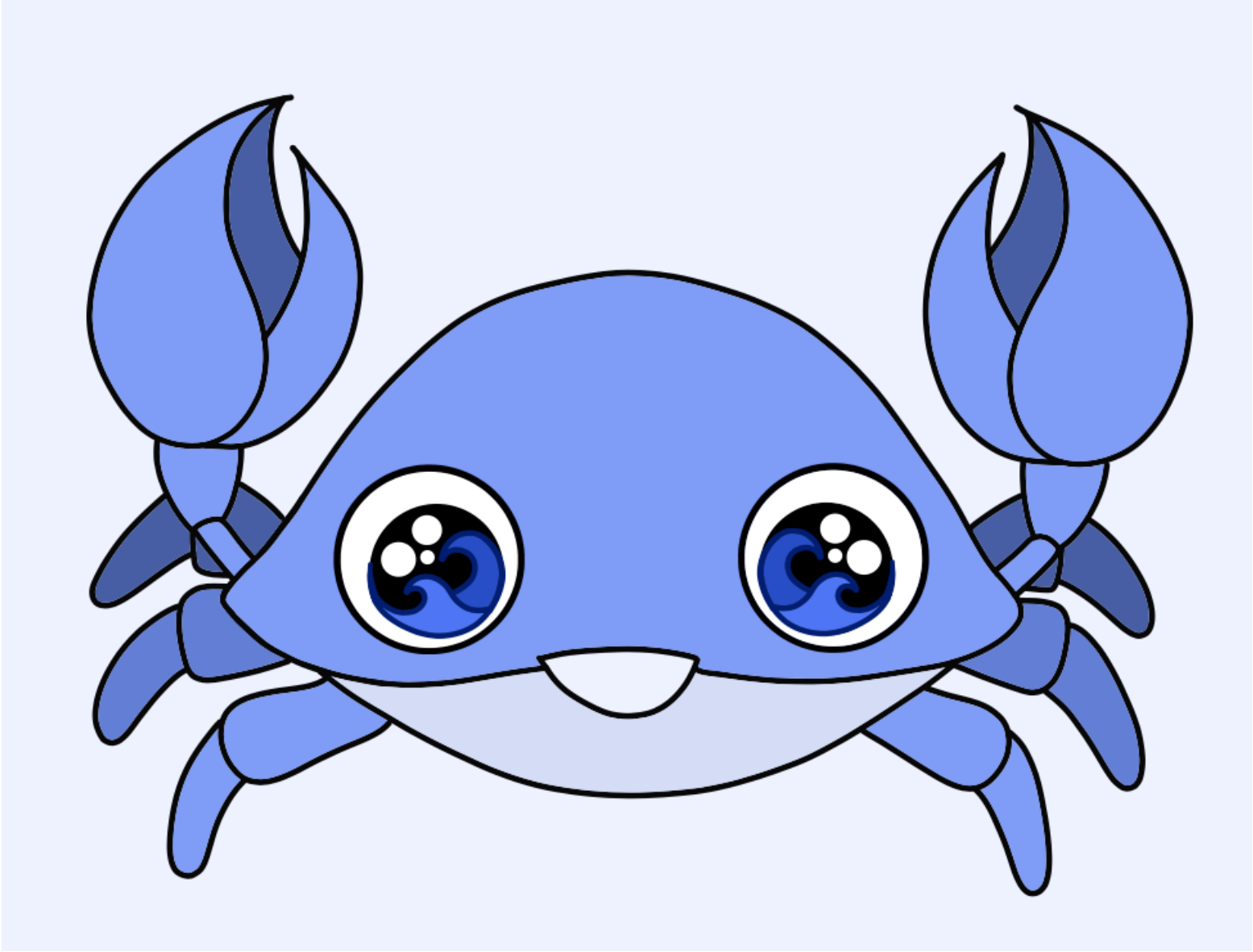


Neoplasia II: Tumor Characteristics

Tumor Characteristics Lecture Objectives

- Define tumor differentiation, and explain the difference between well-differentiated, moderately-differentiated, and poorly-differentiated tumor cells.
- Define anaplasia, and describe what anaplastic cells typically look like.
- Define dysplasia, describe what dysplastic cells look like, and explain why it matters whether cells are mildly, moderately, or severely dysplastic.
- Explain what “growth fraction” means, and list some factors that affect a tumor’s growth fraction.
- Describe the three ways tumors metastasize.
- Compare and contrast grading and staging (just know what they are...don’t memorize tiny details!)

Tumor Characteristics Lecture Outline

- Differentiation, dysplasia, and anaplasia
- Rate of growth
- Metastasis
- Grading and staging

Tumor Characteristics Lecture Outline

- Differentiation, dysplasia, and anaplasia

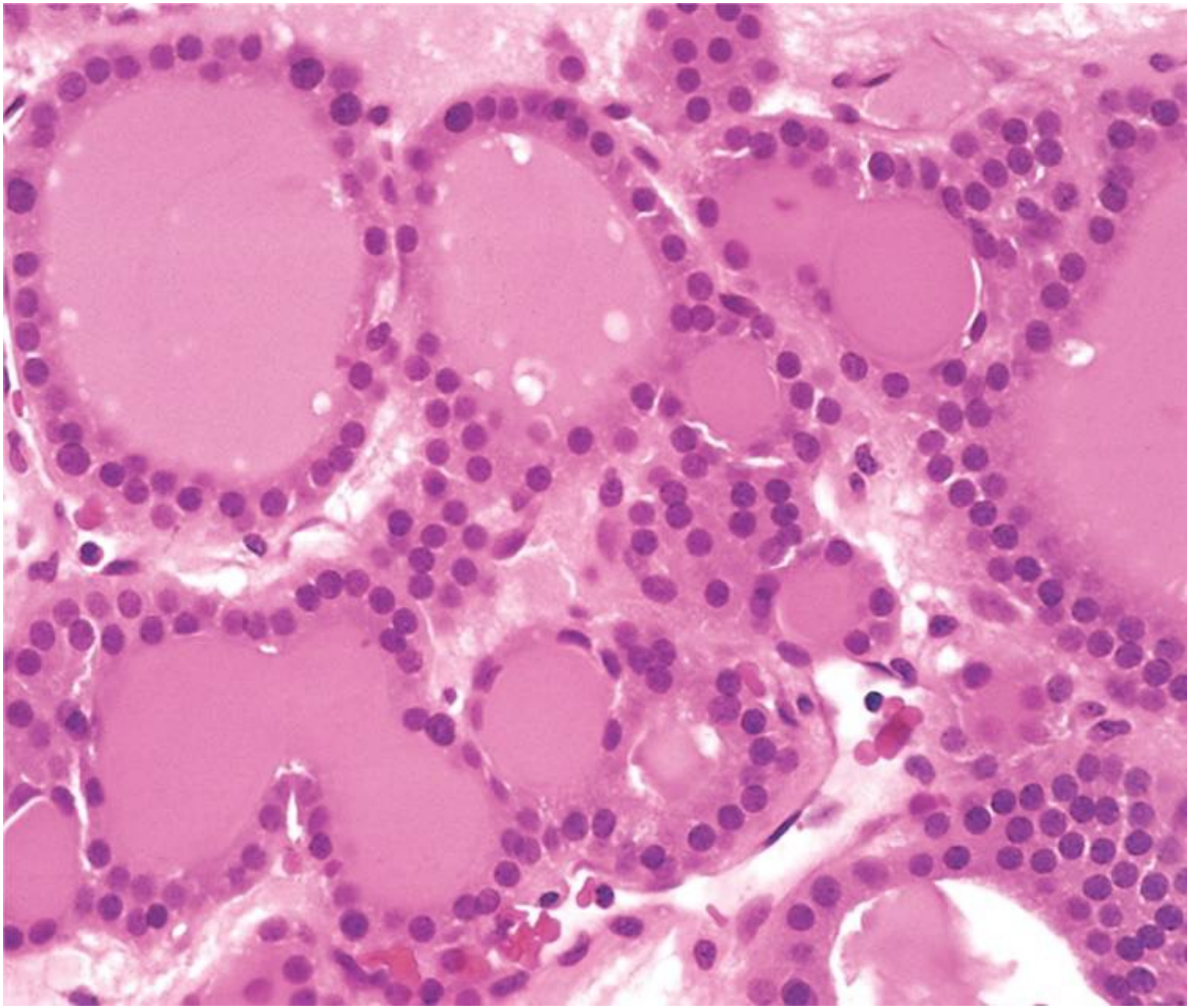
Differentiation

Differentiation = the degree to which tumor cells resemble their cell of origin

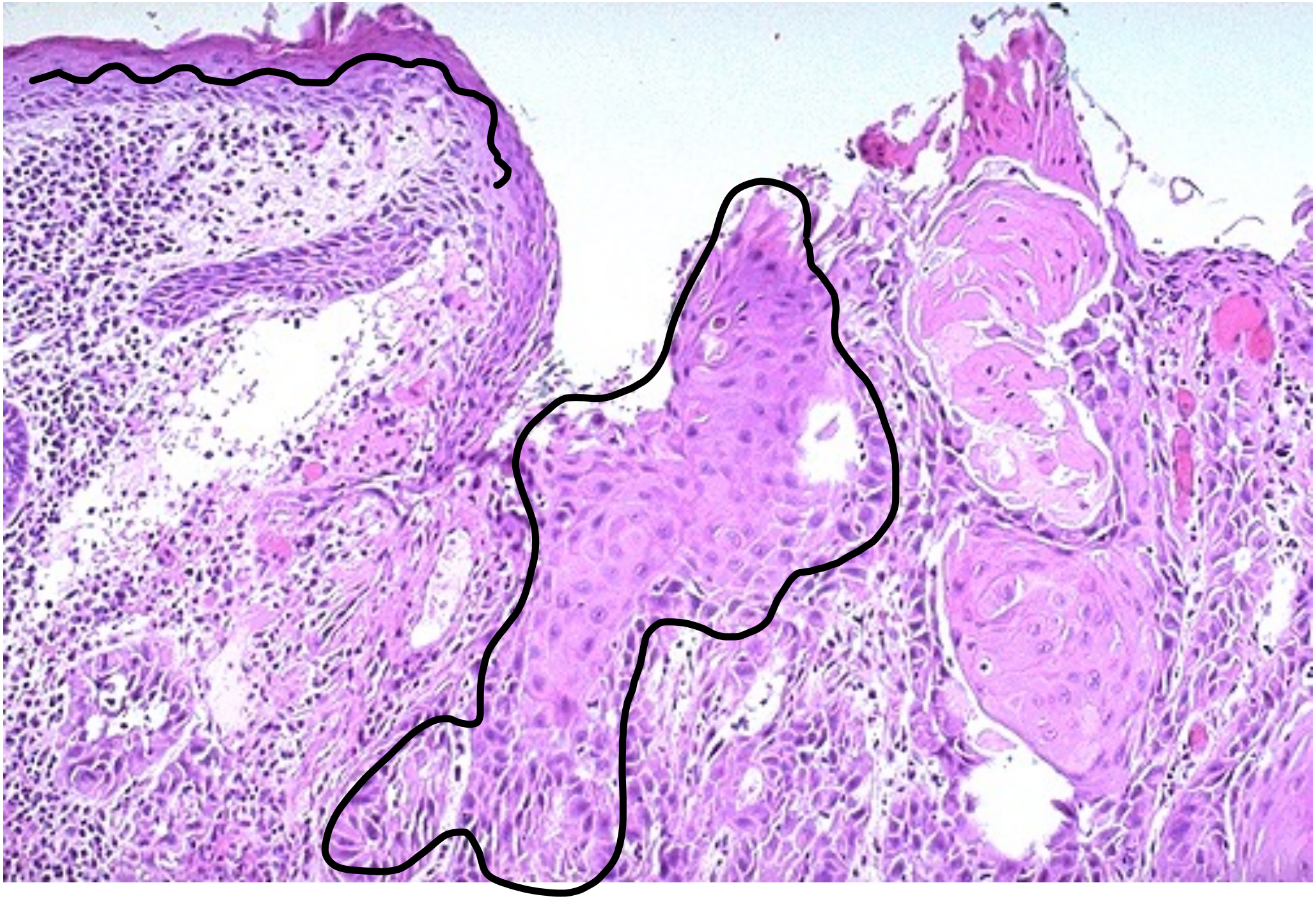
- Well-differentiated: closely resemble
- Moderately-differentiated: sort of resemble
- Poorly-differentiated: barely resemble

