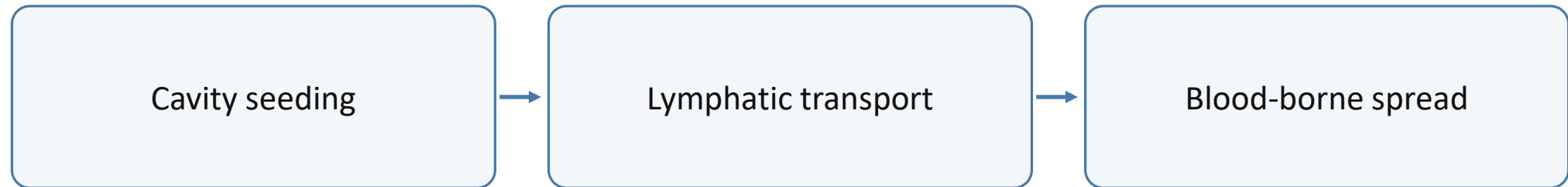


Pathways of Spread

Malignant neoplasms: routes of dissemination



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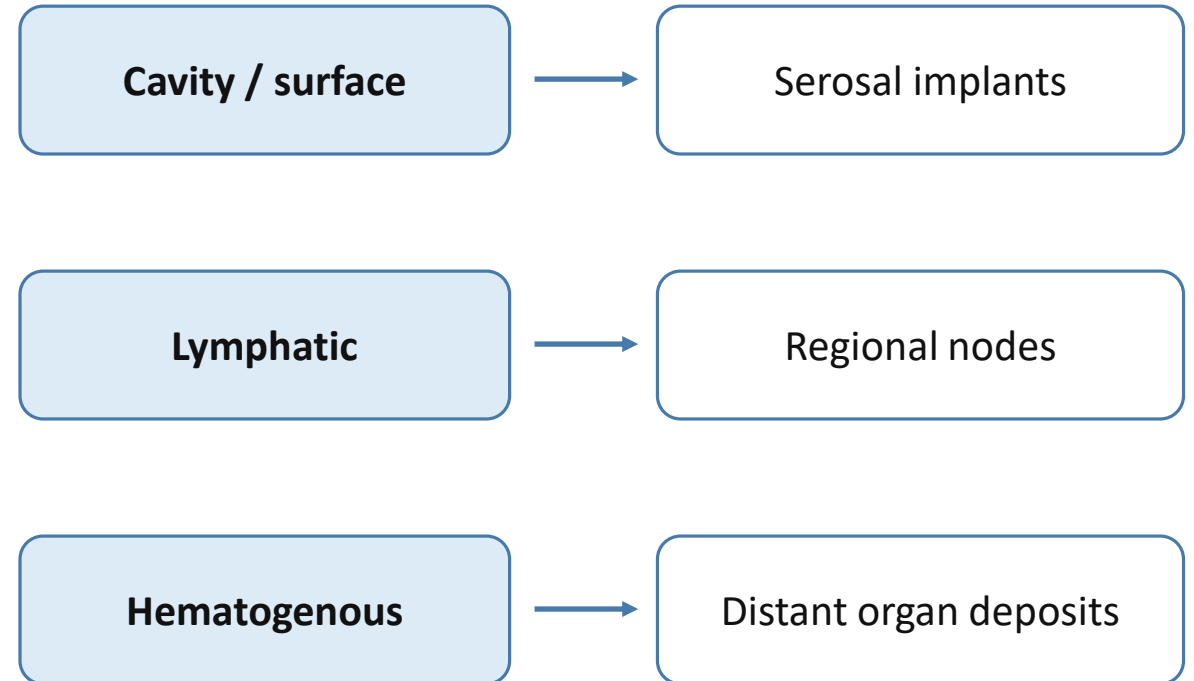
Learning outcomes

- Distinguish direct cavity seeding, lymphatic spread, and hematogenous spread.
- Predict characteristic first sites using regional lymphatic and venous anatomy.
- Interpret sentinel nodes, reactive lymphadenopathy, and tumor in major veins.
- Apply Robbins examples to clinicopathologic scenarios.

