologic barriers.

A frequent location is the gray–white junction

PARENCHYMAL MORPHOLOGY



- Metastases often form at the cortical–subcortical interface.
- The lesion is intraparenchymal rather than dural-based.
- The diagram indicates topography, not a radiologic image.

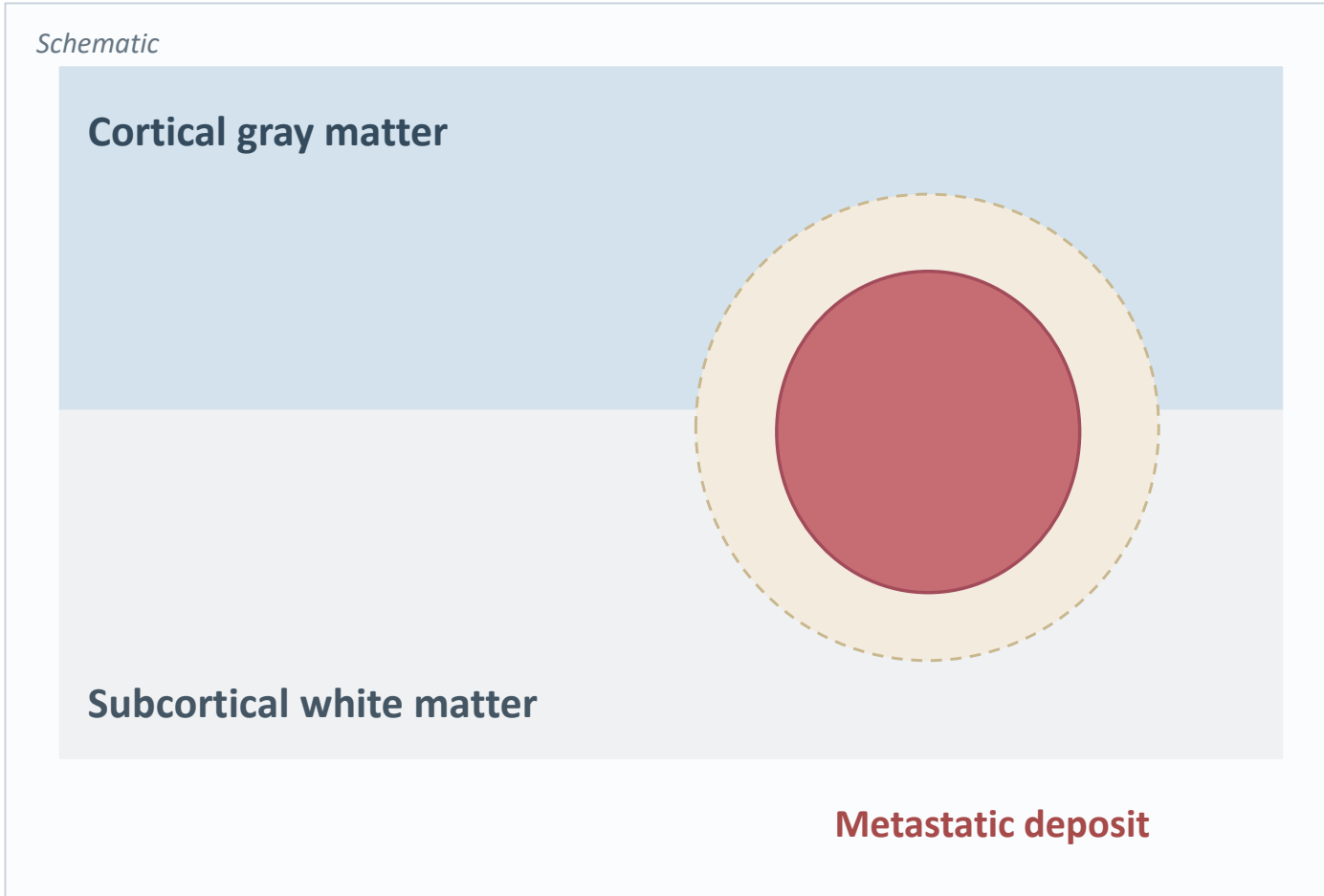
Intraparenchymal metastases are often sharply demarcated

GROSS MORPHOLOGY

- Discrete masses with recognizable borders against brain tissue.
- A sharp macroscopic interface differs from the diffusely infiltrative pattern of some primary brain tumors.
- Circumscription alone does not establish whether a lesion is benign or malignant.

