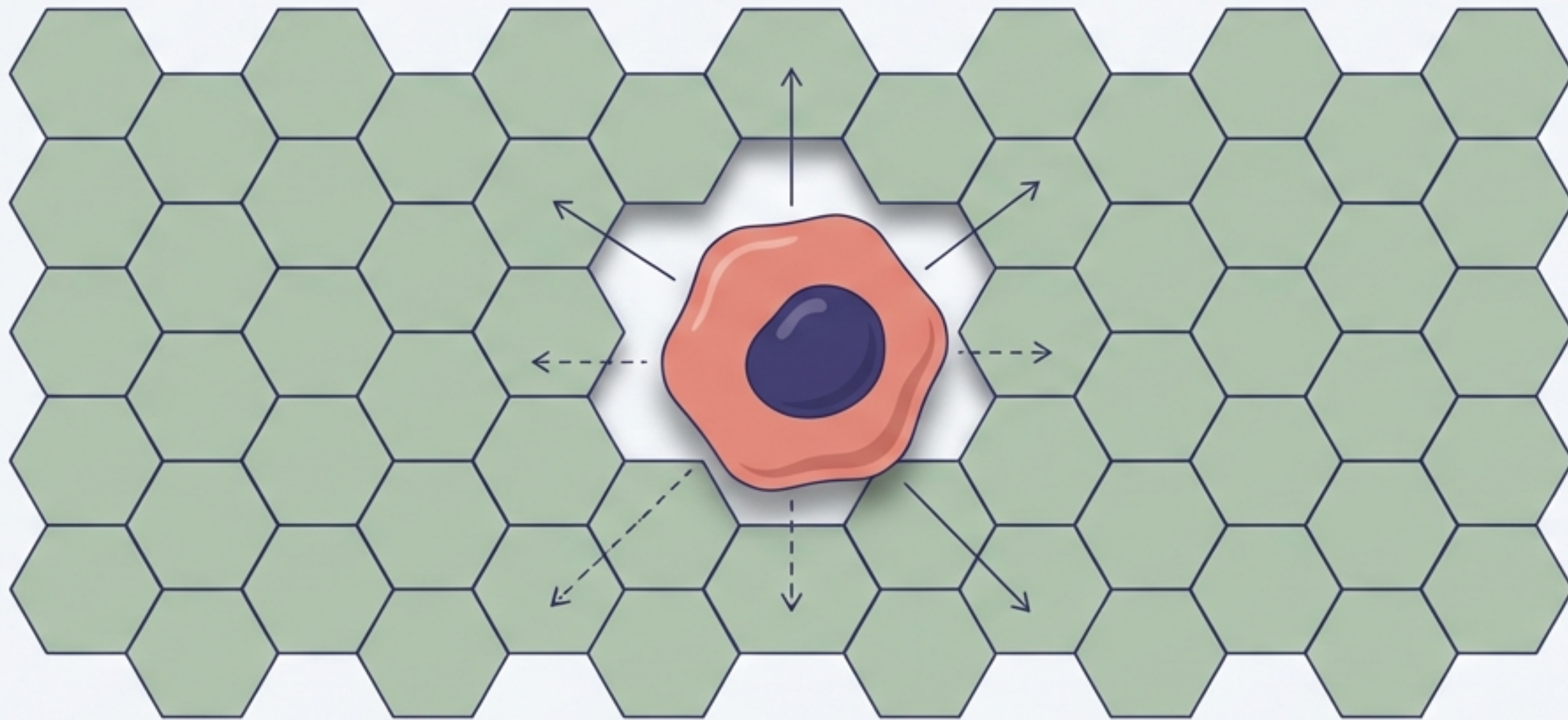


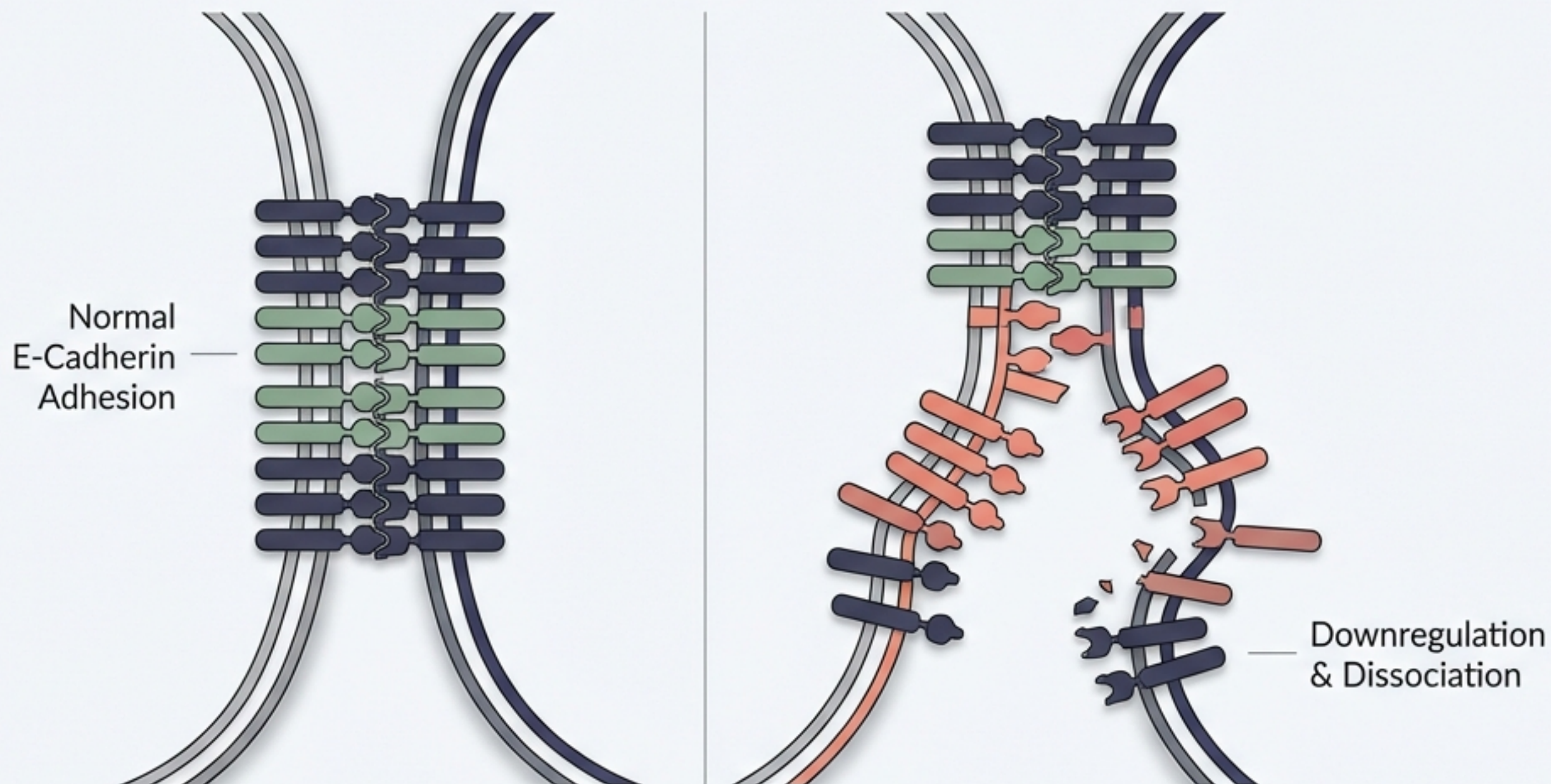
# The Architecture of Malignancy

## From Molecular Escape to Clinical Prognosis

A visual guide to the fundamentals of neoplasia, covering the mechanics of invasion, the routes of metastasis, and the critical distinction between grading and staging.