Three major routes of tumor dissemination

- Direct seeding reaches open body cavities and associated surfaces.
- Lymphatic transport deposits tumor cells in draining nodal basins.
- Hematogenous spread distributes tumor cells through blood vessels.

Schematic

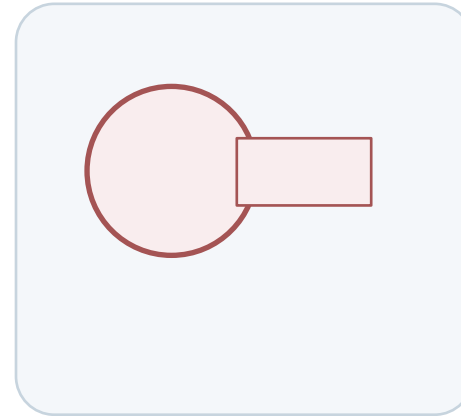


Metastasis requires a discontinuous tumor deposit

- Metastasis denotes spread from a primary tumor to a physically separate site.
- Contiguous extension into adjacent tissue is local invasion, not metastasis.
- Identification of a true metastasis unequivocally establishes malignant behavior.

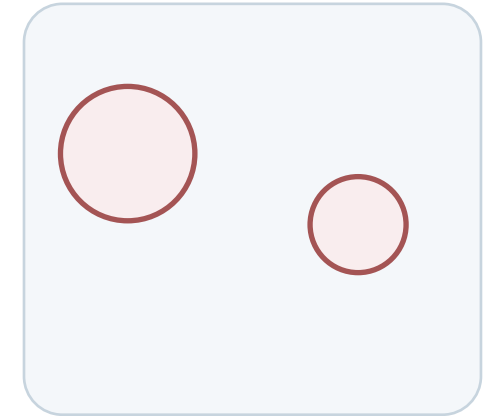
Schematic

Contiguous growth



One connected focus

Discontinuous deposit

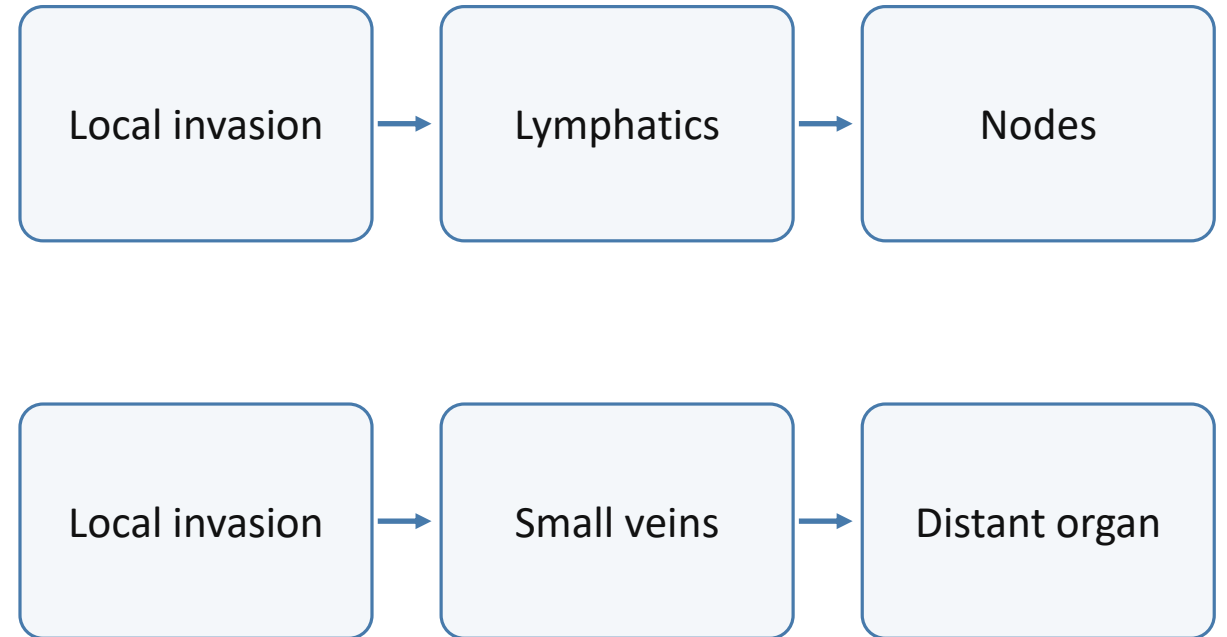


Separate focus

Invasion provides access to routes of dissemination