Benign tumors are usually well-differentiated

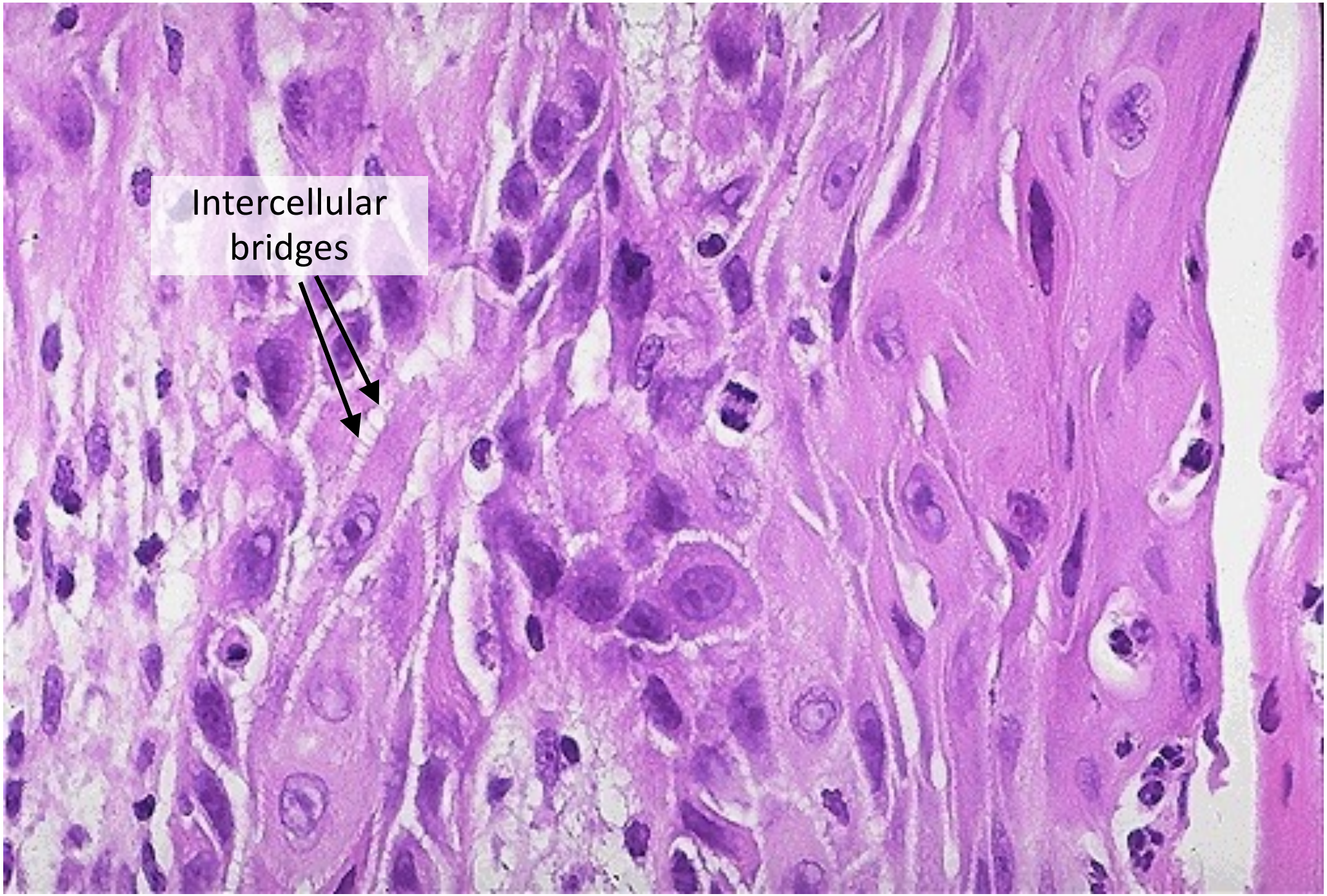
Malignant tumors can show any level of differentiation



Thyroid adenoma, well-differentiated



Squamous cell carcinoma, well-differentiated



Squamous cell carcinoma, poorly-differentiated

Anaplasia

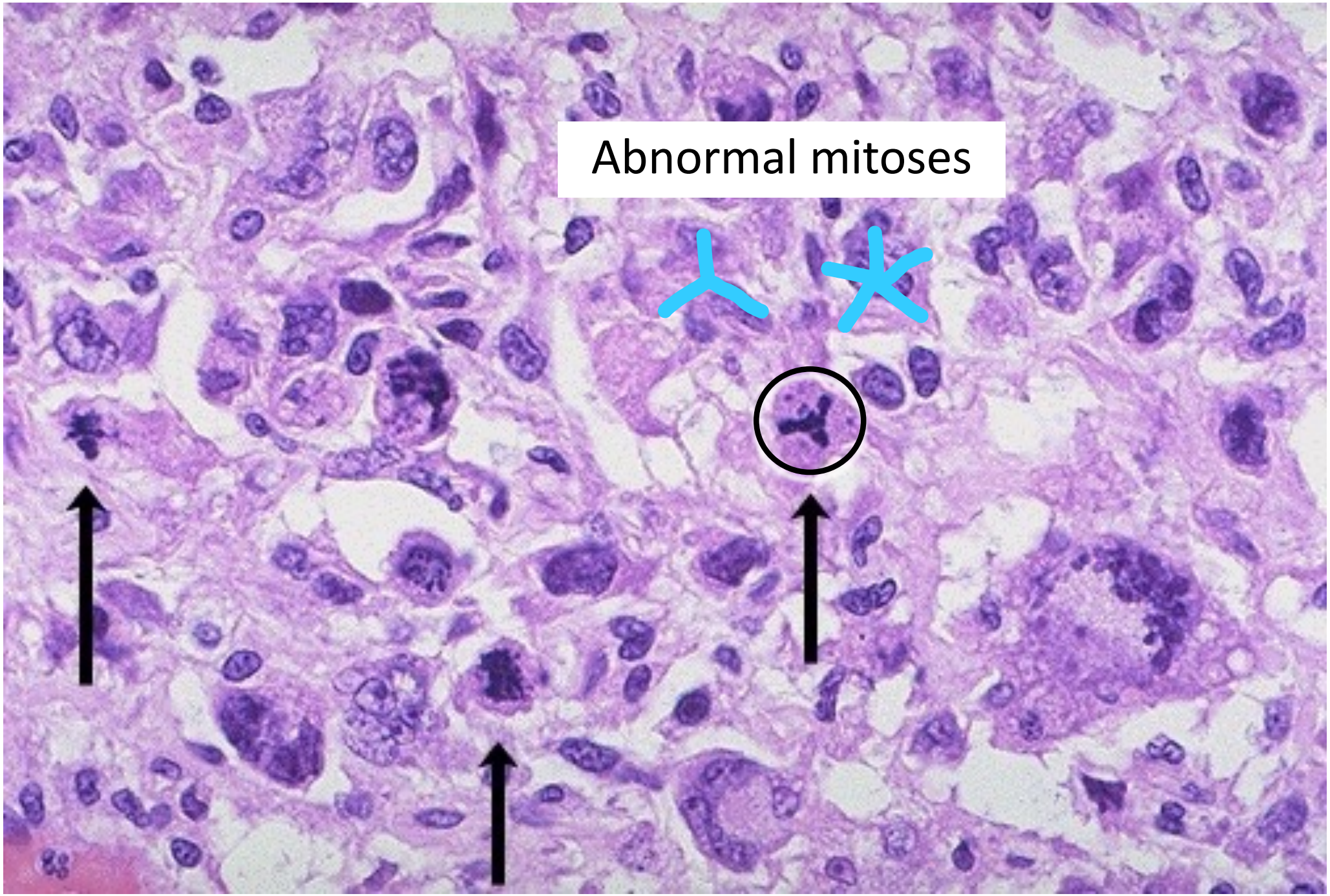
Anaplasia = a state of complete un-differentiation

- Literally, “to grow (-plasia) backwards (ana-)”
- Means tumor cells do not resemble their cell of origin at all
- Almost always indicates malignancy

Characteristics of Anaplastic Cells

- Pleomorphism
- Hyperchromatic, large nuclei
- Bizarre nuclear shapes, distinct nucleoli
- Lots of mitoses, and atypical mitoses
- Architectural anarchy

Anaplastic carcinoma



Lots of mitoses

Dysplasia

Dysplasia = disorderly (dys-) growth (-plasia)

- Used to describe changes in non-neoplastic epithelial cells
- Graded as mild, moderate, or severe
- Next step after severe dysplasia is carcinoma in situ
- ...and the next step after that is invasive carcinoma

Dysplastic cells show:

- Pleomorphism
- Hyperchromatic, large nuclei
- Lots of mitoses
- Architectural anarchy