# The Breach of Adhesion



**Normal State:** Epithelial cells are anchored by cellular adhesion molecules (E-cadherin).

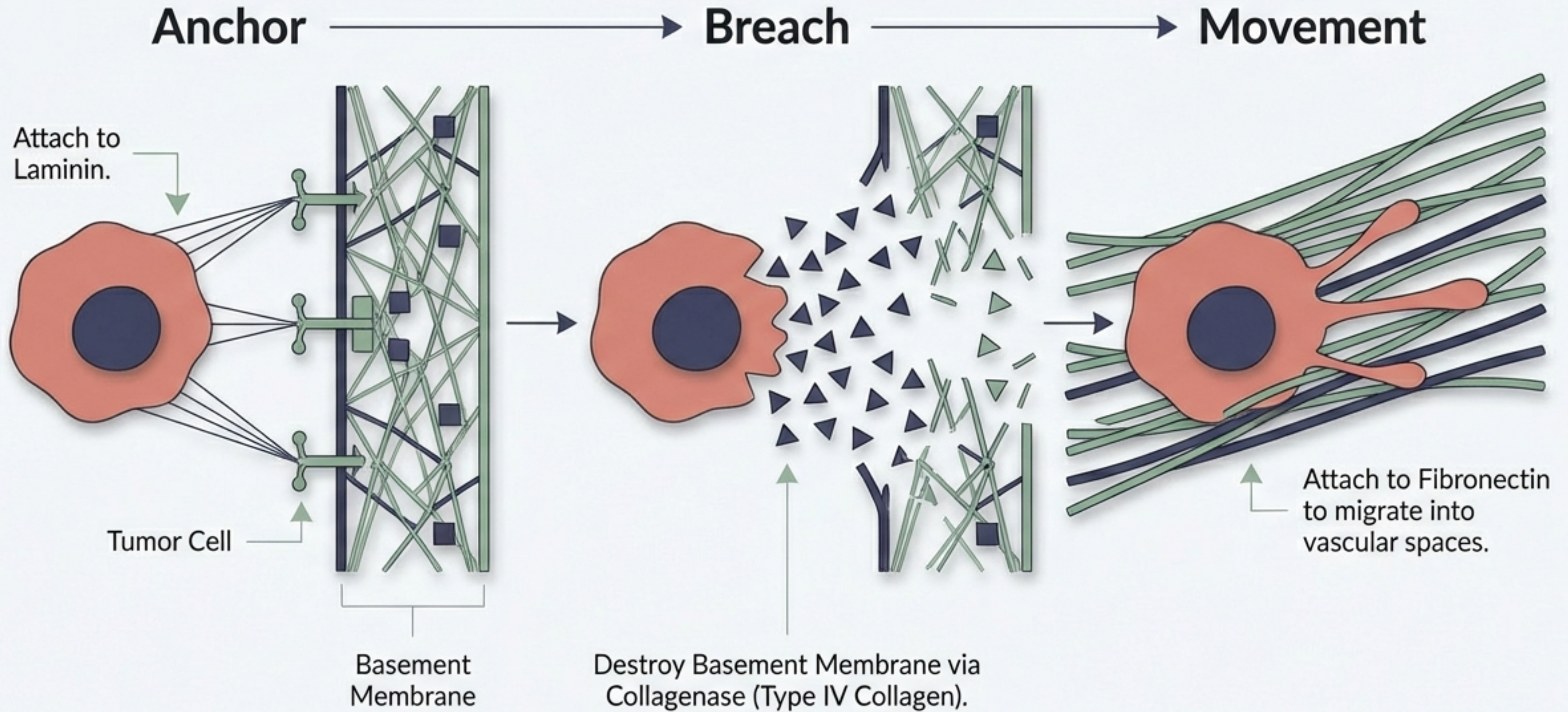


**The Mutation:** Downregulation of E-cadherin results in the dissociation of attached cells.



**Result:** The first step of invasion is physical detachment.

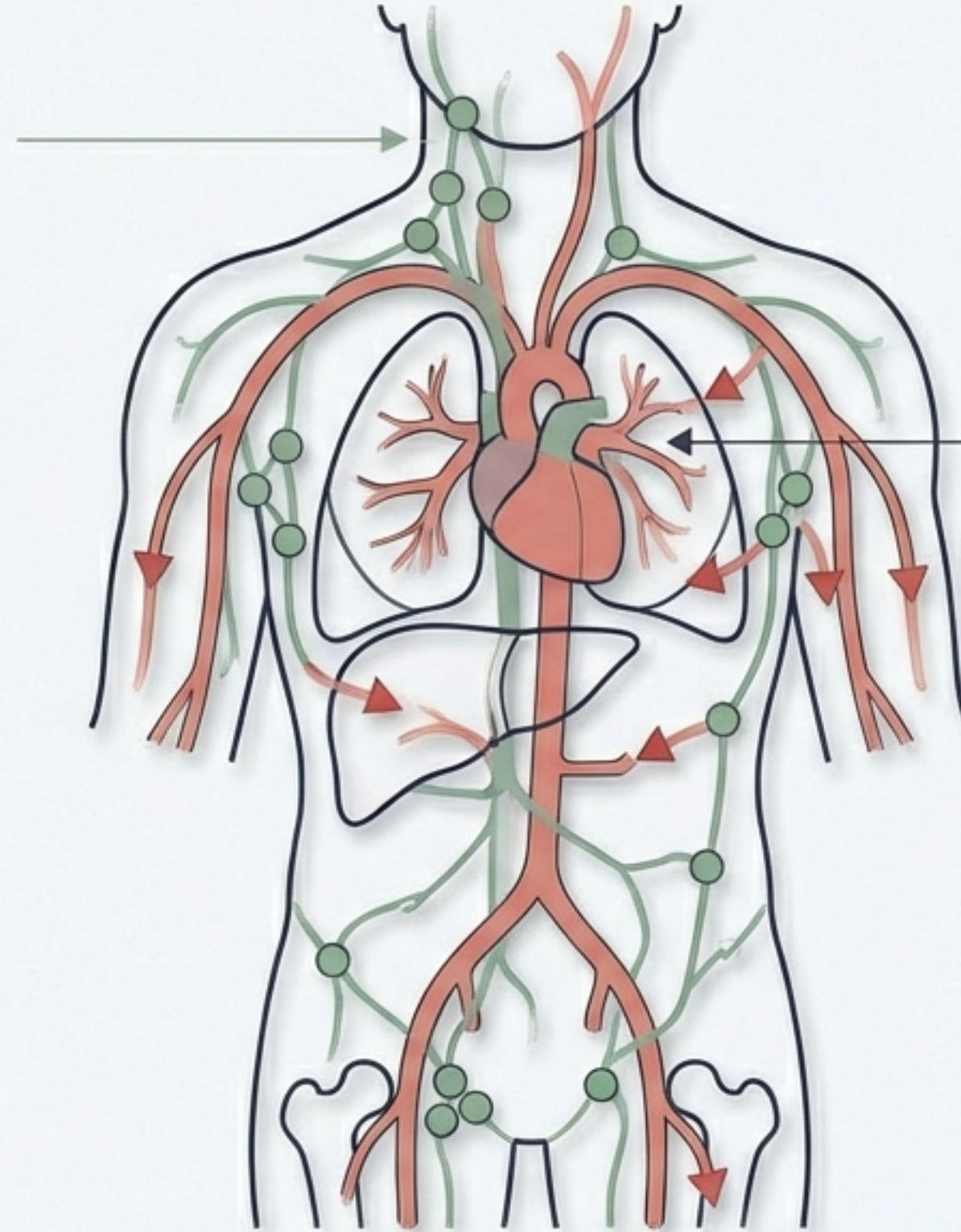
# Destruction and Migration



# The Routes of Metastasis

## Lymphatic Spread

Standard route for **CARCINOMAS**.  