- Malignant cells may breach adjacent tissue barriers and enter lymphatics.
- Vessel penetration allows transport with circulating blood.
- Access to a natural cavity enables implantation on distant surfaces.

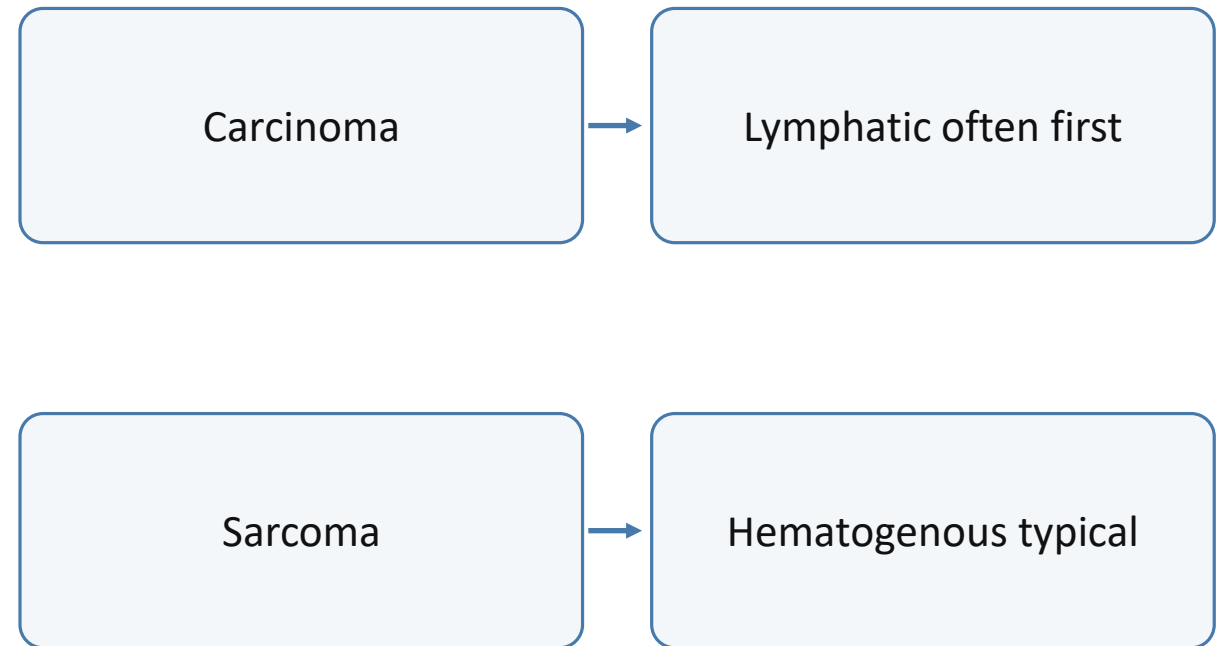
Schematic



Route preference is a tendency, not an absolute rule

- Lymphatic transport is the most common initial route for carcinomas.
- Hematogenous metastasis is especially characteristic of sarcomas.
- Carcinomas may spread through blood; Sarcomas may use lymphatics.

Schematic



Each route produces a different anatomic pattern

- Cavity seeding: Deposits on lining surfaces, often across a large serosal field.
- Lymphatic: Deposits in nodes along regional drainage pathways.
- Hematogenous: Deposits in organs reached by circulating tumor emboli.