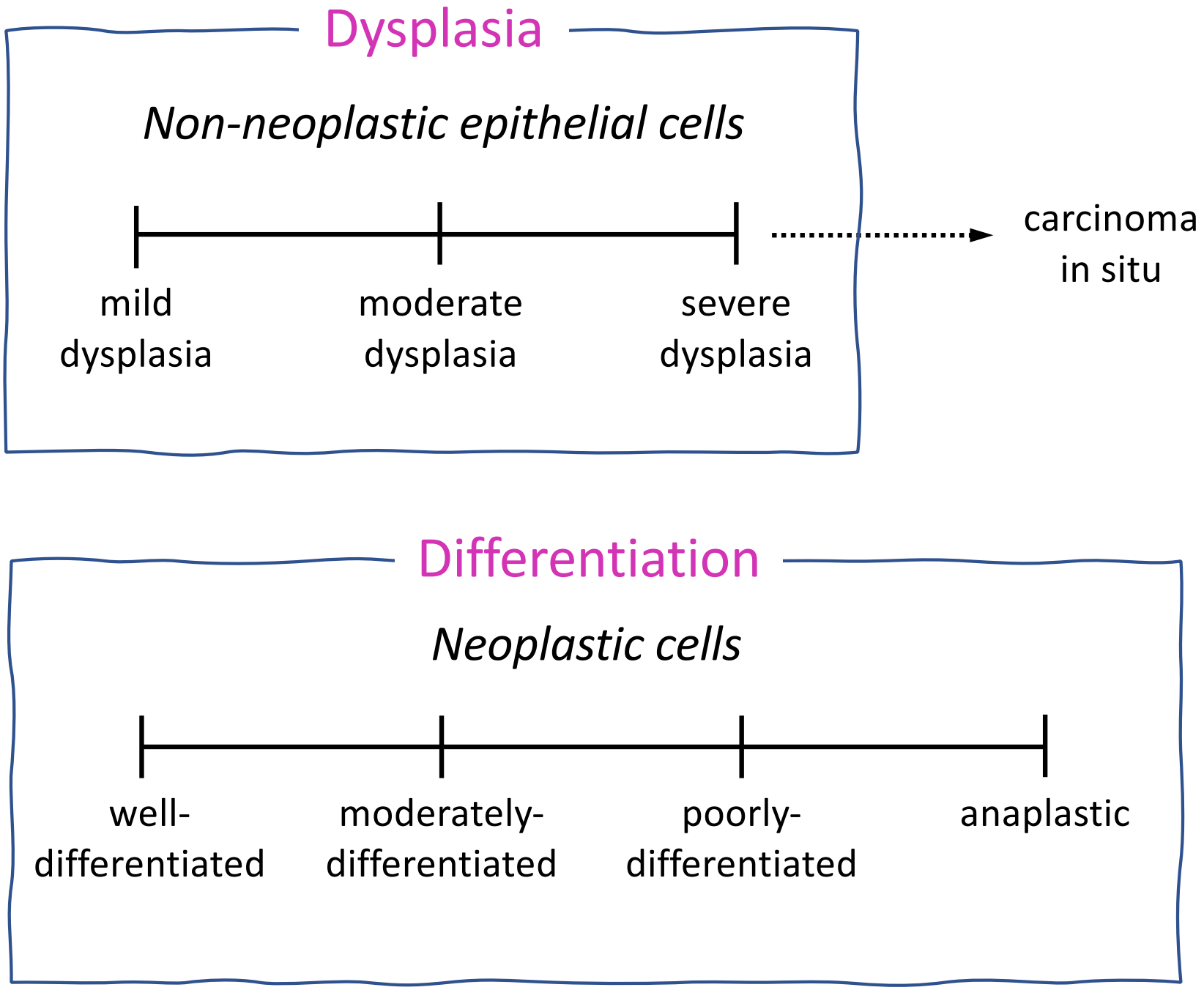
Q. Wait a minute, “dysplasia” sounds suspiciously similar to “differentiation” – what’s the difference?

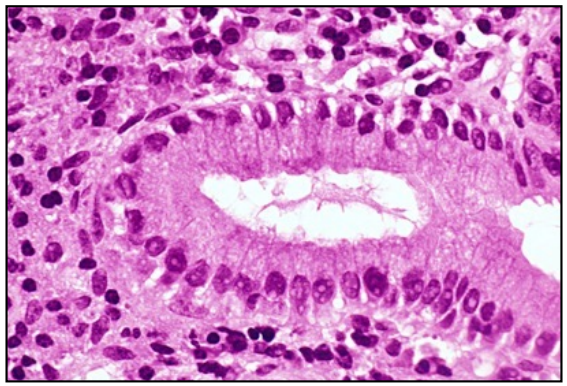
A. Both terms describe whether cells look normal or not!

BUT:

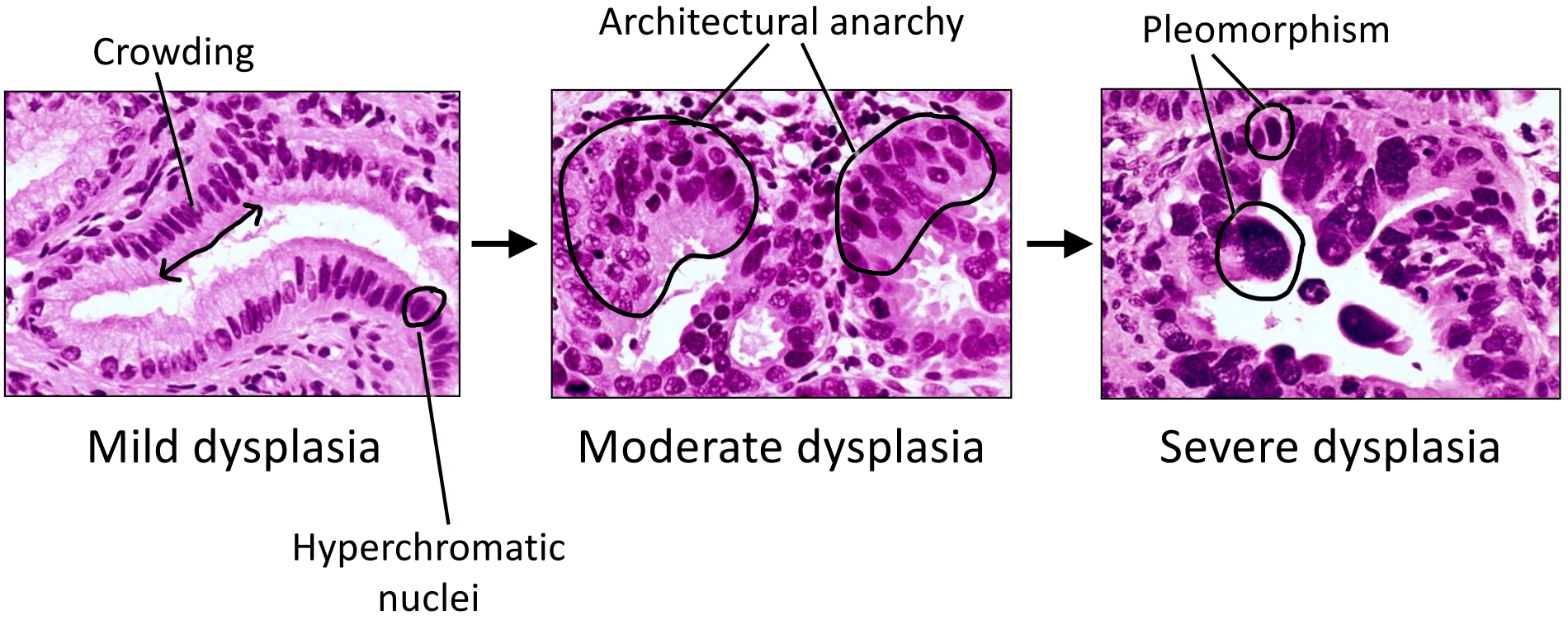
Dysplasia is used to describe non-neoplastic cells, and differentiation is used to describe neoplastic cells.

Dysplasia is used to describe epithelial cells, and differentiation can be used to describe any cell type.


Dysplasia
Non-neoplastic epithelial cells
mild dysplasia
moderate dysplasia
severe dysplasia
carcinoma in situ
Differentiation
Neoplastic cells
well-differentiated
moderately-differentiated
poorly-differentiated
anaplastic