Initial spread to regional  
draining lymph nodes.



## Hematogenous Spread

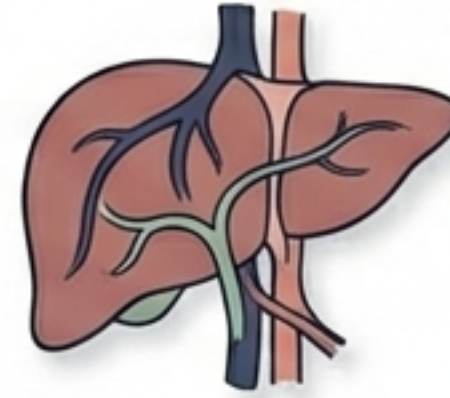
Standard route for **SARCOMAS**.  
Spread via blood vessels;  
typically more aggressive.

# The Hematogenous Exceptions

Carcinomas that invade the vascular highways directly.



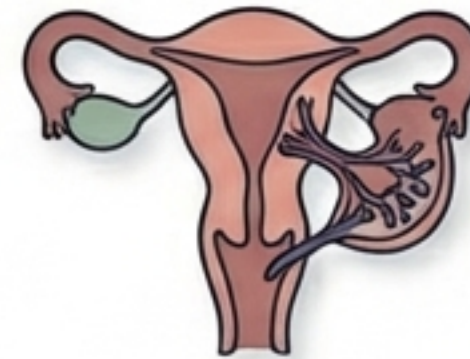
**Renal Cell Carcinoma.**  
Invades Renal Vein.