Edema commonly surrounds the metastatic mass

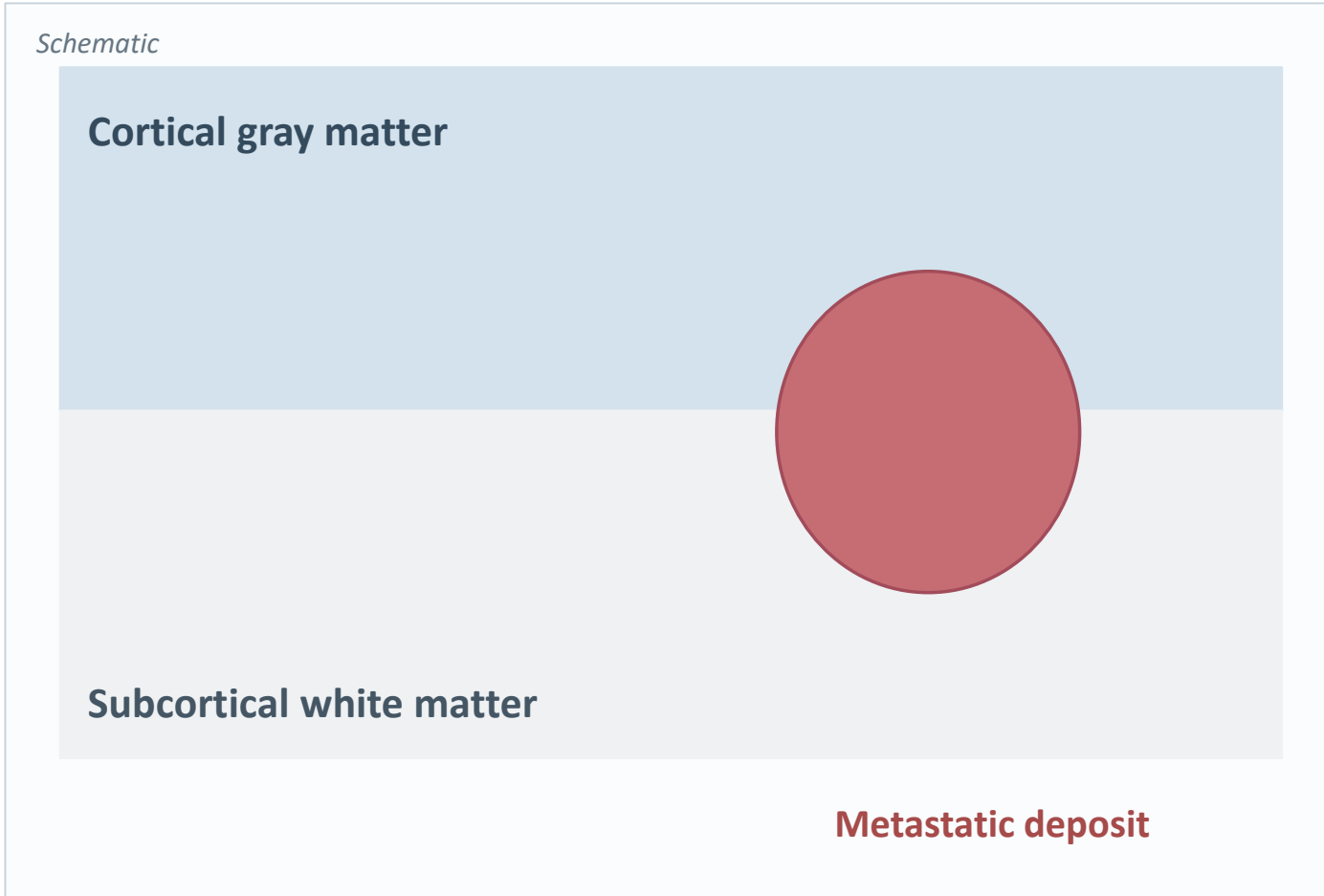
GROSS-CLINICAL CORRELATION



- A zone of surrounding edema is characteristic description.
- The edema extends beyond the gross tumor boundary.
- Local effects can therefore exceed the volume of visible tumor.