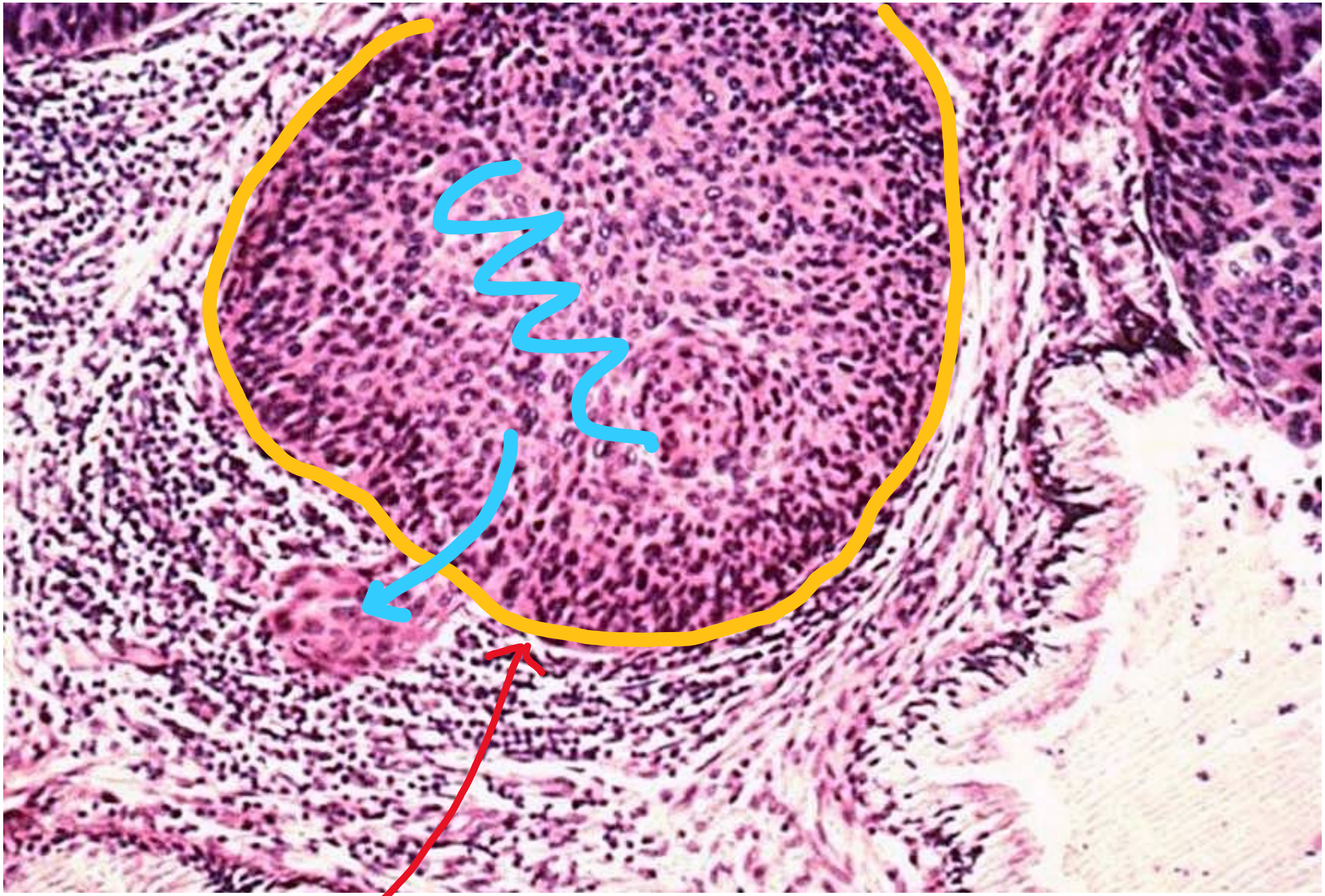
Normal glandular epithelium



Mild dysplasia

Moderate dysplasia

Severe dysplasia



Invasive carcinoma

Tumor Characteristics Lecture Outline

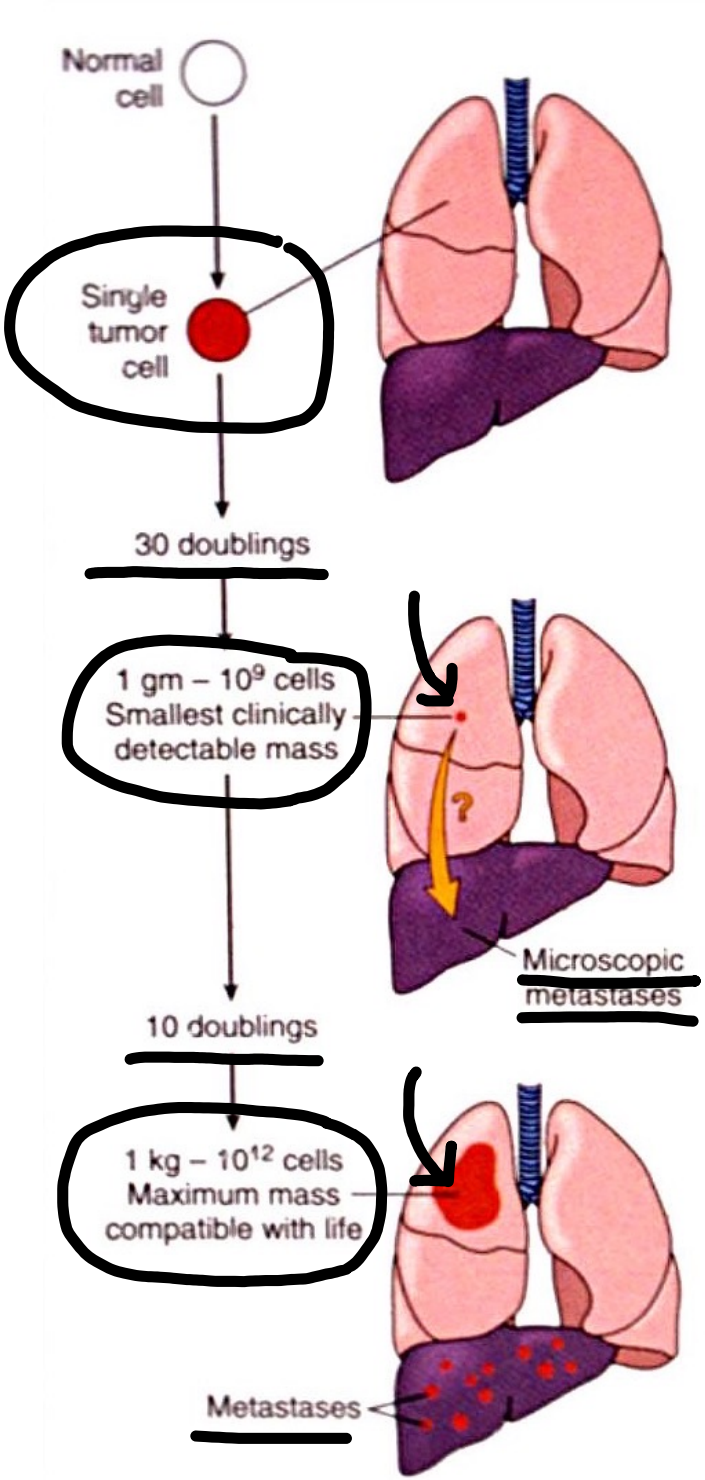
- Differentiation, dysplasia, and anaplasia
- Rate of growth

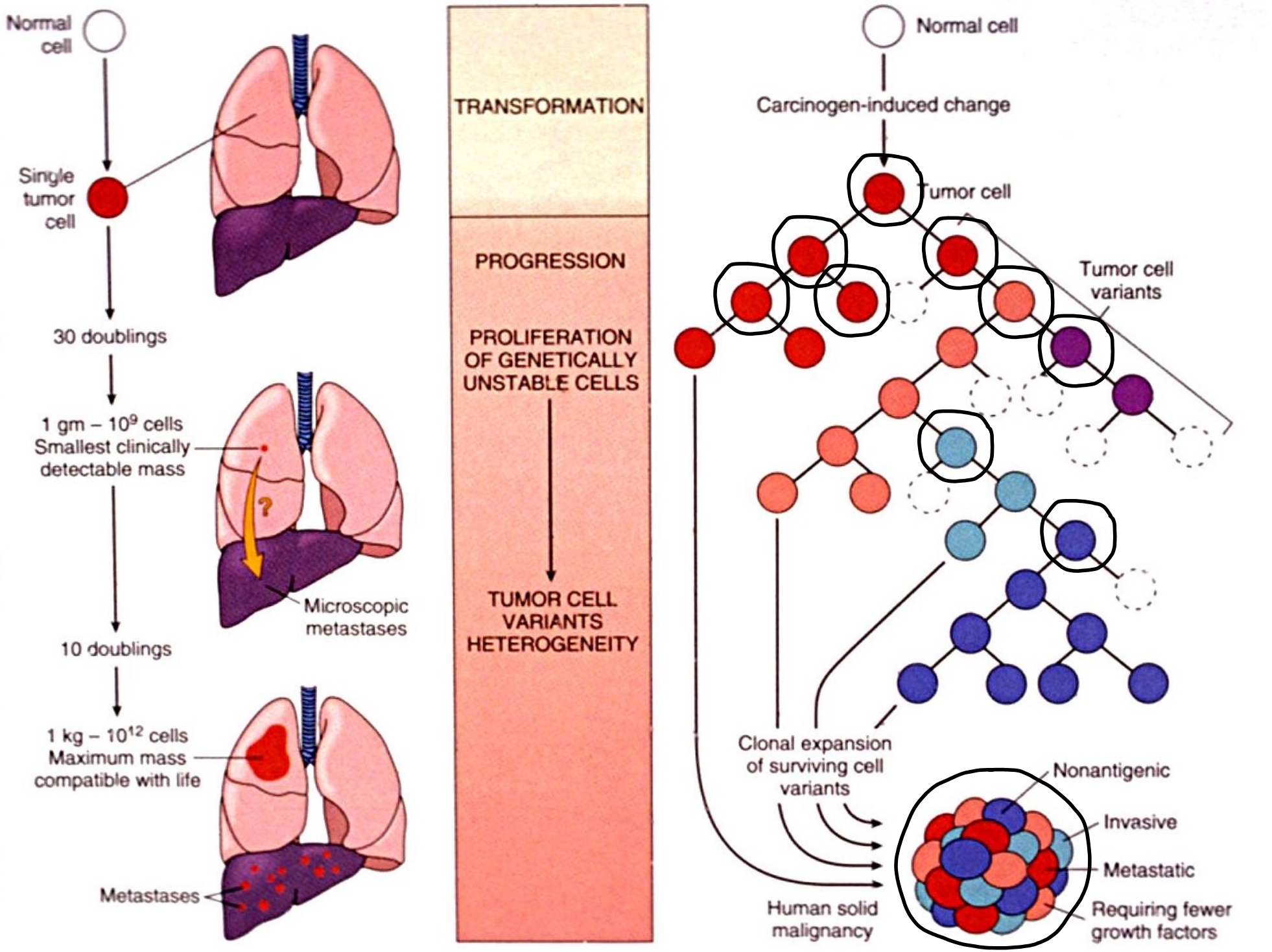
Generalizations about Tumor Growth

- Malignant tumors grow faster than benign ones.
- Poorly-differentiated tumors grow faster than well-differentiated ones.
- Growth is dependent on:
  - Blood supply
  - Hormonal factors
  - Emergence of aggressive sub-clones

Growth Fraction

- Growth fraction (GF) = % of tumor cells that are dividing
- Age of tumor matters
  - Early on (subclinical), GF high.
  - Later (clinically detectable), GF low.
- Type of tumor matters
  - Leukemias, lymphomas, small-cell lung cancer: high GF
  - Breast, colon cancer: low GF
- Important for treatment
  - High GF tumor: treat with chemotherapy/radiation
  - Low GF tumor: treat by debulking


Normal cell
Single tumor cell
30 doublings
1 gm – 10^9 cells
Smallest clinically detectable mass
?
Microscopic metastases
10 doublings
1 kg – 10^{12} cells
Maximum mass compatible with life
Metastases


Normal cell
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Smallest clinically detectable mass
?
Microscopic metastases
10 doublings
1 kg – 10^{12} cells
Maximum mass compatible with life
Metastases
TRANSFORMATION
PROGRESSION
PROLIFERATION OF GENETICALLY UNSTABLE CELLS
TUMOR CELL VARIANTS HETEROGENEITY
Normal cell
Carcinogen-induced change
Tumor cell
Tumor cell variants
Clonal expansion of surviving cell variants
Nonantigenic
Invasive
Metastatic
Requiring fewer growth factors
Human solid malignancy