Schematic

Surface

Implants on lining

Lymphatic

Draining nodes

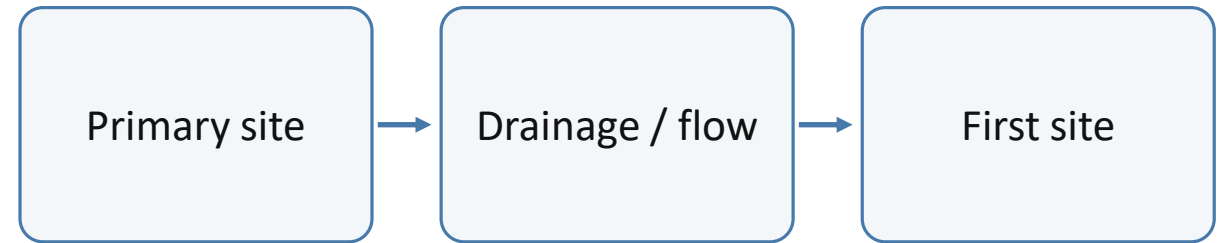
Blood

Organ parenchyma

First destination does not determine every later deposit

- Natural drainage pathways help predict where metastases may first appear.
- Variations in lymphatic drainage can alter regional node involvement.
- Vascular anatomy alone does not explain all cancer-specific organ tropism.

Schematic

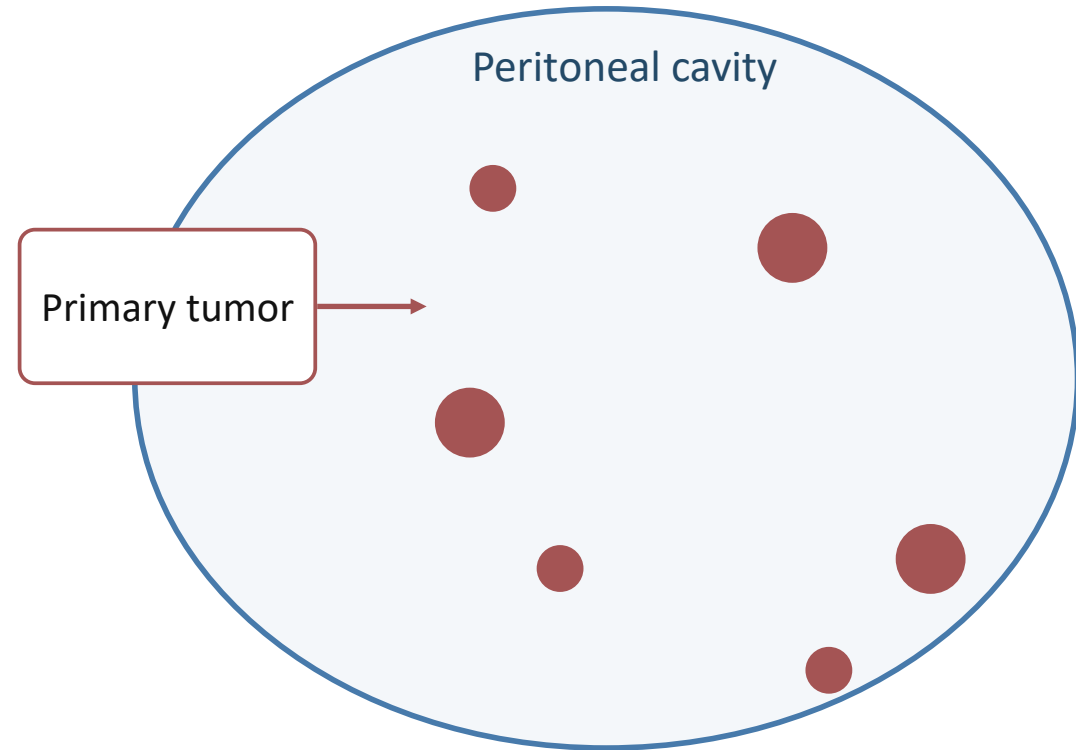


Flow alone does not predict every metastatic site

Seeding exploits a natural “open field”

- Malignant neoplasms can disseminate where an exposed cavity lacks intervening tissue barriers.
- Cells implant on surfaces separated from the primary focus.
- The route differs from continuous tissue infiltration.