The tumor–brain boundary is usually well defined

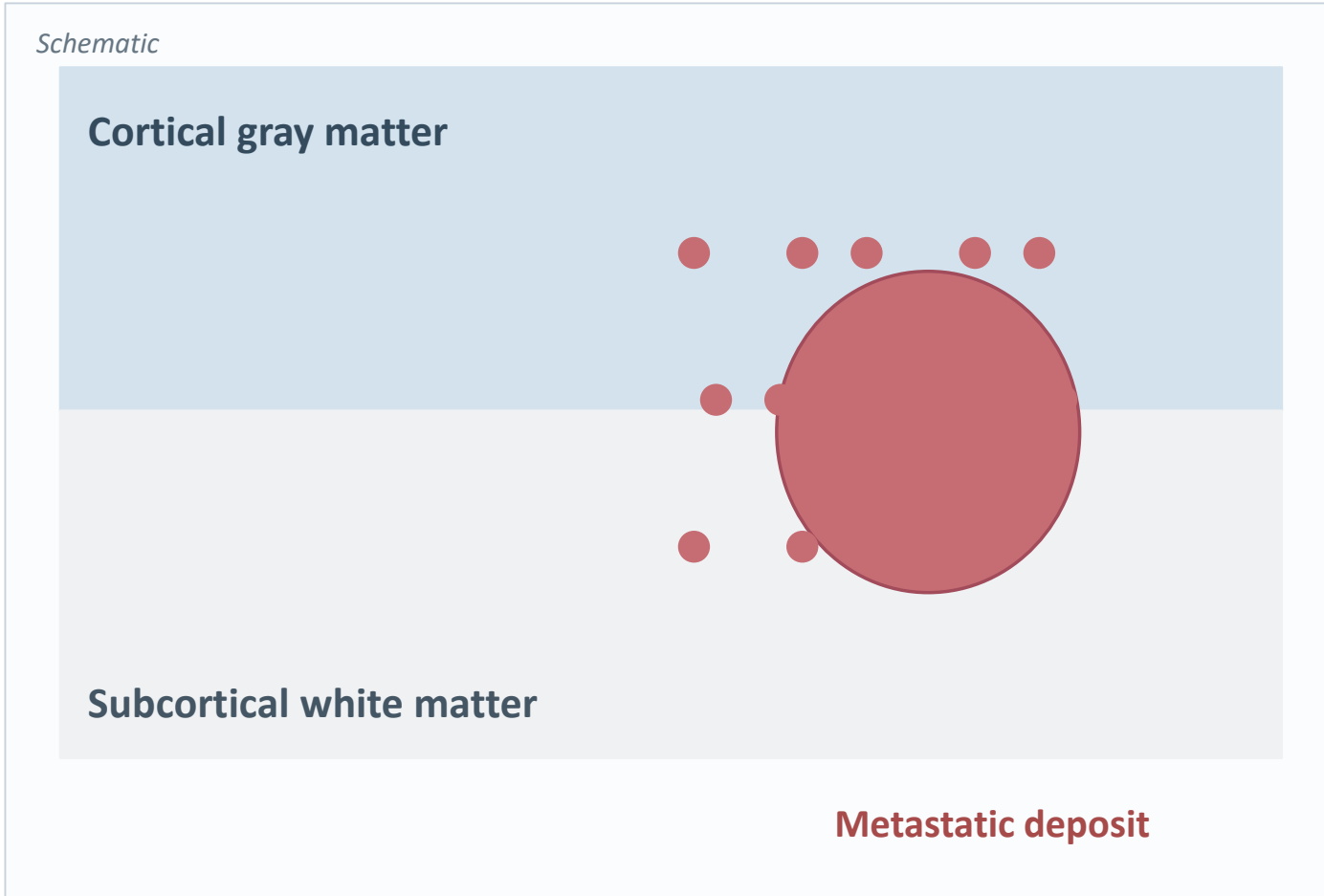
MICROSCOPIC ARCHITECTURE



- The microscopic tumor-to-brain interface can be clearly identified.
- Adjacent brain tissue may differ visibly from the metastatic cellular population.
- Assess this interface at low magnification before cell-level typing.

Melanoma may display a more infiltrative interface

MICROSCOPIC EXCEPTION



- Melanoma is an explicit exception to the usual sharp boundary.
- Isolated tumor cells may extend away from the dominant deposit.
- Do not exclude metastasis solely because infiltration is present.