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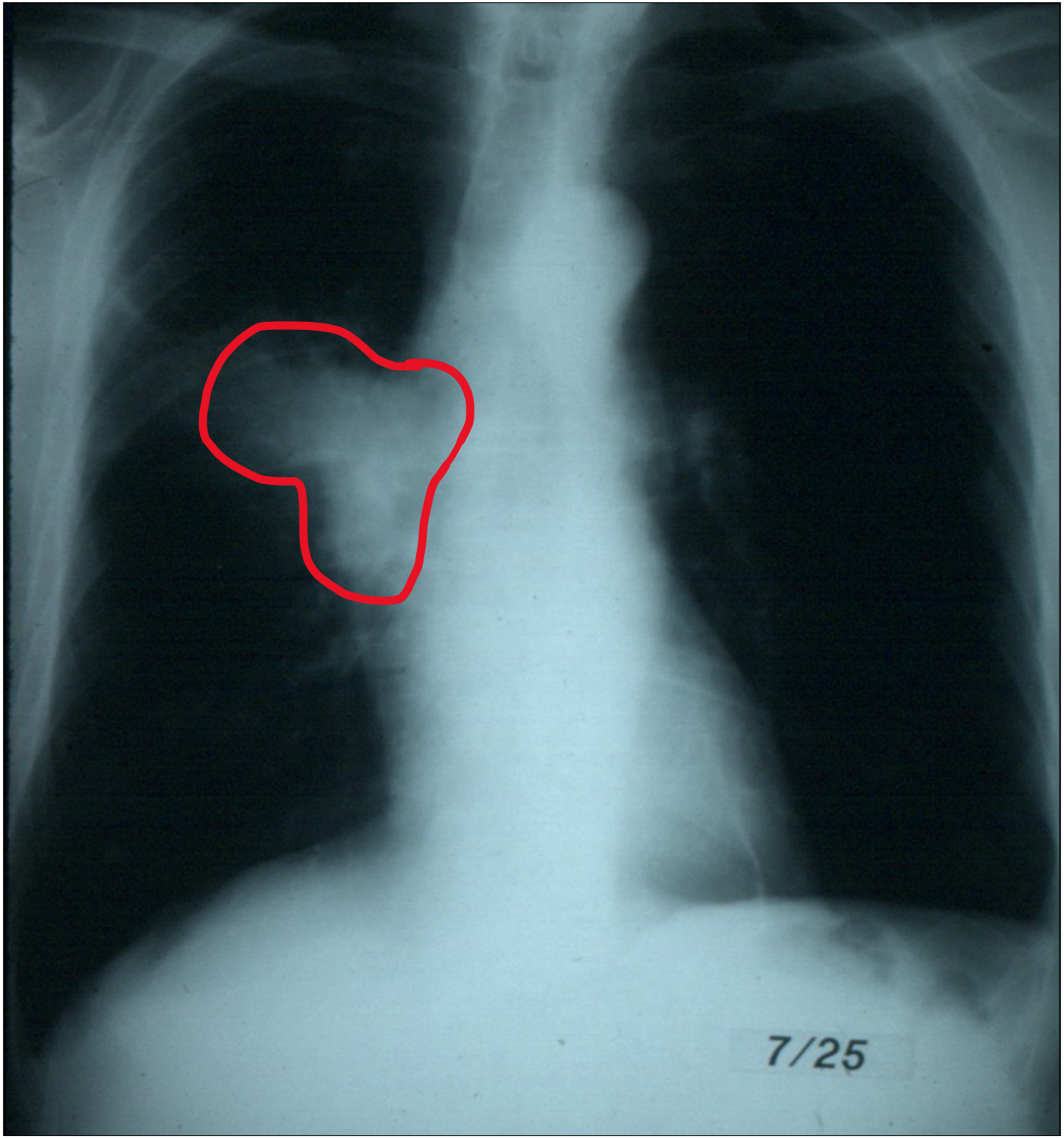
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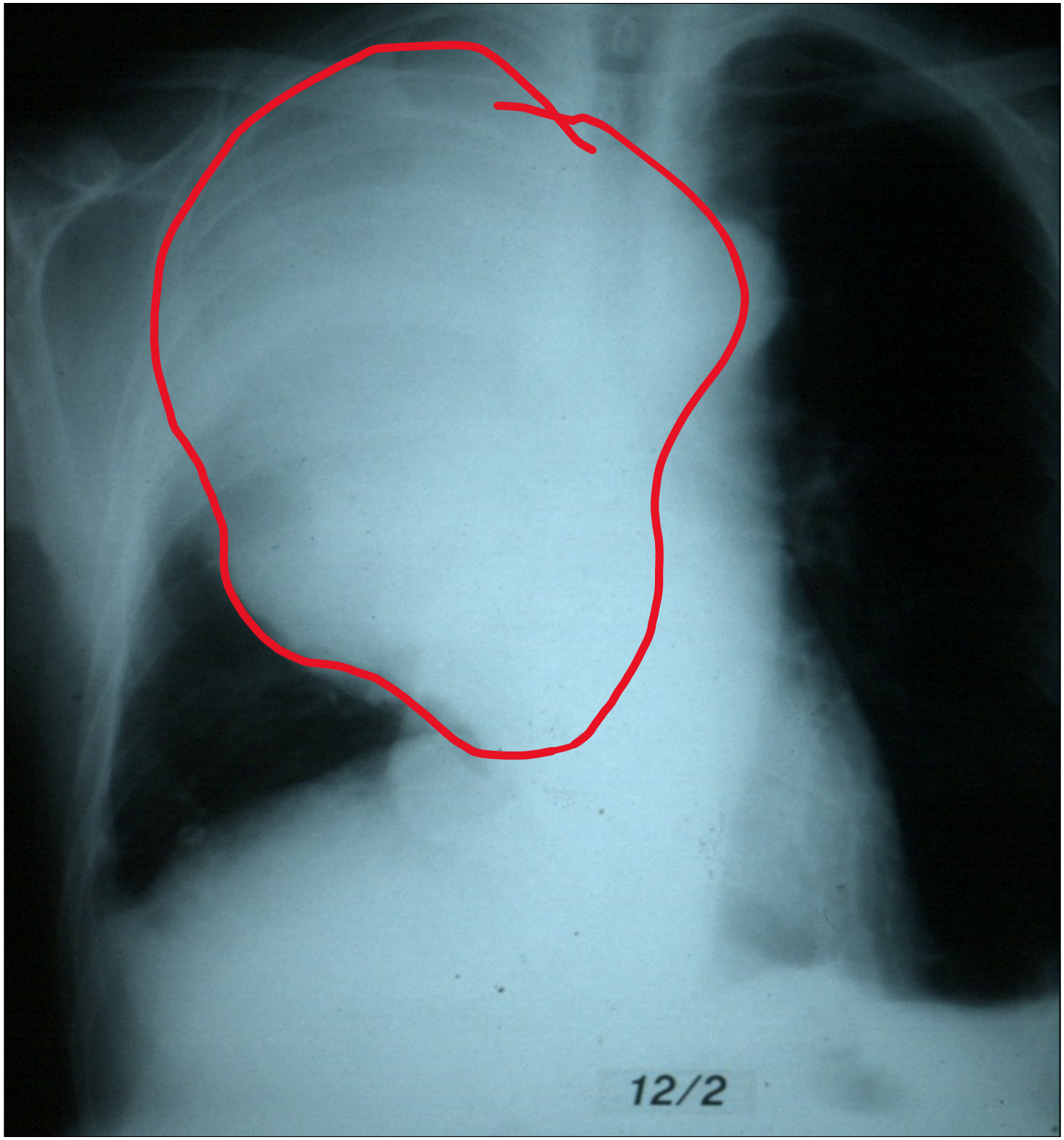
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Tumor Characteristics Lecture Outline

- Differentiation, dysplasia, and anaplasia
- Rate of growth
- Metastasis

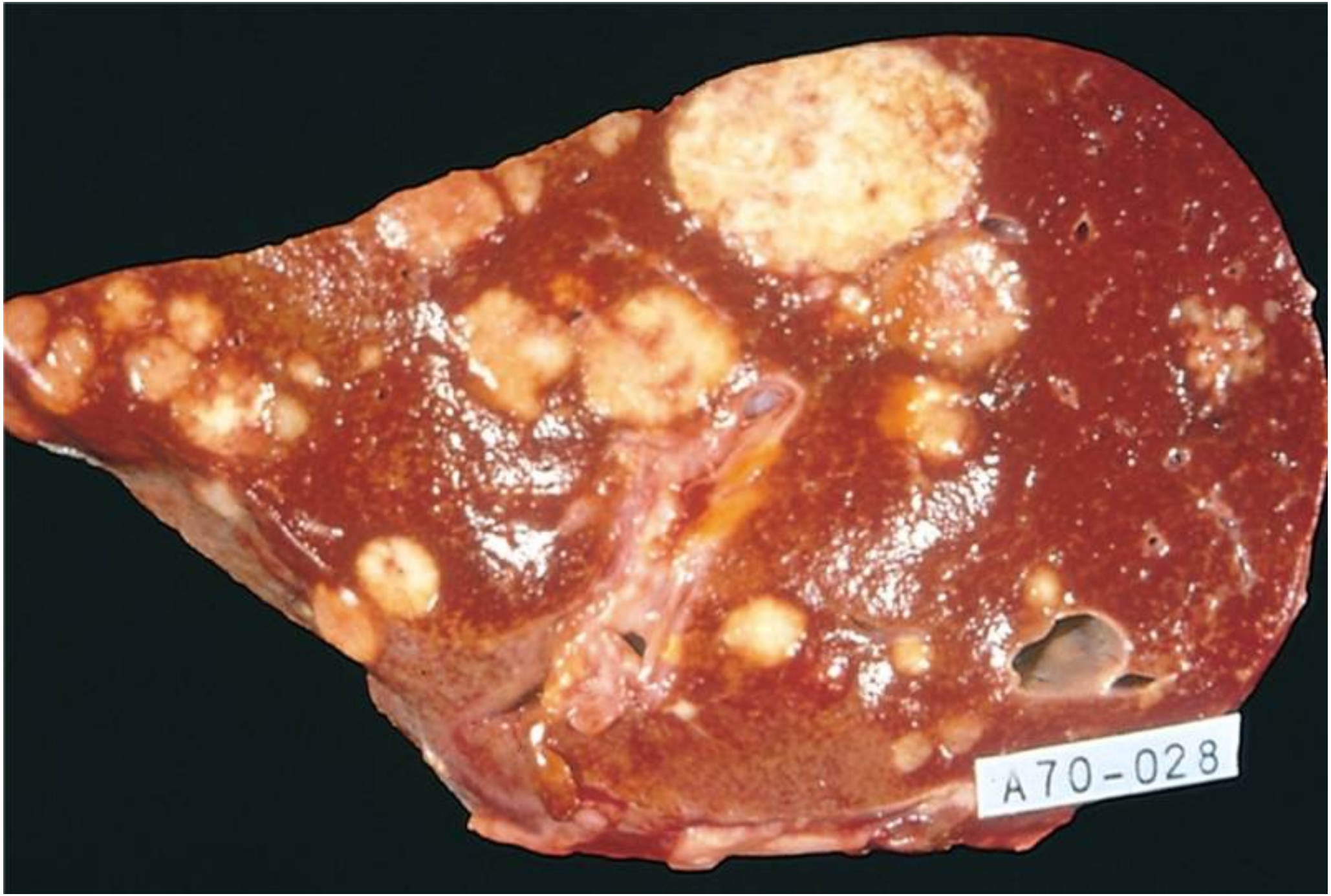
Metastasis

Metastasis = development of secondary tumor implants in distant tissues

Half of all patients with malignancies have mets at the time of diagnosis!!