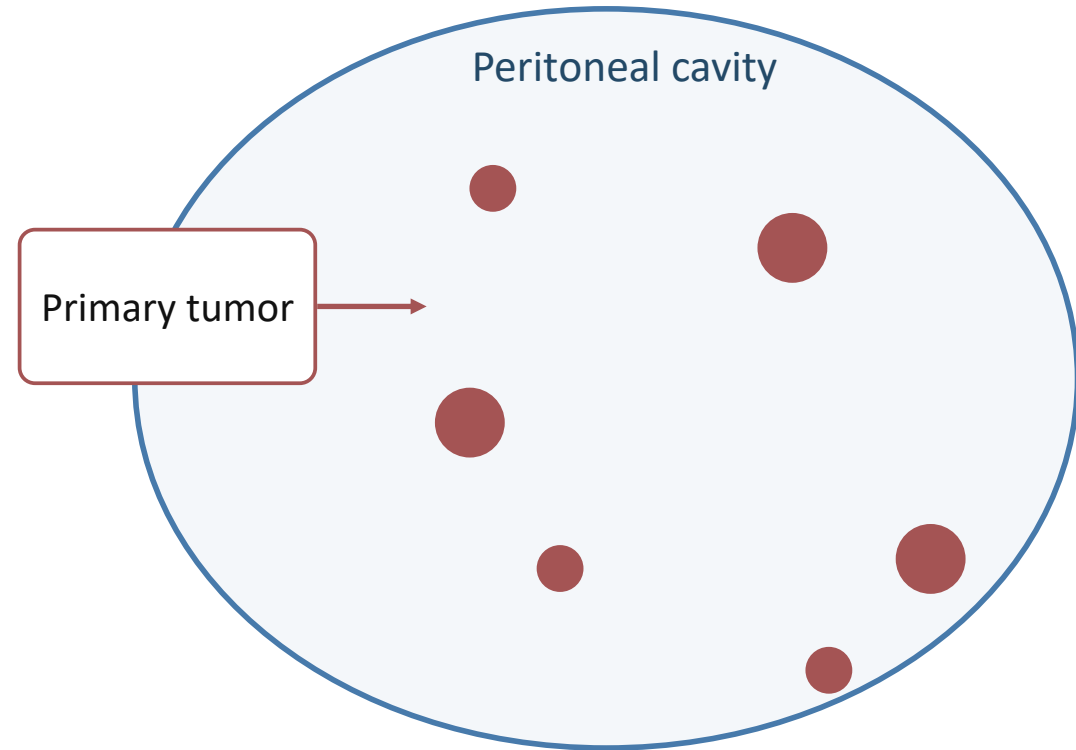
Schematic



The peritoneal cavity is the usual example

- The peritoneum as the most frequently involved body cavity.
- Implants may occupy separated peritoneal and omental surfaces.
- Surface distribution can be extensive despite a localized primary organ site.