**Hepatocellular Carcinoma.**  
Invades Hepatic Vein.



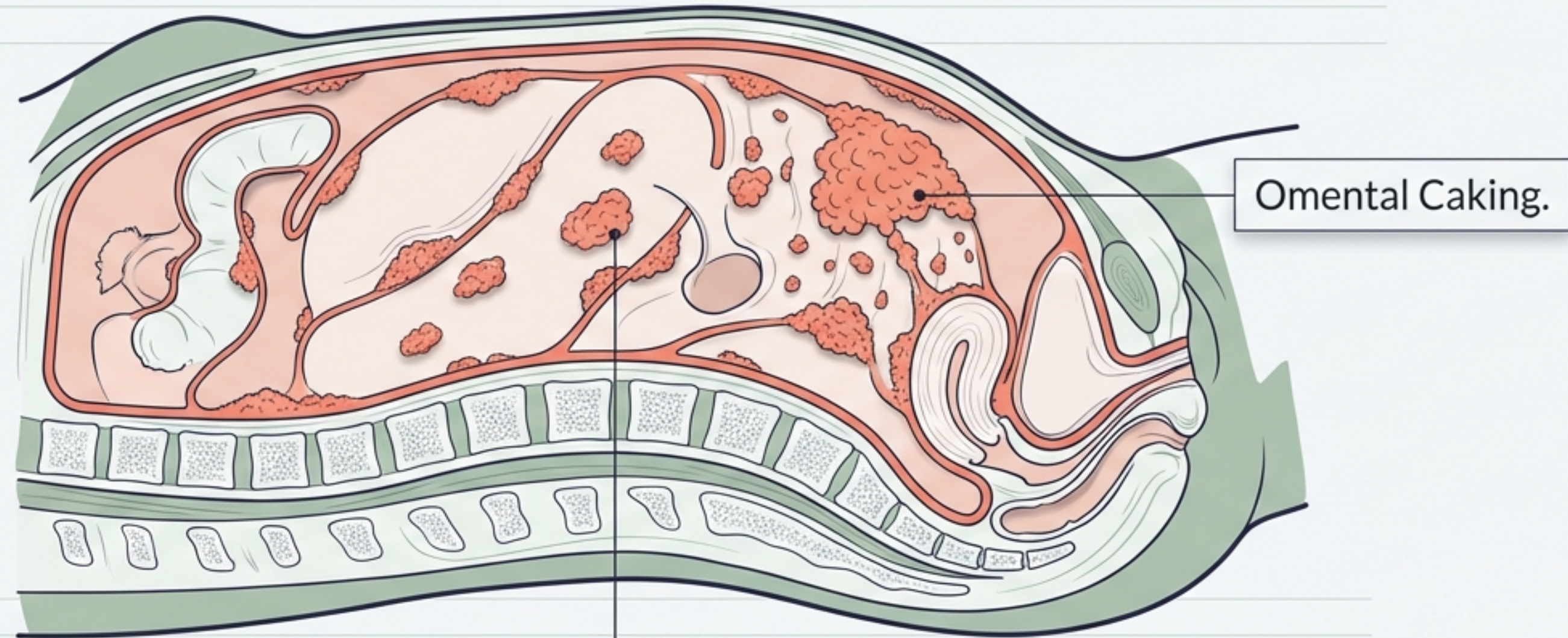
**Follicular Carcinoma of the Thyroid.**



**Choriocarcinoma.**

**Note:** While carcinomas typically prefer lymphatics, these four specific types spread via the blood.

# Seeding the Body Cavities



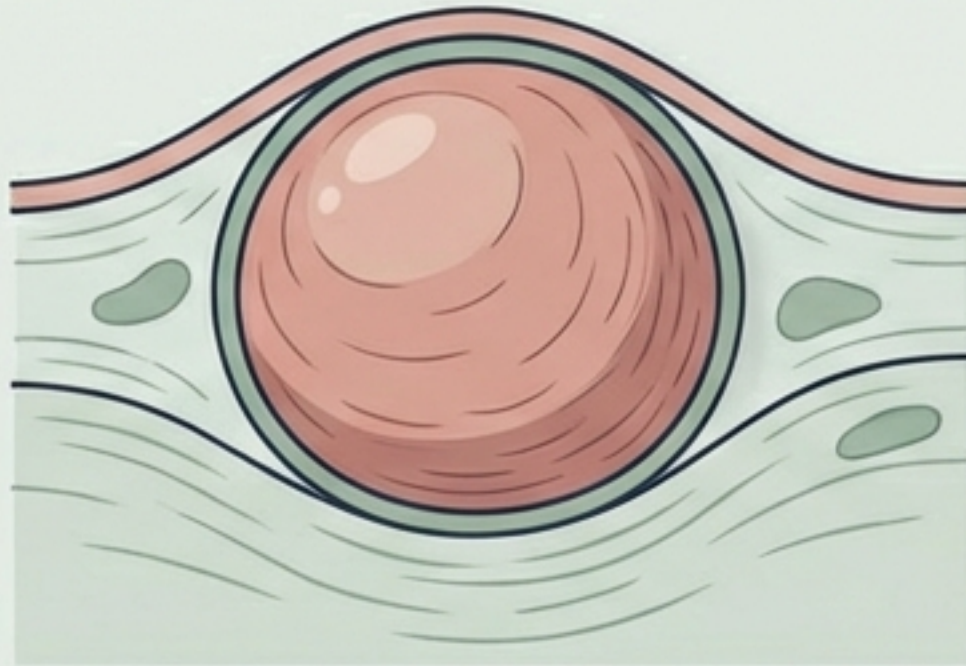
Characteristic of Ovarian Carcinoma.

**Mechanism:** Direct involvement of the peritoneum surface rather than vessel-based transport.

**Omental Caking.**

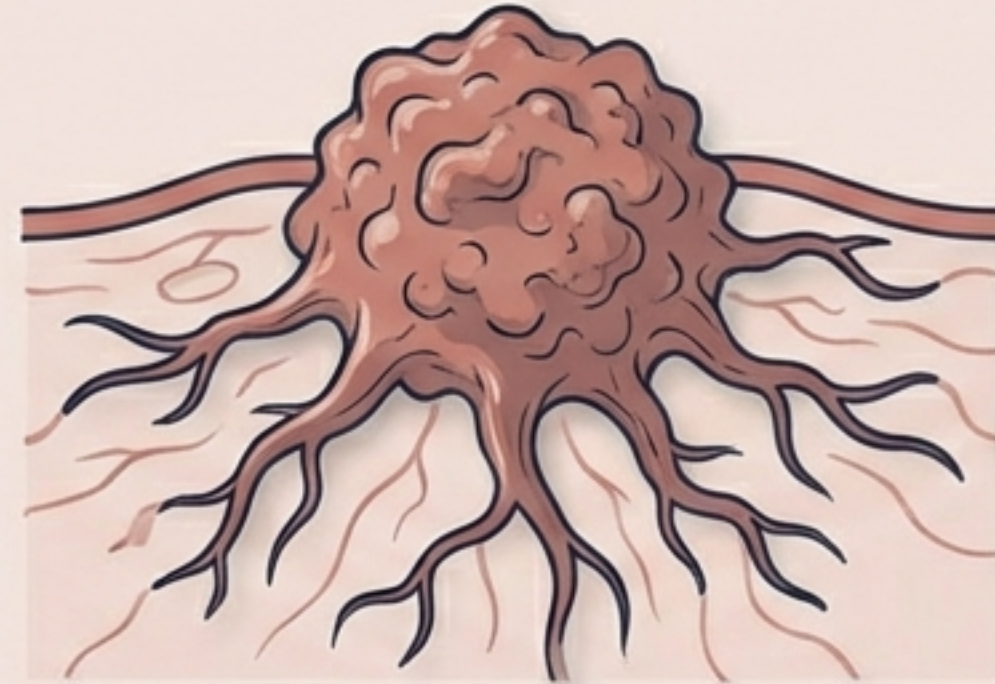
# Clinical Presentation: Macroscopic Features