The speed and location of metastasis is related to:

- Type of tumor
- Size of tumor
- Degree of differentiation of tumor



Liver with multiple metastases

Three Ways Tumors Metastasize

Seeding

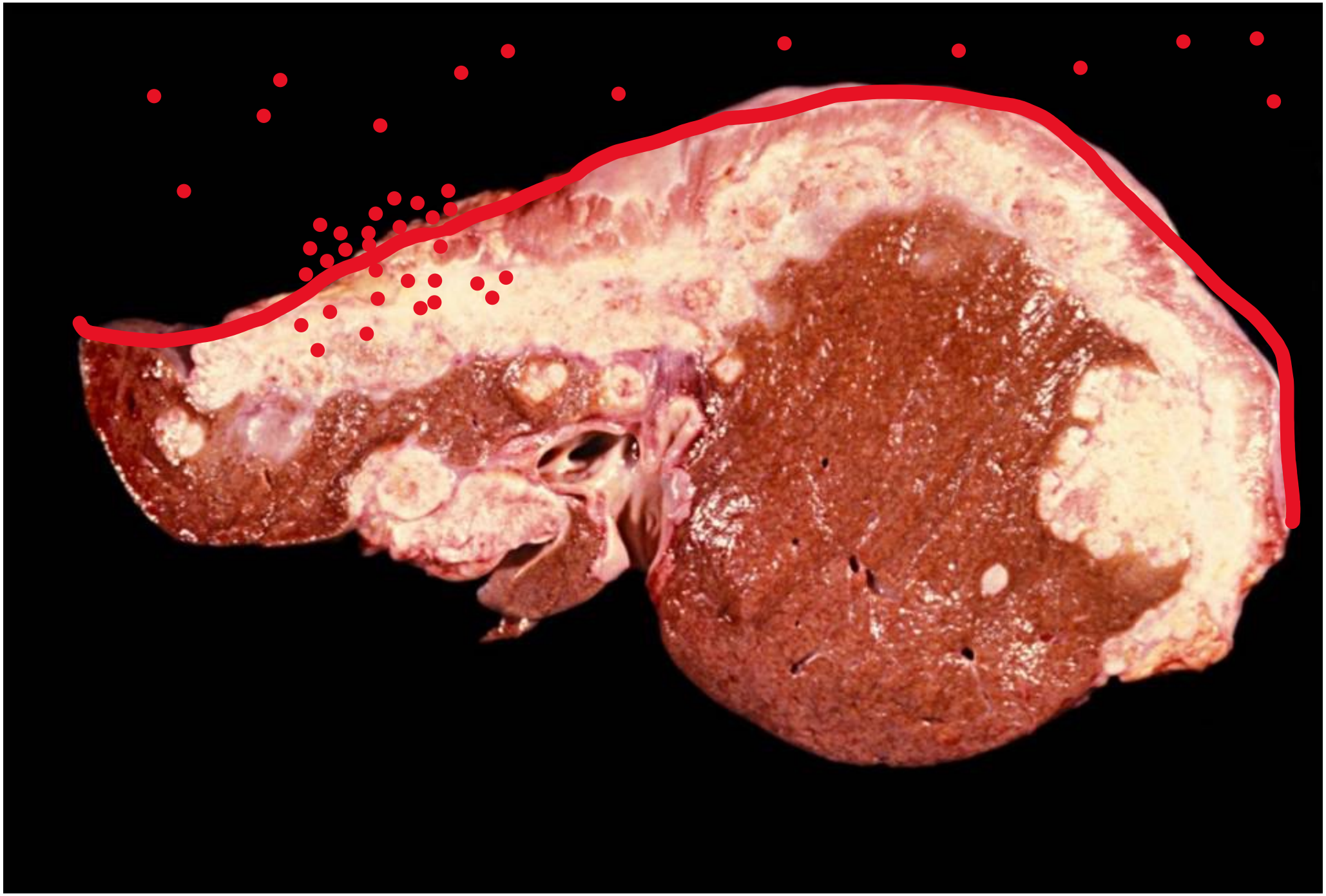
Lymphatic spread

Hematogenous spread

Three Ways Tumors Metastasize

Seeding

- Tumor floats through a body cavity
- Bits break off and implant on peritoneal surfaces
- Ovarian cancer can spread easily this way



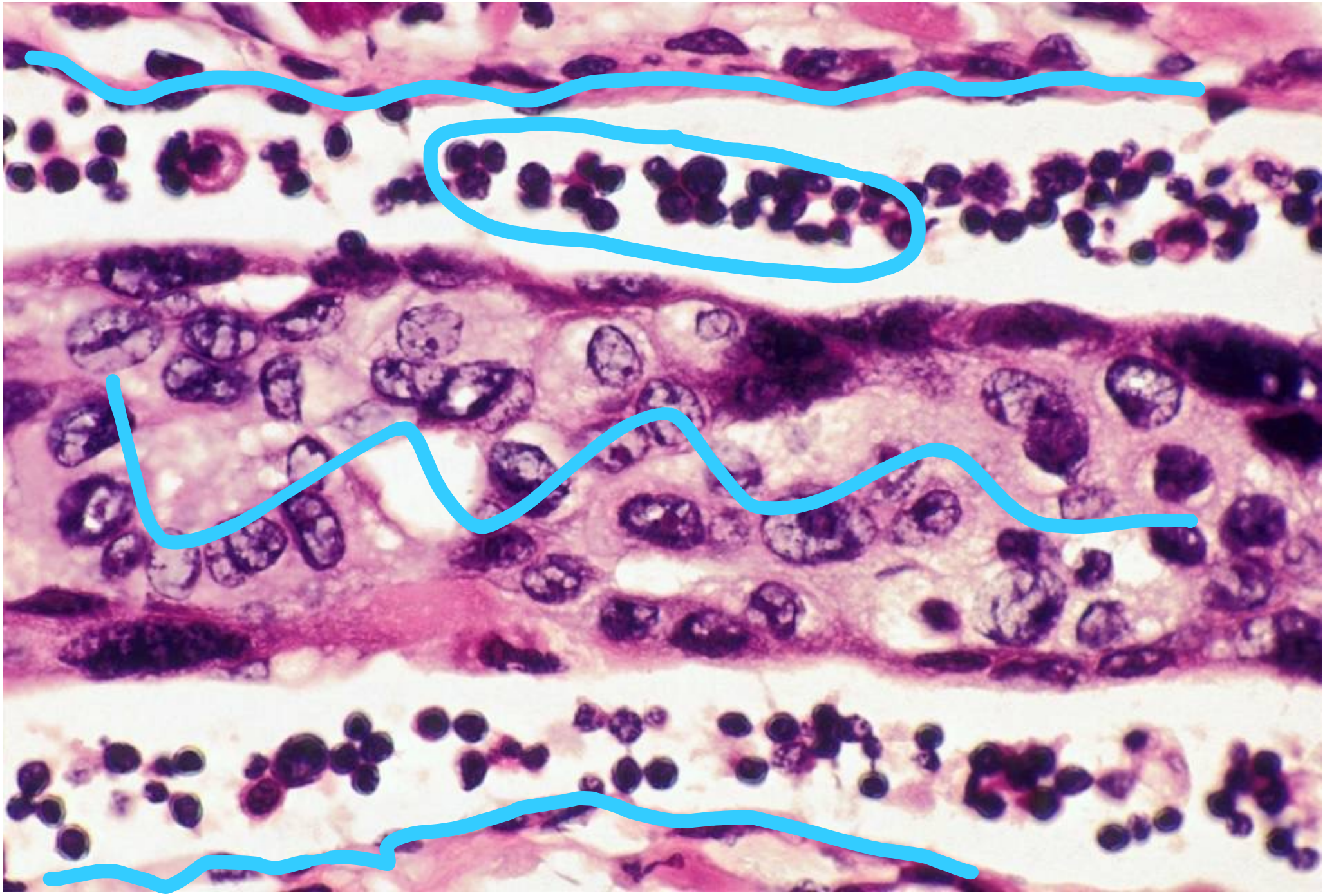
Liver seeded with metastatic ovarian carcinoma