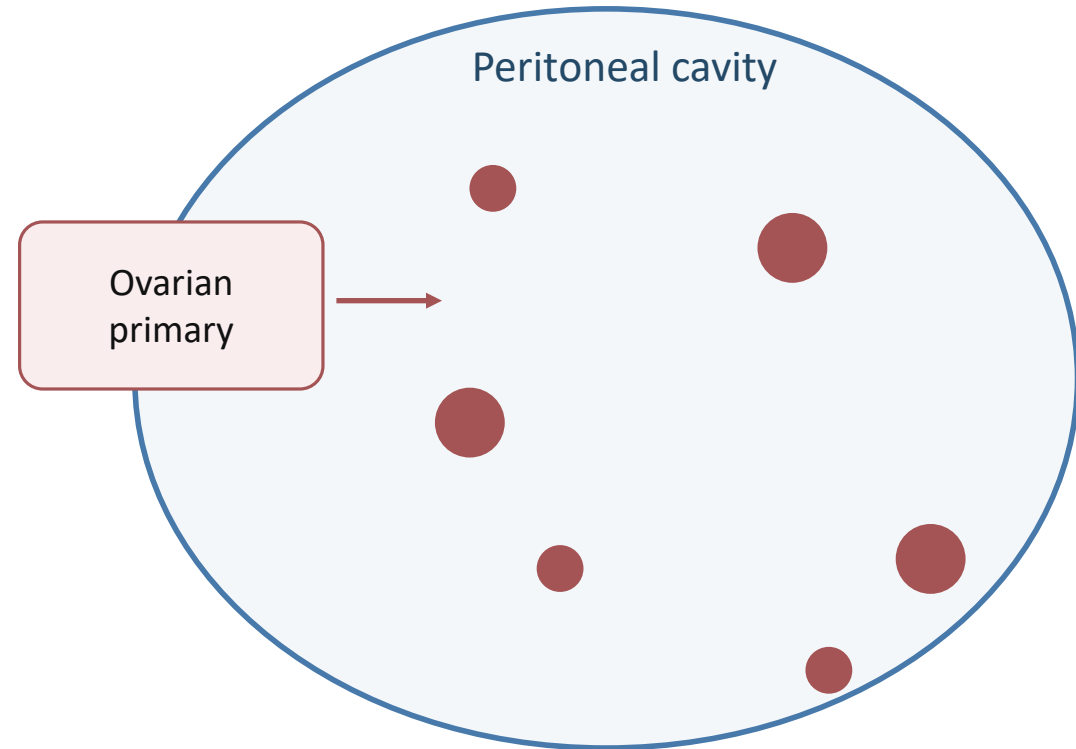
Schematic



Ovarian carcinoma characteristically seeds peritoneum

- Ovarian carcinoma is a characteristic example of cavity dissemination.
- Carcinoma cells implant on peritoneal surfaces rather than requiring a direct contiguous front.
- Widespread deposits may create a substantial tumor coating.