## BENIGN



Slow growing  
Well circumscribed & Distinct  
**Mobile** (moves easily within tissue)

## MALIGNANT

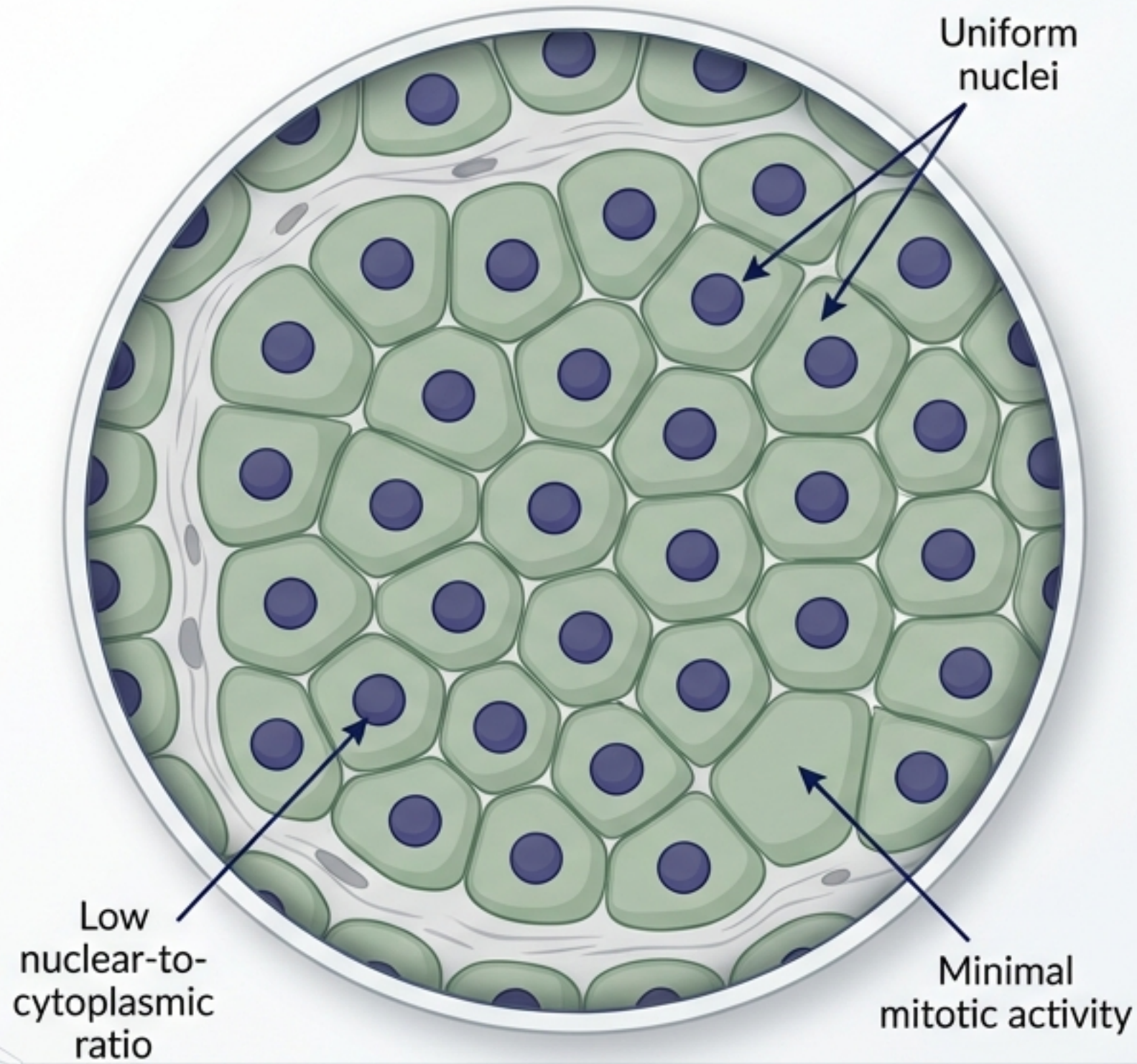


Rapid growing  
Poorly circumscribed & Infiltrative  
**Fixed** to surrounding tissues