Three Ways Tumors Metastasize

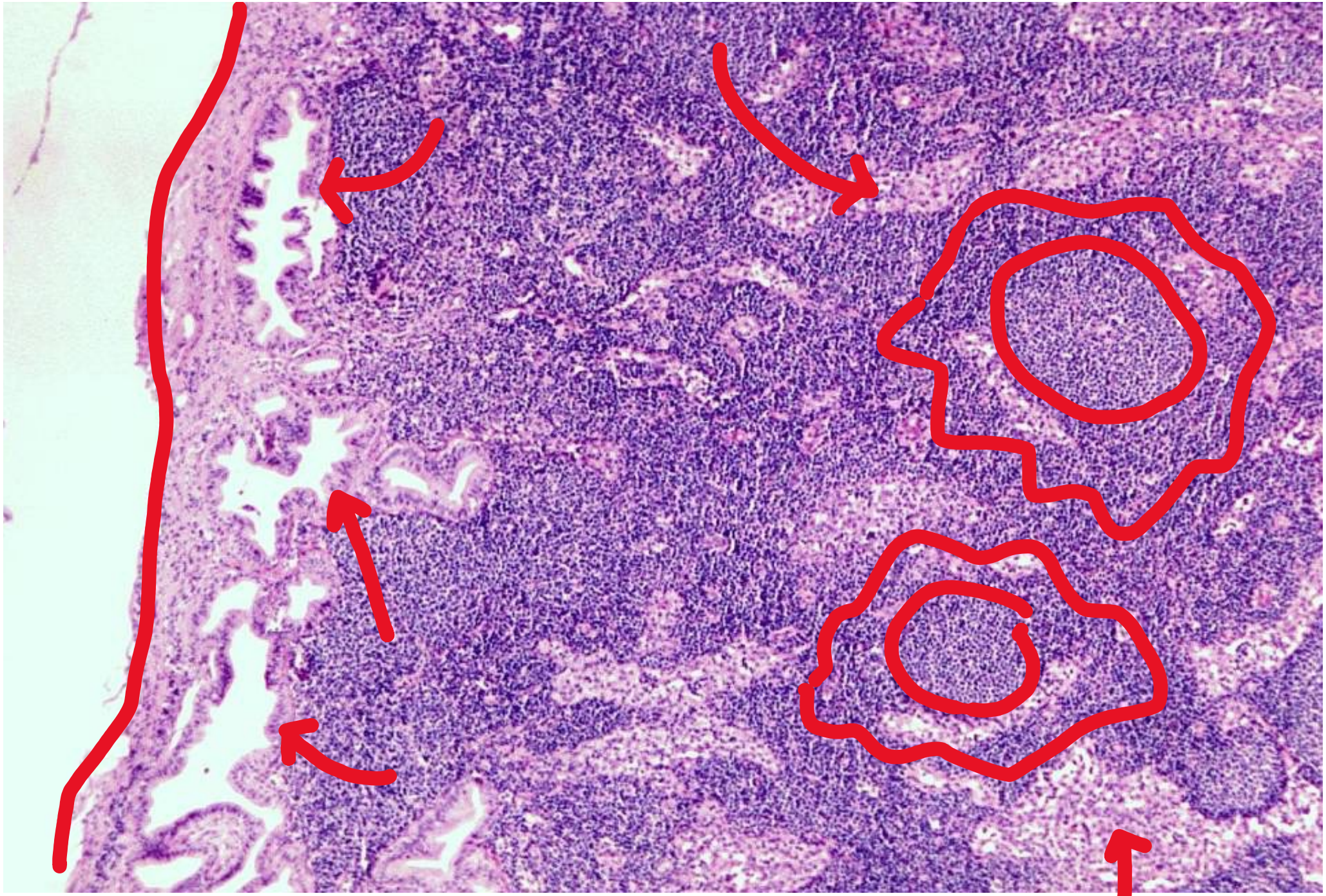
Seeding

Lymphatic spread

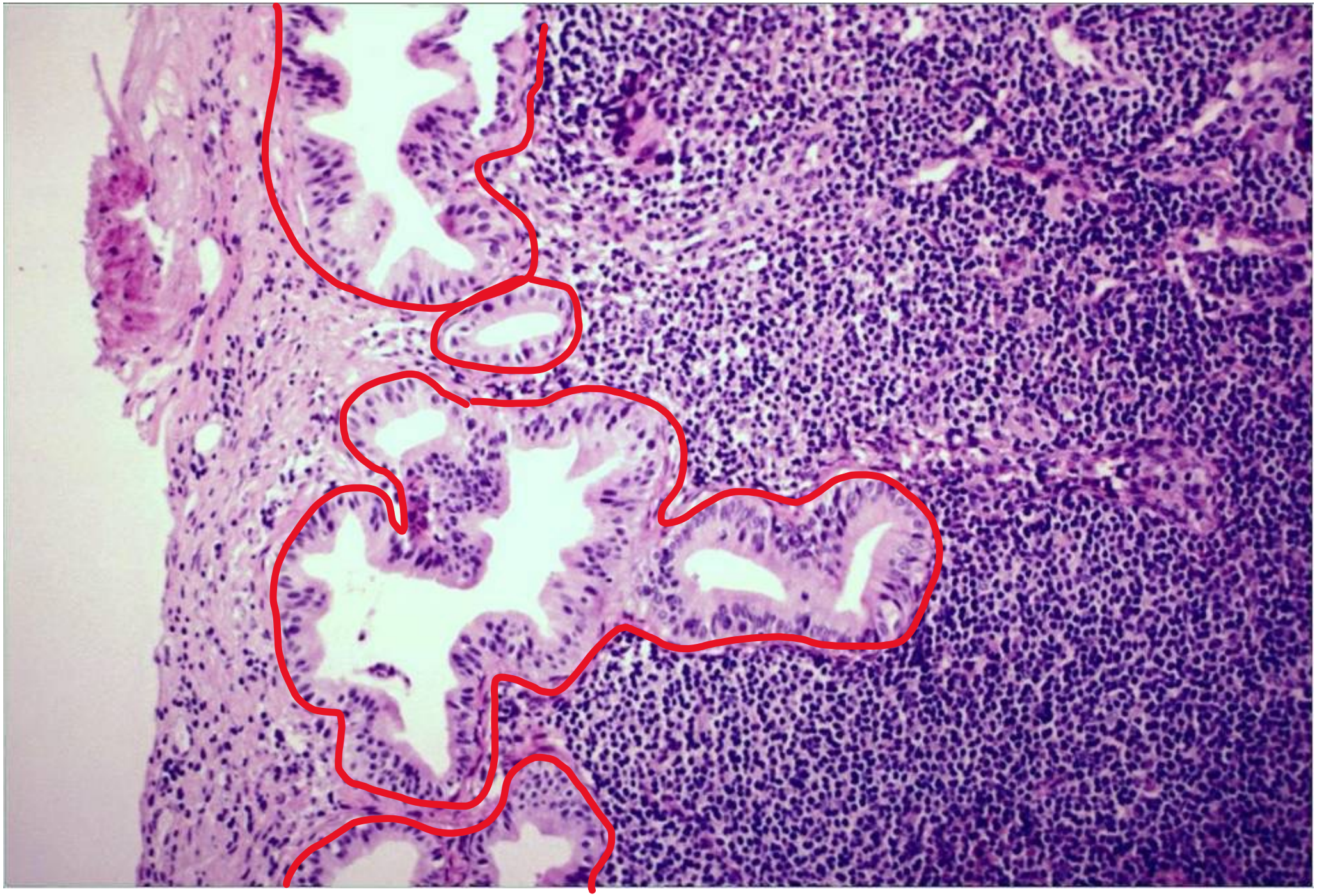
- Tumor spreads through lymphatics
- Sentinel lymph node first
- Carcinomas prefer to spread this way



Tumor in lymphatic



Tumor in lymph node



Tumor in lymph node

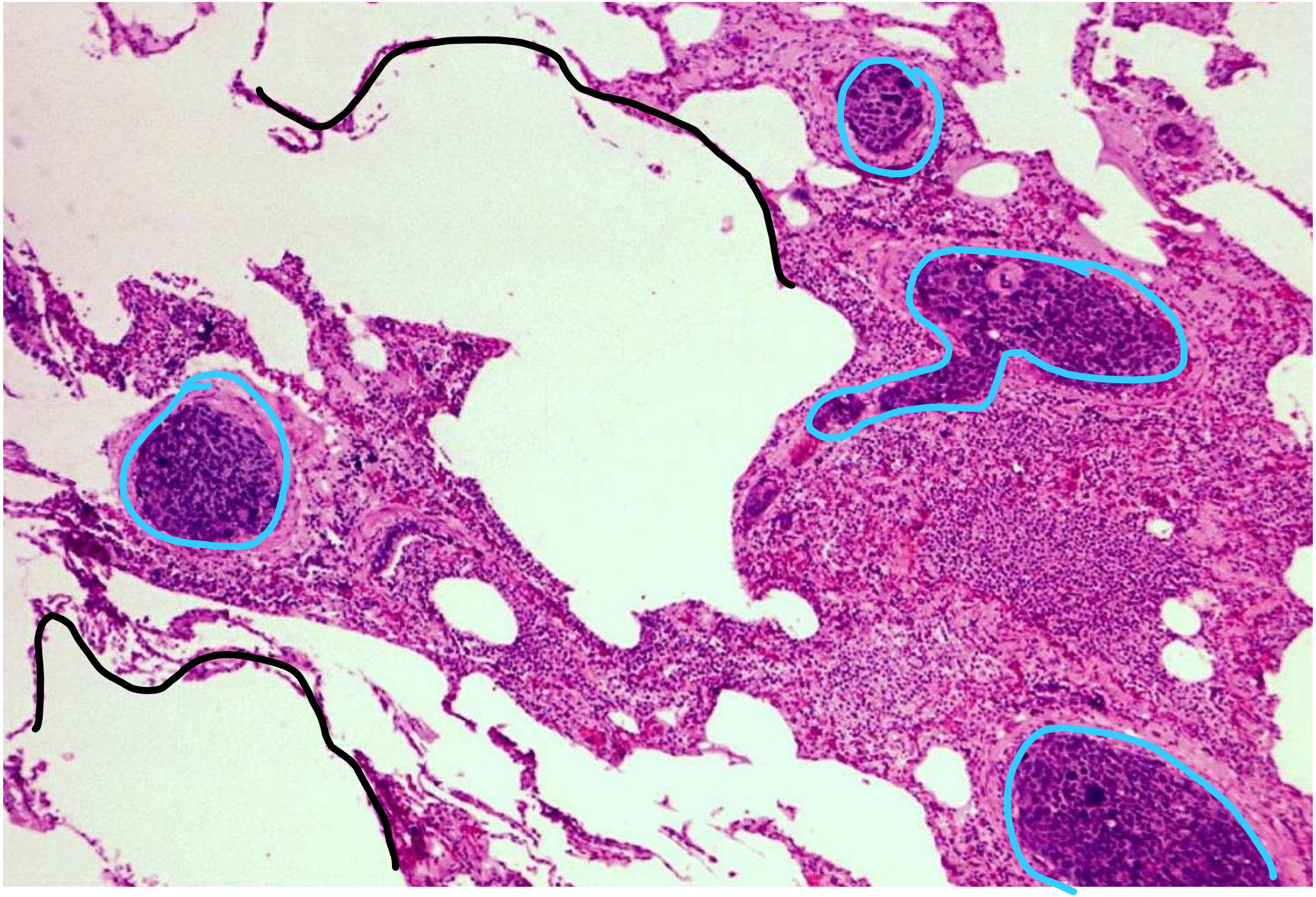
Three Ways Tumors Metastasize

Seeding

Lymphatic spread

Hematogenous spread

- Tumor spreads through blood vessels
- Liver and lungs are the most common destinations
- Sarcomas prefer to spread this way



Sarcoma metastatic to lung

Neoplasia Outline

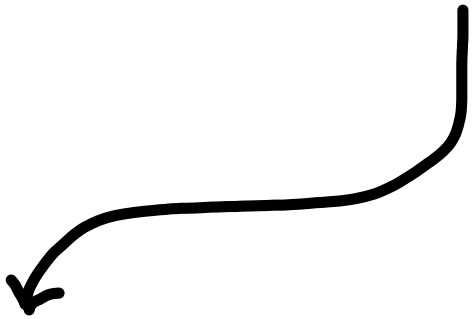
- Differentiation, dysplasia, and anaplasia
- Rate of growth
- Metastasis
- Grading and staging

Grading and Staging

- Used for malignant tumors
- Useful for determining treatment and prognosis
- Grading
  - Tells you how nasty the tumor looks
  - Use microscope
  - Can be useful in some tumors
- Staging
  - Tells you how far the tumor has spread
  - Use imaging
  - Very useful in most tumors

Grading system for breast cancer*

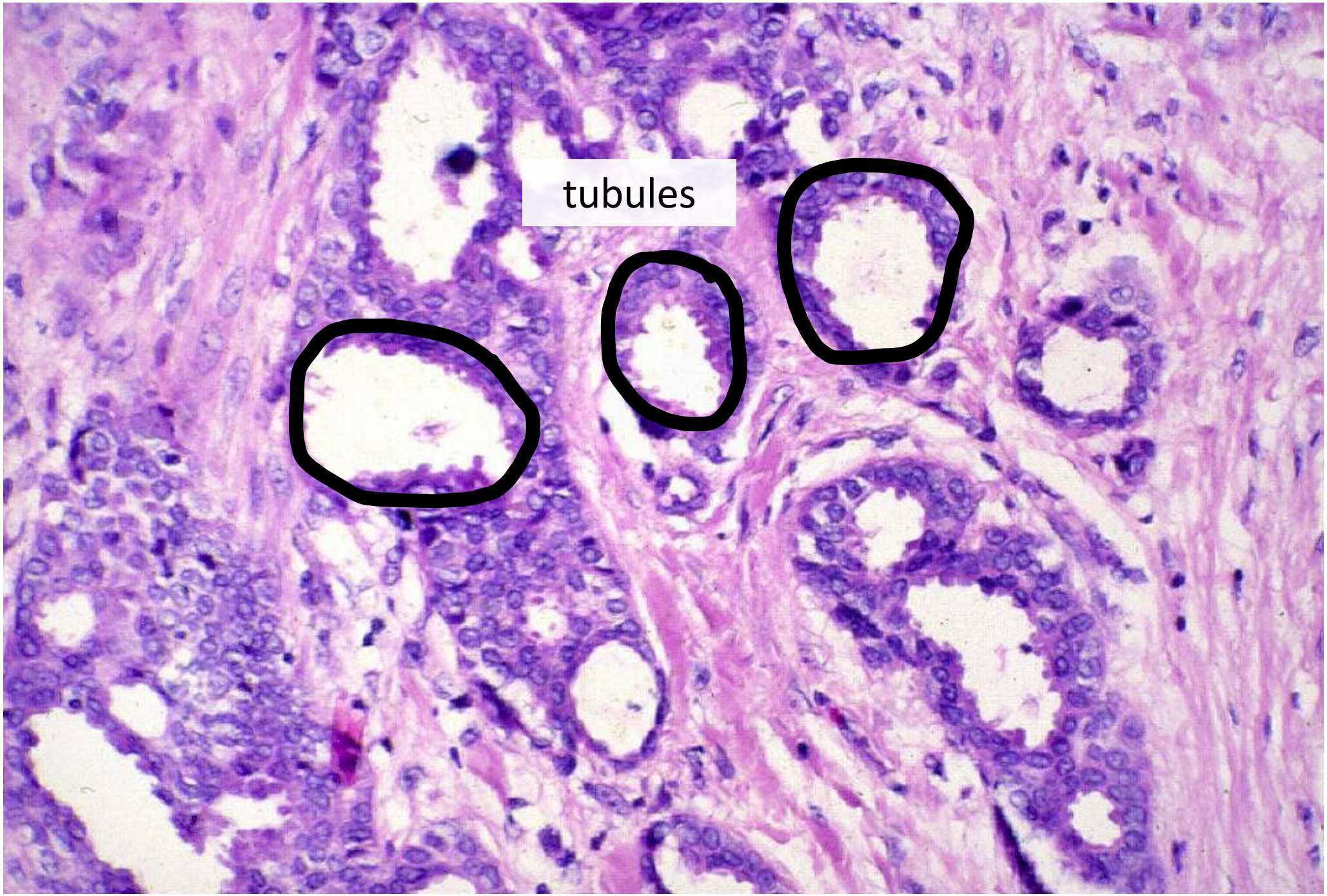
Tubules		Pleomorphism		Mitoses	
lots of tubules	1	small, uniform cells	1	0-9 mitoses/10 hpf	1
some tubules	2	larger, less uniform cells	2	10-19 mitoses/10 hpf	2
rare tubules	3	markedly pleomorphic cells	3	≥20 mitoses/10 hpf	3