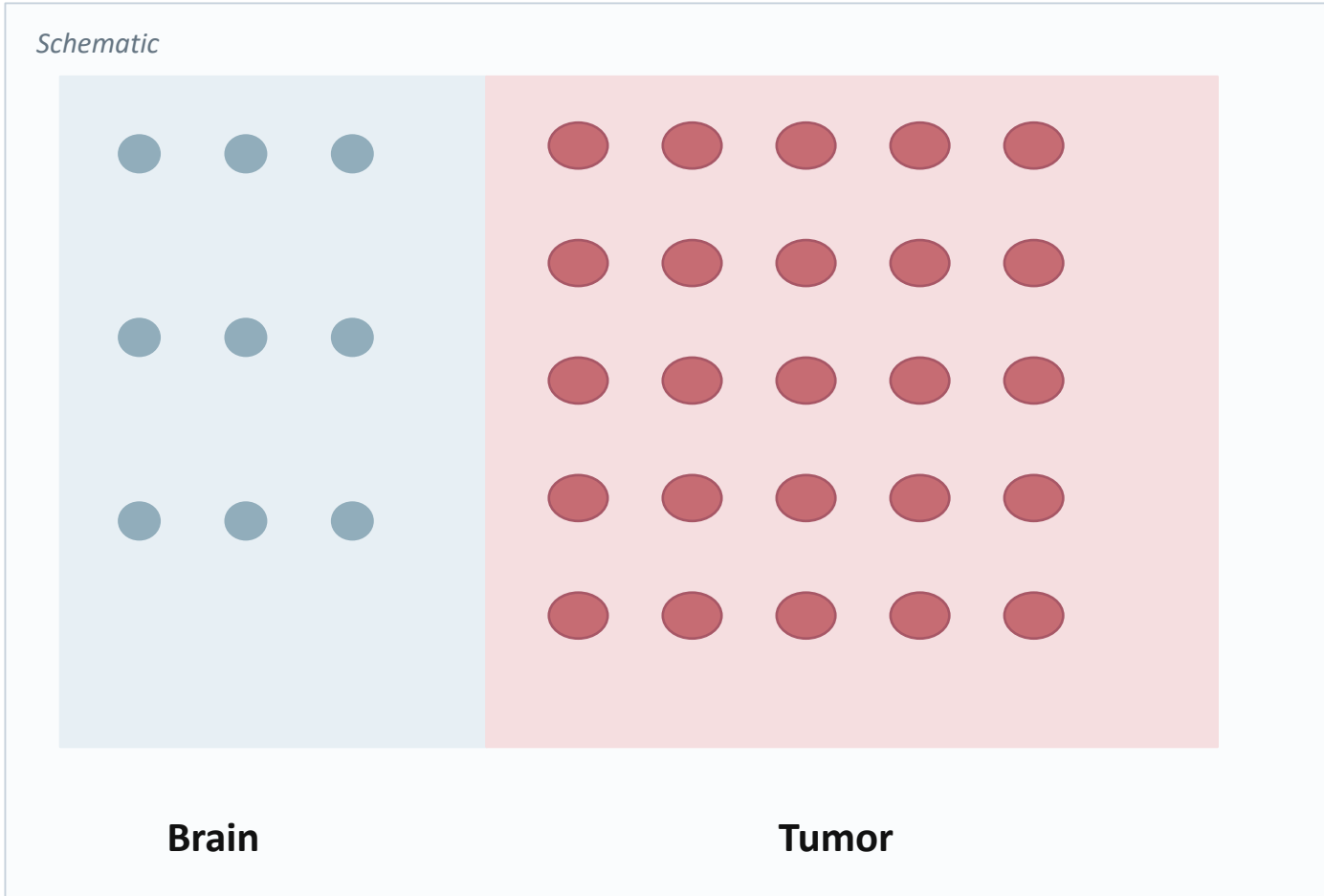
Many metastases preserve their parent tumor architecture

HISTOLOGIC IDENTITY

- A metastatic gland-forming carcinoma may retain its glandular organization.
- Recognizable differentiation can connect the intracranial lesion with a known extracranial malignancy.
- Interpret architectural resemblance together with the clinical history and tissue findings.

A distinct tumor population can abut neural tissue

HISTOLOGIC REASONING



- Low-power evaluation identifies the relationship between the lesion and brain parenchyma.
- Microscopic tumor morphology may resemble an extracranial primary.
- The illustration is diagrammatic and does not represent an observed specimen.

Poor differentiation may conceal the primary lineage

DIAGNOSTIC LIMITATION

- Some CNS metastases are poorly differentiated and lack an obvious parent-tumor architecture.
- Site-of-origin interpretation becomes harder when distinct morphologic features are lost.
- Additional tissue workup may be necessary rather than guessing the primary from histology alone.

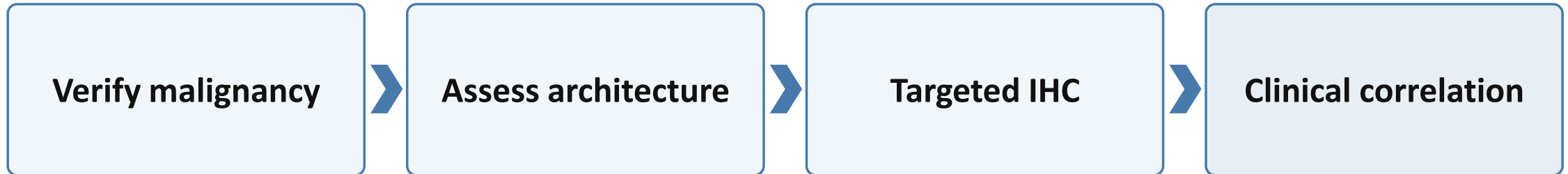
An unknown primary is a recognized presentation

UNKNOWN PRIMARY

- Roughly 10% of brain metastases present without an identified primary malignancy.
- The diagnostic problem is to determine tumor type and likely extracranial origin.
- This percentage is a textbook contextual estimate, not a contemporary universal rate.

Unknown-primary workup follows a tissue-centered logic

DIAGNOSTIC APPROACH



- Immunohistochemistry can help further subtype an undifferentiated metastasis.
- Marker choice depends on microscopic findings and relevant clinical possibilities.