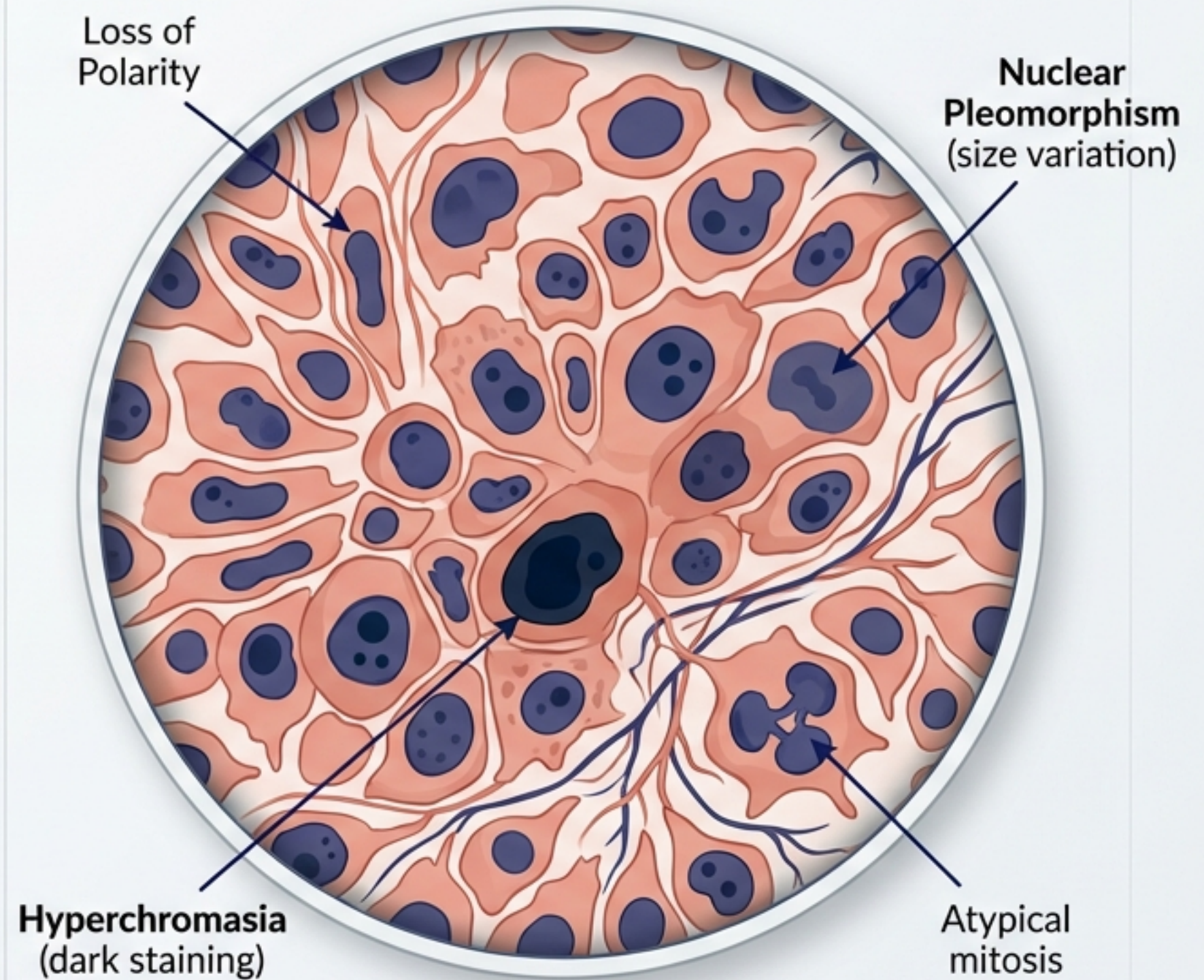
Clinical exam suggests, but **Biopsy** confirms.

# Histologic Features: The Microscopic Truth

BENIGN



MALIGNANT



# The Hallmark of Malignancy

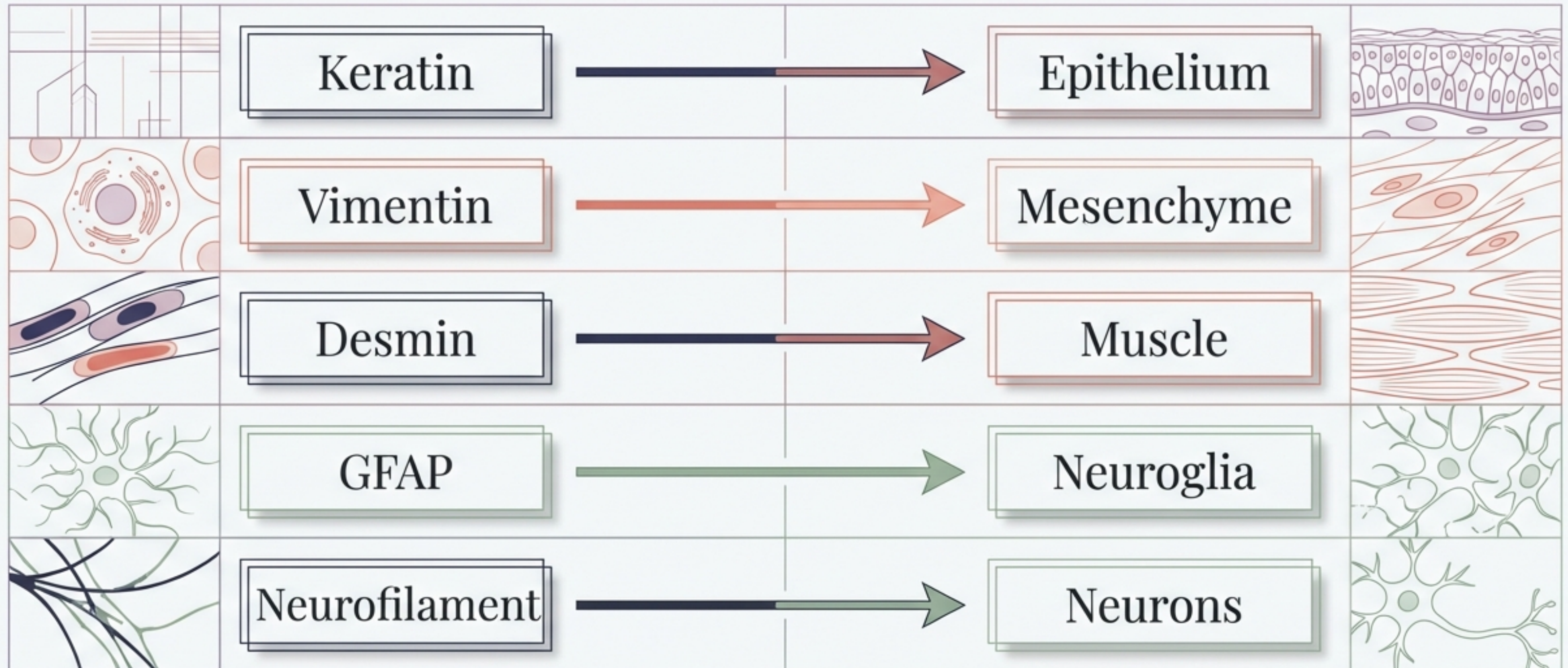
# Metastatic Potential

**Benign tumors never metastasize.**

Regardless of growth rate or local invasion, the ability to spread to distant sites is the definitive proof of malignancy.

# Immunohistochemistry: Intermediate Filaments

Used to characterize undifferentiated tumors difficult to classify by sight alone.