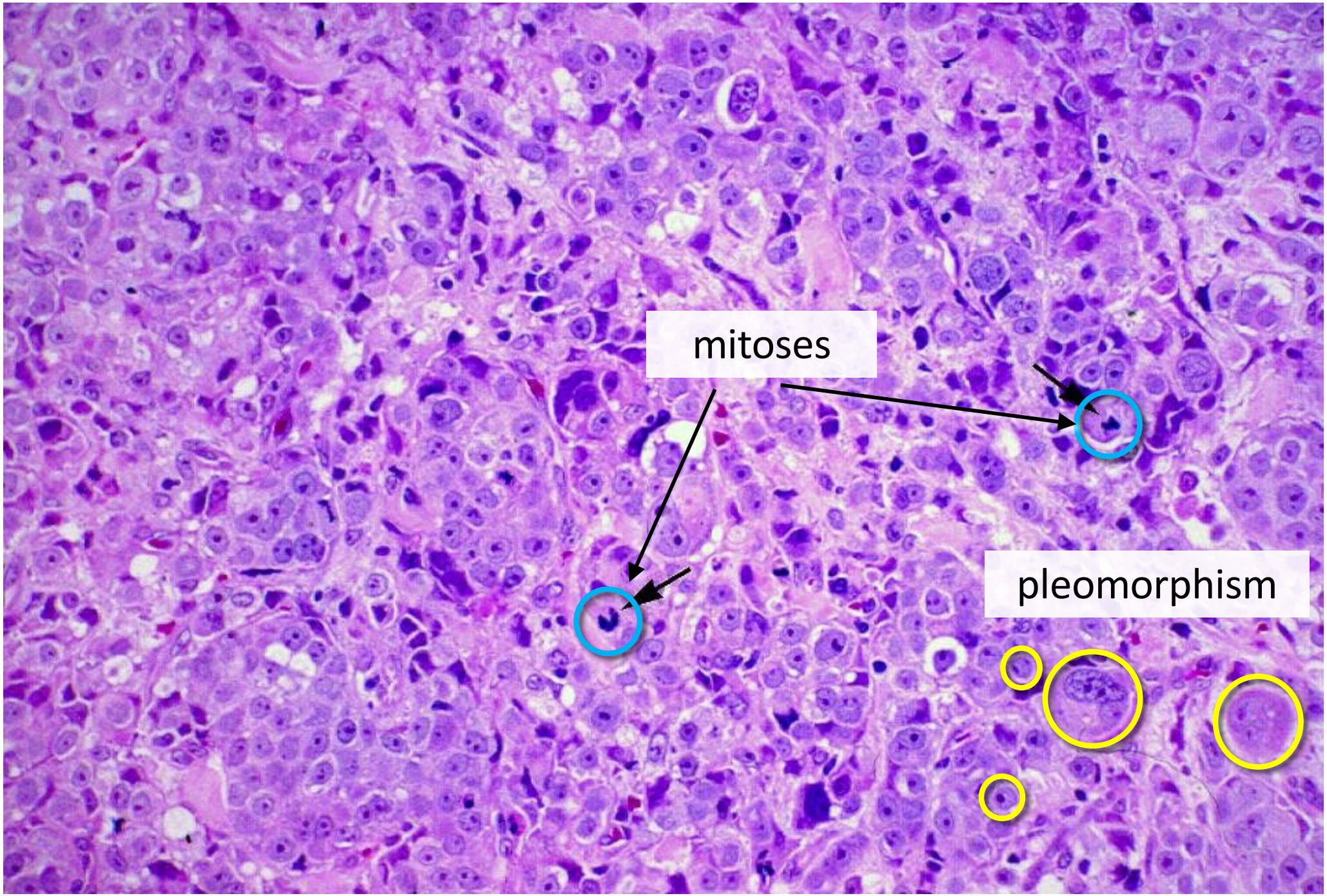
add all points together

Score	Grade	5y survival
3-5	Low grade	>95%
6-7	Intermediate grade	80%
8-9	High grade	60%

*Don’t memorize this slide!! It’s just here to give you an example of how the system works.

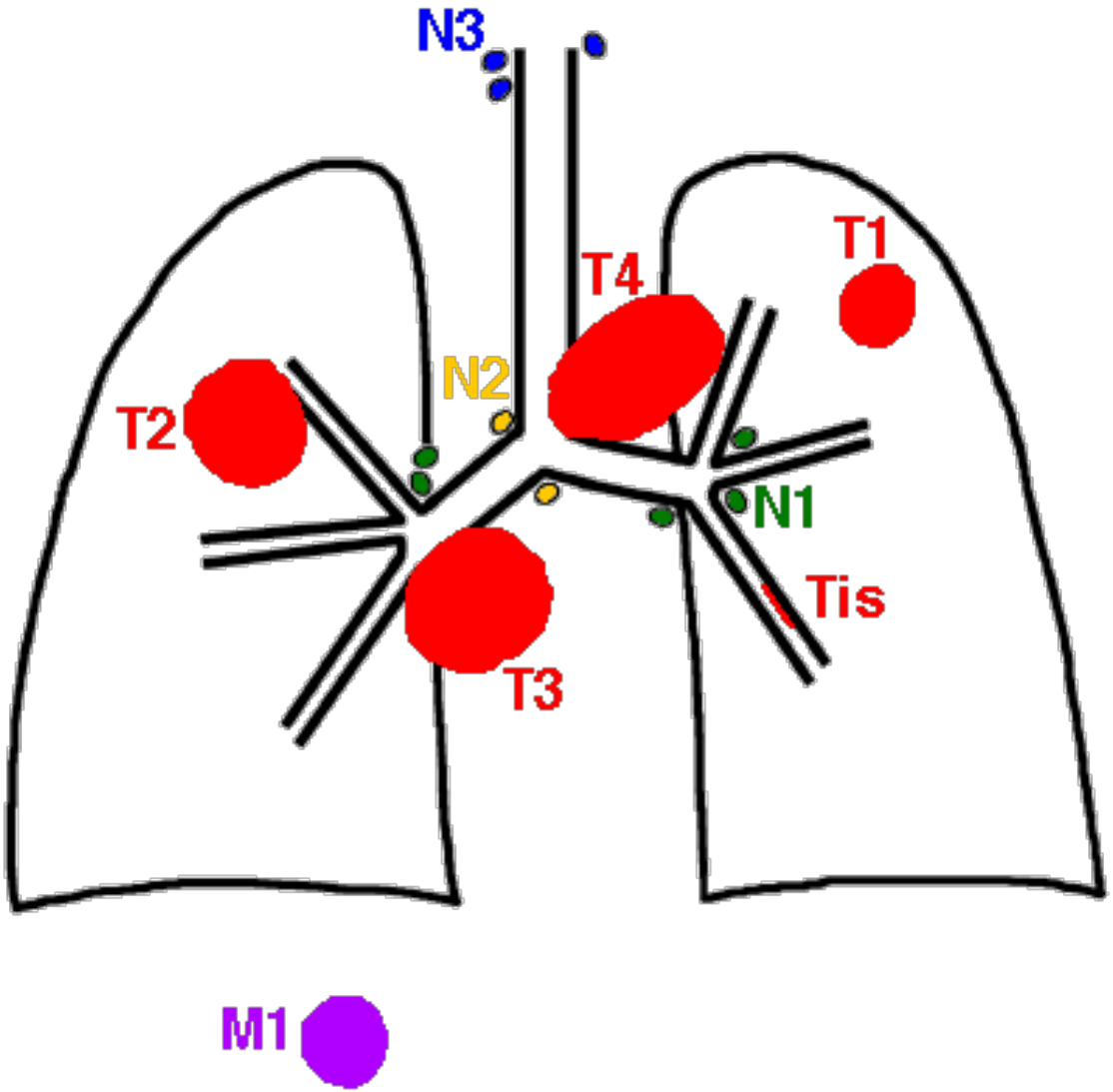


Breast carcinoma low grade



Breast carcinoma high grade

TNM staging system for non-small cell lung cancer



T = Tumor size

Tis – in situ tumor
T1 – small tumor
T2 – larger tumor
T3 – larger or invasive tumor
T4 – very large/very invasive

N = Nodes

N0 – no lymph node involvement
N1 – a few regional nodes
N2 – lots of regional nodes
N3 – distant nodes

M =Metastases

M0 – no metastases
M1 – metastases

TNM staging system for non-small cell lung cancer*

Stage	T	N	M	Treatment	5y survival
Stage 0	Tis	N0	M0	Surgery only	75%
Stage I	T1 or T2	N0	M0	Surgery ± radiation	50%
Stage II	T1 T2 T3	N1 N1 N0	M0 M0 M0	Surgery and radiation ± chemotherapy	30%
Stage III	T1 or T2 T3 Any T T4	N2 N1 or N2 N3 Any N	M0 M0 M0 M0	Chemotherapy ± radiation to debulk Maybe surgery	10%
Stage IV	Any T	Any N	M1	Palliative care Maybe chemo or radiation	<2%

*Don't memorize this slide!! It's just here to give you an example of how the system works.