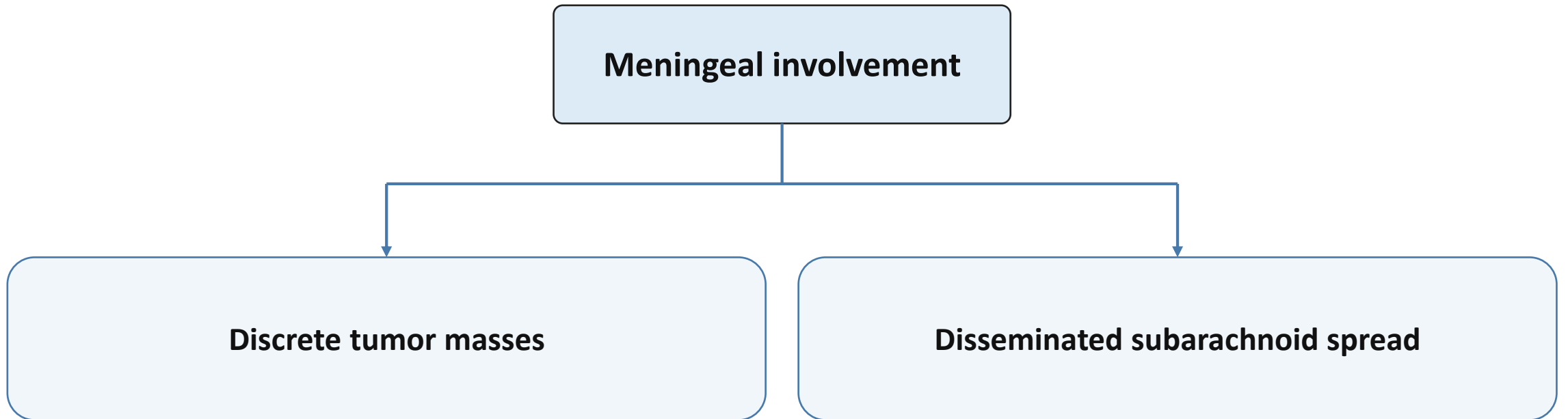
The source does not prescribe a specific IHC panel, and none is invented here.

Immunohistochemistry supports, but does not replace, diagnosis

DIAGNOSTIC PRINCIPLES

- Robbins explicitly identifies immunohistochemistry as helpful for subtyping metastases of unknown primary.
- Interpret a marker pattern in the context of morphology and the clinical distribution of disease.
- No single generic marker is sufficient to establish the primary site of every poorly differentiated metastasis.

Meningeal metastasis can have two patterns

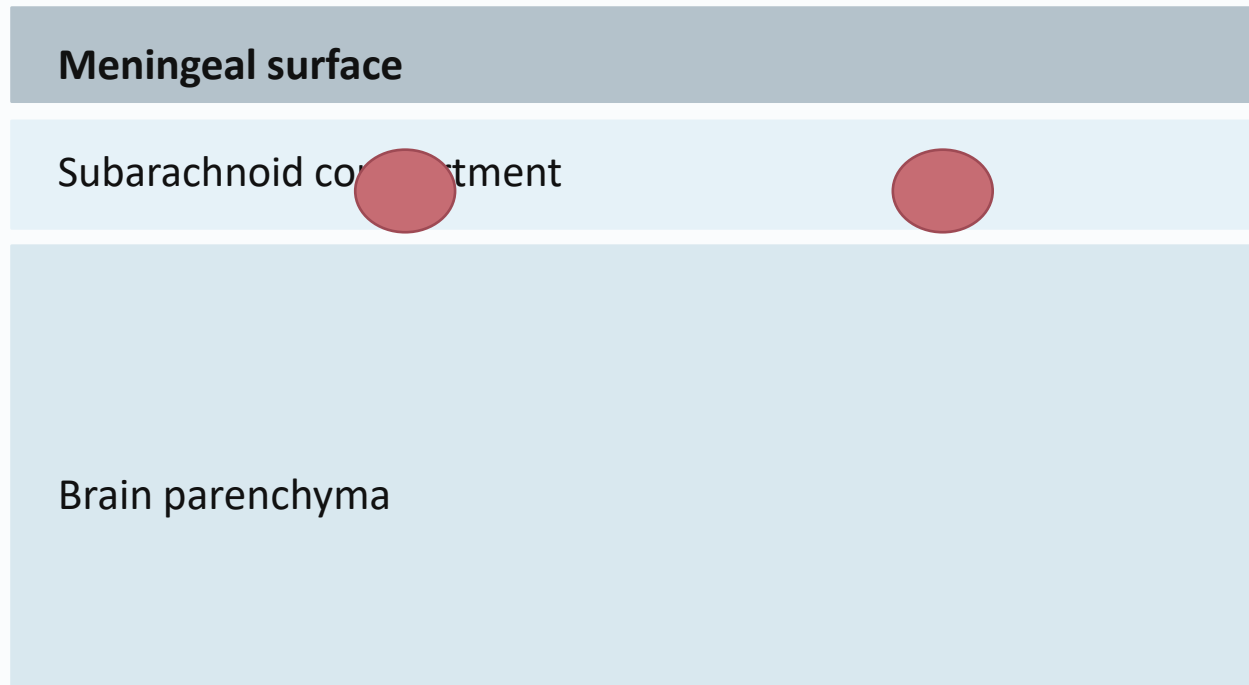


The diffuse pattern is termed meningeal carcinomatosis.