# Targeted Tumor Markers

**PSA**

Prostatic Specific Antigen

**Prostatic Epithelium**



**ER (Estrogen Receptor)**

**Breast Epithelium**



**Thyroglobulin**

**Thyroid Follicular Cells**



**Chromogranin**

**Neuroendocrine cells**

(e.g., Small cell carcinoma, Carcinoid)



**S-100**

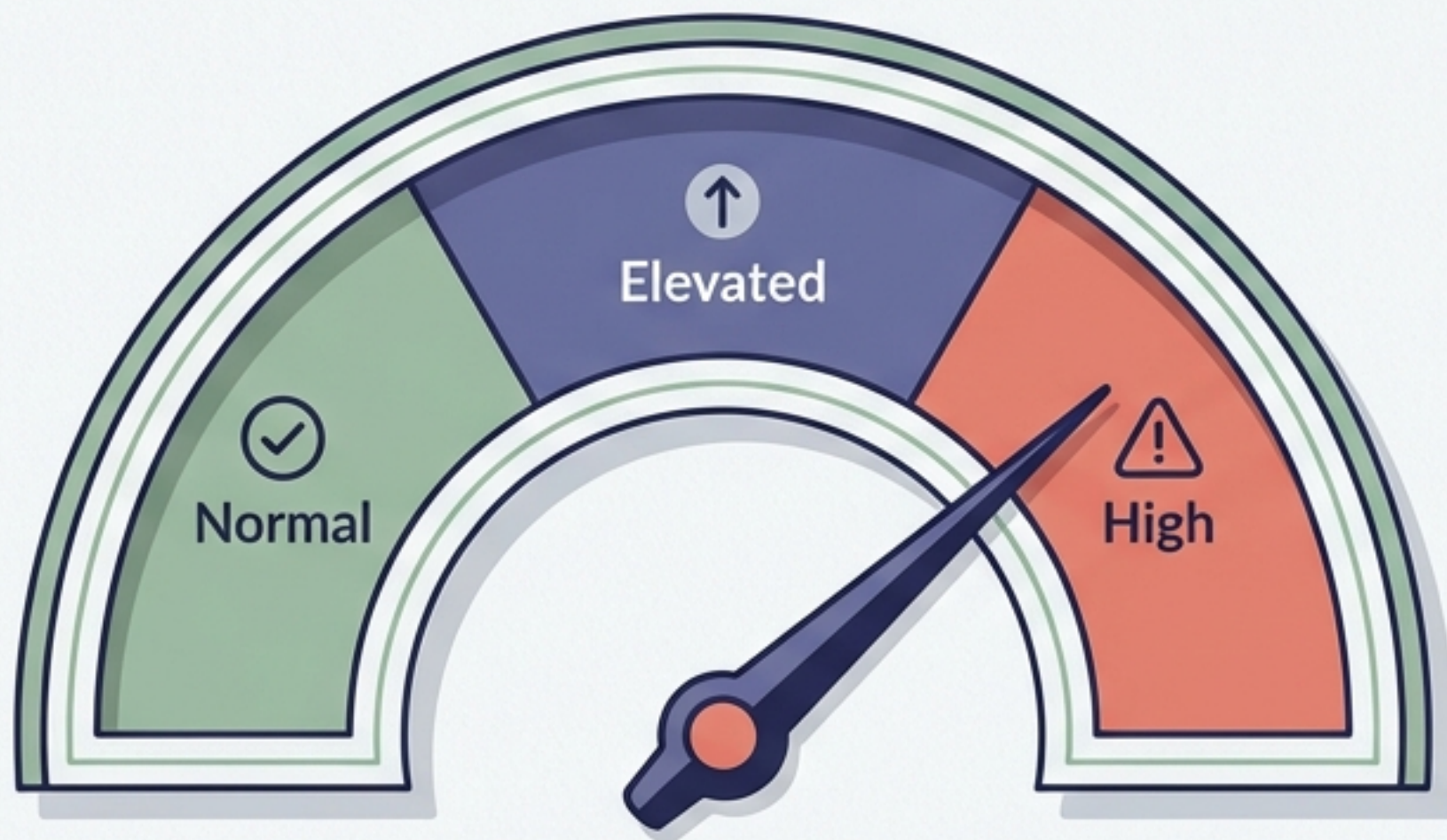
**Melanoma, Schwannoma,  
Langerhans cell histiocytosis**



# Serum Tumor Markers

Proteins released by the tumor into the serum.

## PSA Level



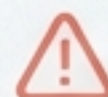
**Screening:** Detecting potential issues.



**Monitoring:** Tracking response to treatment.



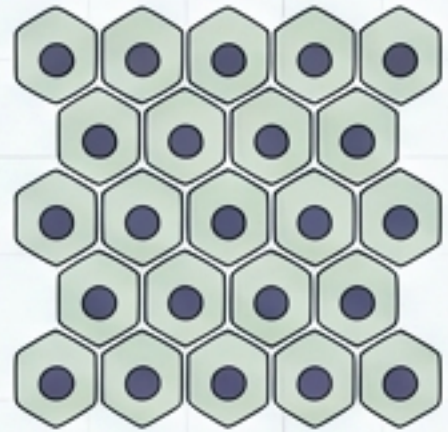
**Recurrence:** Watching for spikes after remission.



**Elevated levels are a warning, not a diagnosis.**  
Elevated levels are a warning, not a diagnosis.  
Biopsy is required for diagnosis of carcinoma.

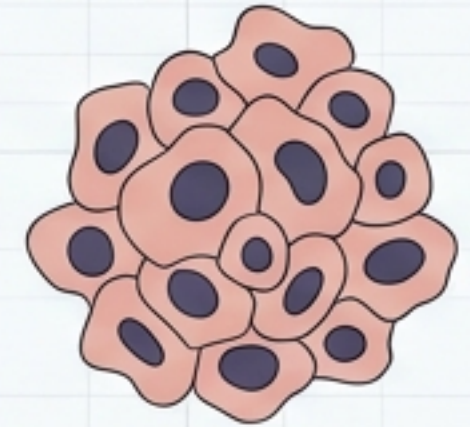
# Grading the Tumor

**Low Grade**



- Well Differentiated.
- Resembles normal parent tissue.

**High Grade**

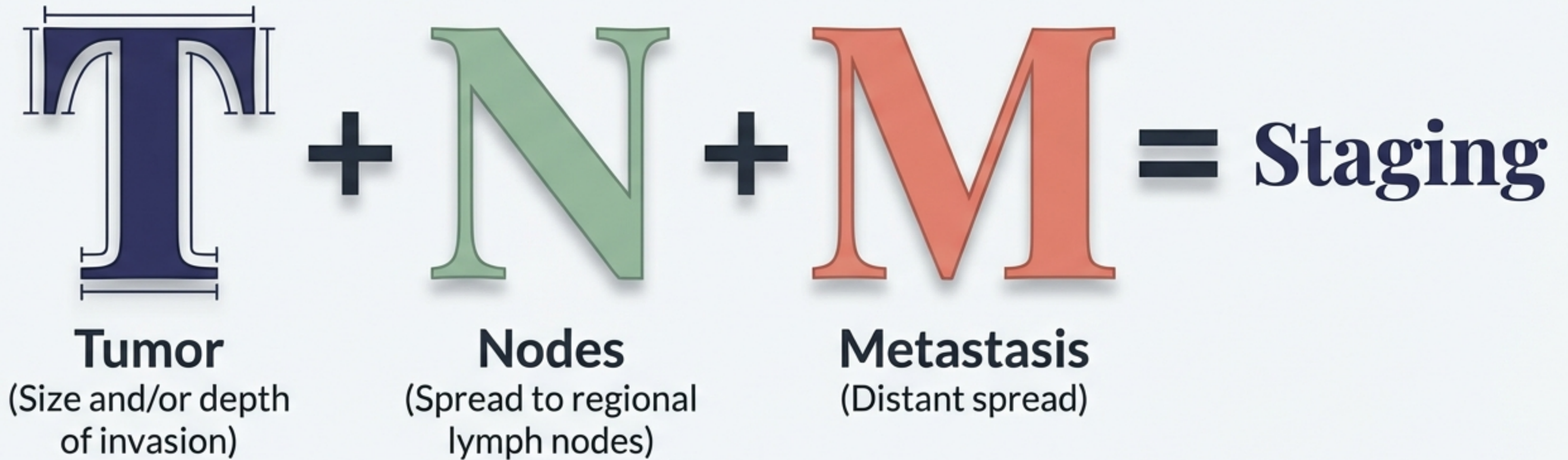


- Poorly Differentiated.
- Anaplastic.
- Does not resemble parent tissue.

**Better Prognosis**

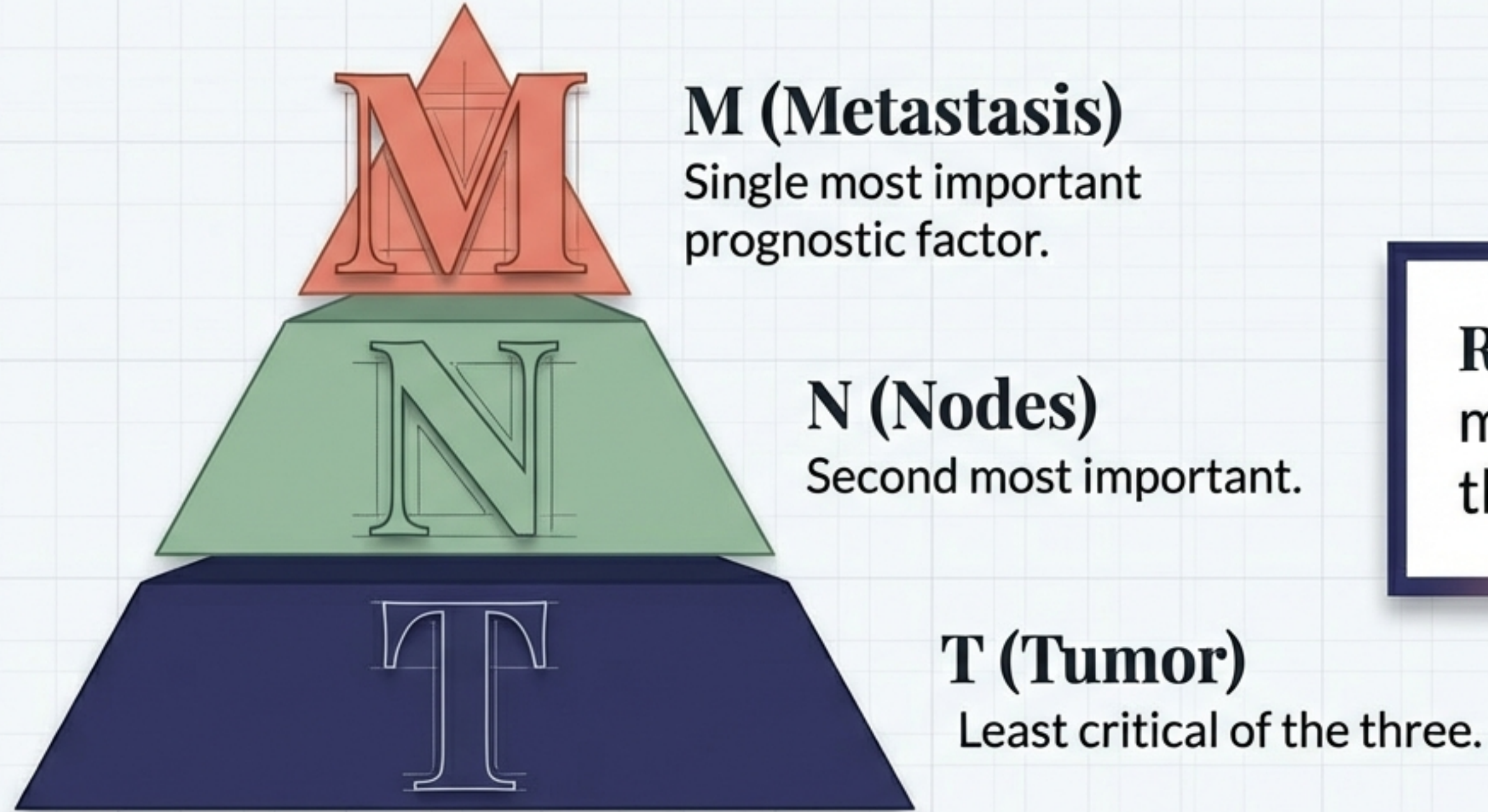
**Worse Prognosis**

# Staging the Cancer: The TNM System



Staging is determined after final surgical resection.

# The Prognostic Hierarchy



**Rule:** Staging is more important than Grading.

The degree of spread defines the future.