Discrete tumor nodules may involve the meninges

MENINGEAL PATTERN

Schematic



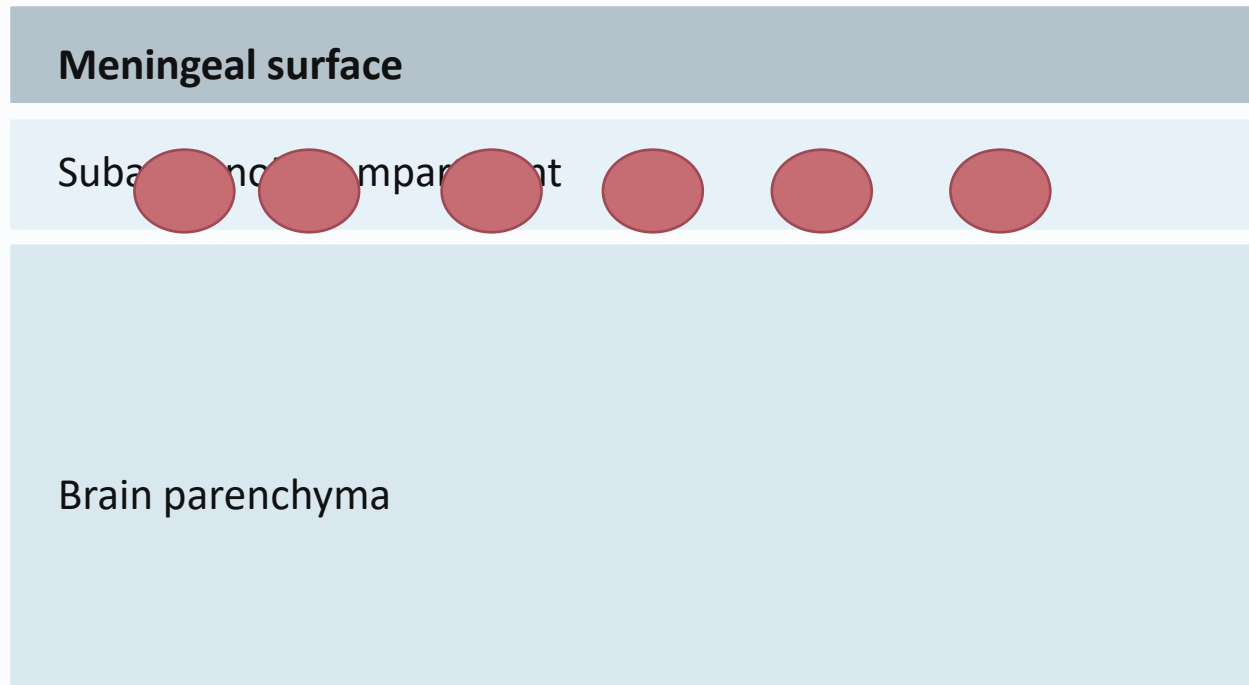
Tumor deposits on meningeal surfaces

- Metastatic tumors may produce focal meningeal masses.
- The site is external to the brain parenchyma.
- The differential includes primary dural-based tumors.

Meningeal carcinomatosis is disseminated surface disease

MENINGEAL PATTERN

Schematic



Tumor deposits on meningeal surfaces

- Widespread tumor deposits involve the subarachnoid compartment.
- The gross appearance may resemble a meningitis-like distribution.
- This pattern differs from a single discrete intracerebral mass.

“Meningitis-like” describes distribution, not infection

TERMINOLOGY

- The term meningeal carcinomatosis denotes metastatic malignant cells involving meningeal surfaces.
- Diffuse involvement can mimic the distribution of inflammatory meningitis.
- The histologic substrate remains malignancy rather than a primary infectious process.

The brain, cord and roots can all be studded with tumor

GROSS DISTRIBUTION

- The Robbins morphology section describes nodules on the brain surface.
- Deposits can also occur on the spinal cord and intradural nerve roots.
- Anatomically extensive spread explains why manifestations can involve multiple neurologic levels.

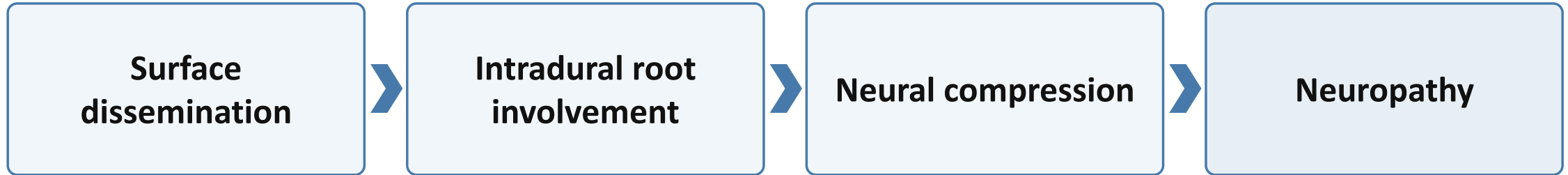
Lung and breast carcinoma are frequent meningeal sources

PRIMARY ASSOCIATIONS

- The two primary tumors specifically emphasized are lung and breast carcinomas.
- A patient with either malignancy and new multifocal neuropathies warrants consideration of meningeal involvement.
- The primary-site pattern supports suspicion but is not itself diagnostic.

Meningeal nodules may impair neural structures

CLINICOPATHOLOGIC MECHANISM



- Cranial and spinal nerve involvement can follow meningeal tumor deposition.
- The pattern is anatomically different from a parenchymal cerebral mass lesion.

Cranial neuropathy is a possible manifestation

CLINICAL EFFECT

- Involvement of cranial nerve pathways can produce deficits referable to affected nerves.
- Multiple neurologic deficits can indicate more diffuse meningeal disease.
- Correlate symptoms with anatomic distribution instead of attributing all findings to one parenchymal mass.

Spinal neuropathy follows intradural root involvement

CLINICAL EFFECT

- Meningeal deposits may involve intradural spinal nerve roots.
- Compression or injury at nerve roots can generate spinal neuropathic symptoms.
- Simultaneous cranial and spinal involvement is a clue to disseminated meningeal disease.

Two metastatic patterns produce different findings

INTEGRATIVE COMPARISON

Dimension	Parenchymal metastasis	Meningeal carcinomatosis
Anatomic focus	Within brain tissue	Brain, cord and nerve-root surfaces
Morphologic pattern	Demarcated mass, edema	Discrete surface nodules or diffuse deposits
Clinical emphasis	Effects of an intracranial mass	Cranial/spinal neuropathies
Textbook treatment statement	Localized treatment may help a solitary lesion	Diffuse meningeal disease is challenging to treat

Parenchymal metastases often behave as mass lesions

CLINICAL PRESENTATION

- The clinical presentation is related to space occupied by tumor and surrounding tissue response.
- Anatomical location determines which brain functions may be disrupted.
- The metastasis may be the first manifestation of previously unrecognized systemic cancer.

Edema amplifies the effect of a parenchymal deposit

MECHANISM OF SYMPTOMS

- A zone of edema around many intracerebral metastases.
- The symptomatic region can extend beyond the microscopic tumor itself.
- Interpret the lesion's consequences as a combination of tumor location, tumor mass and adjacent tissue response.

CNS disease can precede discovery of the primary tumor

INITIAL PRESENTATION

- The neurologic presentation may lead to recognition of an underlying extracranial cancer.
- A new intracranial mass should not be assumed to represent a primary CNS neoplasm without adequate evaluation.
- The possibility of occult systemic malignancy is particularly important when pathology resembles carcinoma.

Clinical history changes diagnostic probability

PRETEST PROBABILITY

- A known lung, breast, melanoma, renal or gastrointestinal malignancy makes metastasis a major consideration.
- Nevertheless, the intracranial lesion still requires an evidence-based differential diagnosis.
- Clinicopathologic concordance is strongest when morphology supports the known primary.

Brain metastasis versus meningioma: Compartment first

ADJACENT ROBBINS CONTEXT

Feature	Metastatic deposit	Meningioma
Site	Can be parenchymal or meningeal	Usually attached to dura
Growth relation	Parenchymal deposit often demarcated	Usually compresses adjacent brain
Origin	Secondary from systemic malignancy	Primary meningotheelial neoplasm
Diagnostic lesson	Do not infer origin from a mass alone	Dural location is not exclusive to meningioma

Meningioma features are taken from the adjacent Chapter 28 section.

A dural-based mass is not automatically a meningioma

DIFFERENTIAL DIAGNOSIS

- The adjacent Robbins meningioma section explicitly mentions metastases among tumors that can grow as dura-based masses.
- Anatomic site alone cannot establish meningotheelial lineage.
- Microscopic analysis and patient history remain necessary for reliable classification.

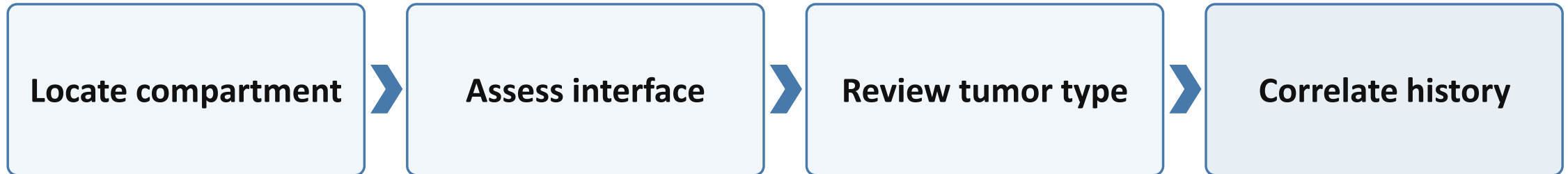
Poorly differentiated morphology requires restraint

DIAGNOSTIC PITFALL

- A high-grade-appearing tumor in brain tissue can be difficult to classify by architecture alone.
- Determine whether the tissue represents a secondary tumor before attaching a primary CNS tumor label.
- Use additional testing only to address a well-defined differential; Avoid unsupported marker claims.

A practical pathology assessment sequence

INTEGRATED APPROACH



- Compartment and interface guide the morphologic interpretation.
- Undifferentiated tumors may then require targeted immunohistochemistry.

Localized treatment can benefit solitary brain metastasis

CLINICAL IMPLICATIONS

- Local treatment of solitary brain metastases generally improves quality and duration of life.
- The claim is specific to an appropriately selected solitary lesion.
- Do not generalize this textbook statement to all multifocal or meningeal disease.

Diffuse meningeal metastasis is therapeutically challenging

CLINICAL IMPLICATIONS

- Meningeal carcinomatosis can extend across brain, spinal cord and intradural roots.
- Its disseminated surface distribution complicates localized management.
- Robbins explicitly characterizes this presentation as frequently difficult to treat.

Case 1: A sharply circumscribed brain lesion

A patient with a previously diagnosed lung carcinoma presents with a new intracerebral mass. The resected tissue has a well-defined interface with adjacent brain and surrounding edema.

DISCUSSION QUESTIONS

- Which anatomic and morphologic findings favor metastasis?
- What does the known extracranial carcinoma contribute to interpretation?

Case 1: Pathologic interpretation

CASE DISCUSSION

- Lung is a frequent primary site for brain metastasis in the Robbins account.
- A demarcated intraparenchymal mass with edema fits the described metastatic morphology.
- The clinical history and tissue phenotype must be correlated before assigning the origin.

Case 2: An infiltrative pigmented tumor

A patient with a history of melanoma has a brain lesion whose microscopic boundary is less sharply defined than expected for most metastases.

DISCUSSION QUESTIONS

- Does infiltrative growth exclude metastasis?
- Which textbook exception is directly relevant?

Case 2: Recognizing an exception

CASE DISCUSSION

- Melanoma metastases may be more infiltrative than other brain metastases.
- A non-sharp tumor interface should therefore not exclude a metastatic diagnosis.
- The known melanoma history remains important in classifying the lesion.

Case 3: Cranial and spinal neuropathies

A patient with breast carcinoma develops clinical abnormalities involving cranial and spinal nerve distributions. Meningeal deposits are identified along intradural nerve roots.

DISCUSSION QUESTIONS

- Which metastatic compartment is primarily affected?
- What mechanism links the anatomic disease distribution to the symptoms?

Case 3: A meningeal pattern

CASE DISCUSSION

- Breast carcinoma is one of the principal sources associated with meningeal carcinomatosis.
- Tumor deposits on intradural roots provide a mechanism for cranial and spinal neuropathies.
- This is diffuse surface disease rather than an isolated intracerebral mass.

Diagnostic checklist for a CNS metastatic lesion

MICROSCOPIC AND CLINICAL INTEGRATION

Question	Why it matters
Where is the tumor?	Parenchymal, dural or subarachnoid location changes the differential.
What is its interface?	Sharp boundaries are common; Melanoma can be infiltrative.
Does it resemble a primary?	Differentiation may preserve parent-tumor architecture.
Is a systemic primary known?	Clinical correlation narrows the plausible sites of origin.
Is the lesion poorly differentiated?	Targeted immunohistochemistry may assist subtyping.

Three pathology patterns to distinguish

Parenchymal metastasis

- A discrete intracerebral mass
- Often near gray–white junction
- Common edema and defined border

Meningeal spread

- Discrete meningeal nodules
- May involve brain and spinal surfaces
- Diffuse form is carcinomatosis

Melanoma exception

- May be more infiltrative
- A diffuse interface does not negate metastasis
- Use history and lineage correlation

The four most defensible lecture conclusions

SYNTHESIS

- Brain metastases are frequently secondary carcinomas from lung, breast, melanoma, kidney or gastrointestinal tract.
- Parenchymal metastases are often demarcated lesions with a zone of surrounding edema.
- Diffuse meningeal carcinomatosis can involve intradural roots and produce cranial or spinal neuropathies.
- Poorly differentiated metastases, especially without an identifiable primary, often benefit from immunohistochemical subtyping.

References and source boundaries

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026). Chapter 28, “The Central Nervous System,” p. 1184, “Metastatic Tumors.”
- Same textbook, Chapter 7, “Neoplasia,” pp. 242–244 and 273–276: metastatic pathways, invasion and metastatic cascade.
- The deck contains native editable conceptual schematics, not diagnostic microscopy or patient imaging.
- The original chapter PDF was unavailable; extracted textbook text was reviewed, but PDF figure/page cross-check was not performed.