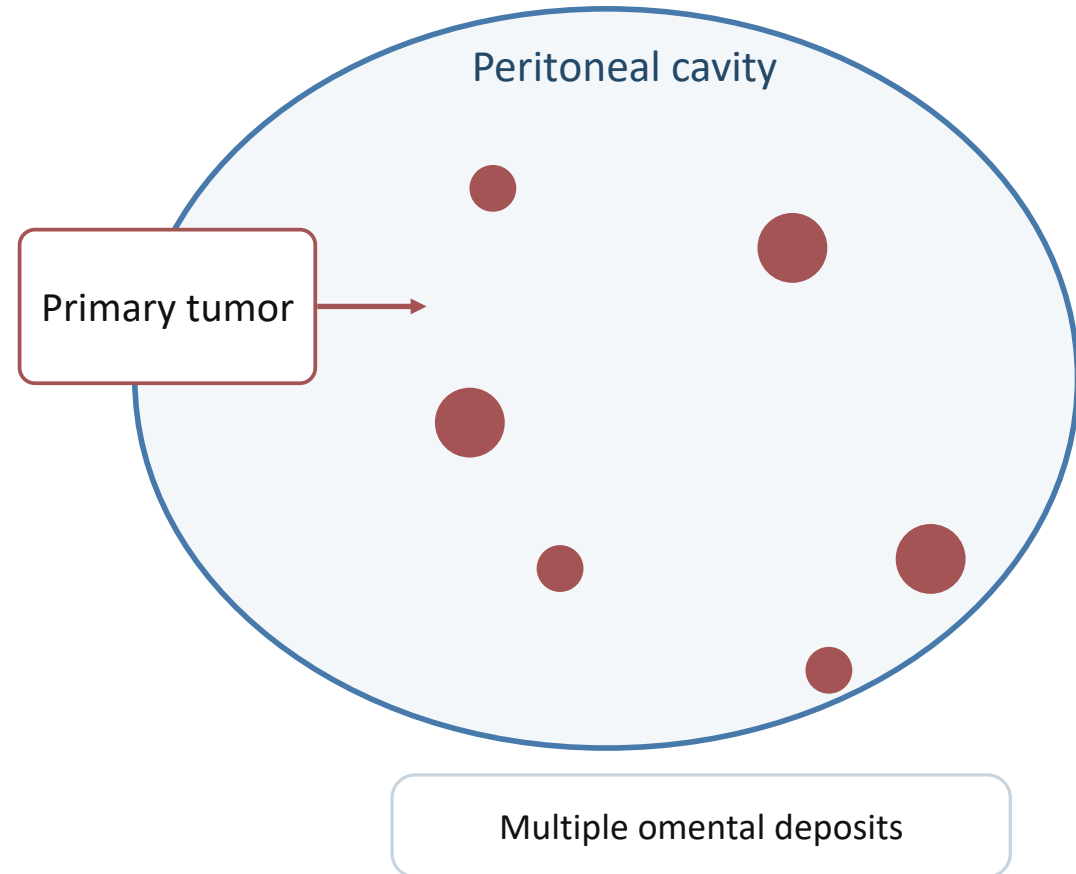
Schematic



Omental involvement may be multifocal

- Numerous omental nodules can result from metastatic ovarian carcinoma.
- The distribution illustrates multiple surface implants, not one growing mass.
- Multiple implants on the same peritoneal surface demonstrate dissemination beyond the primary site.

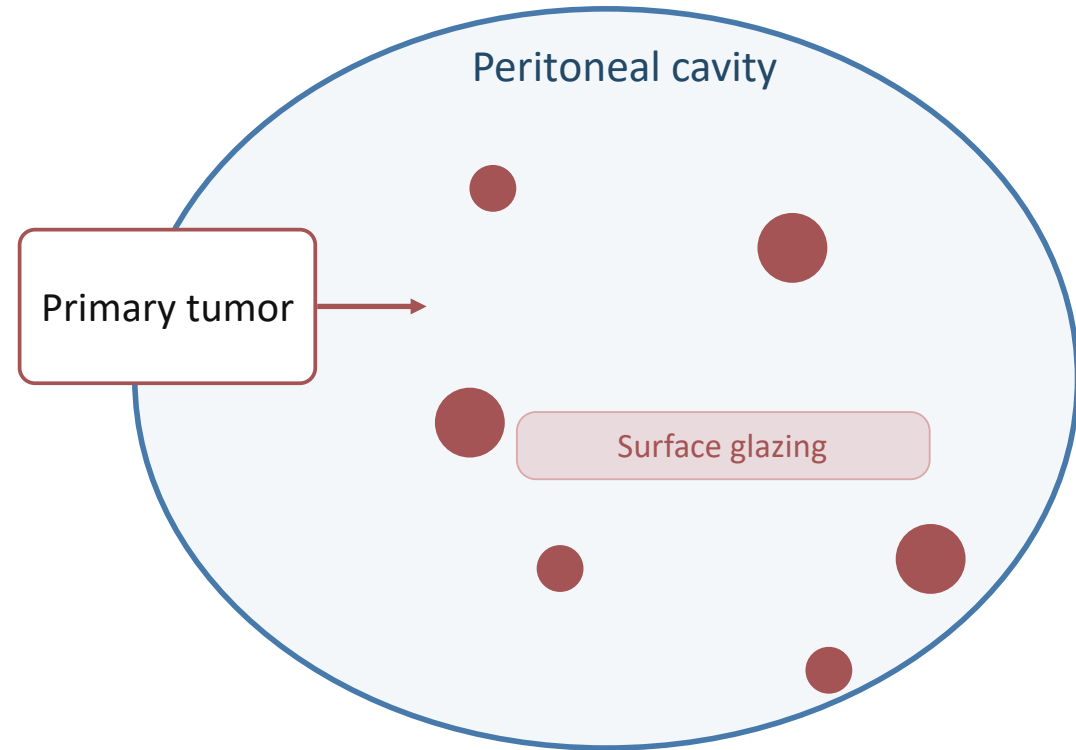
Schematic



Subtle surface “glazing” may accompany nodules

- Omental involvement can combine obvious nodules with subtle surface glazing.
- The deposits may be associated with a gelatinous matrix.
- Inspection must not depend solely on recognizing discrete large masses.

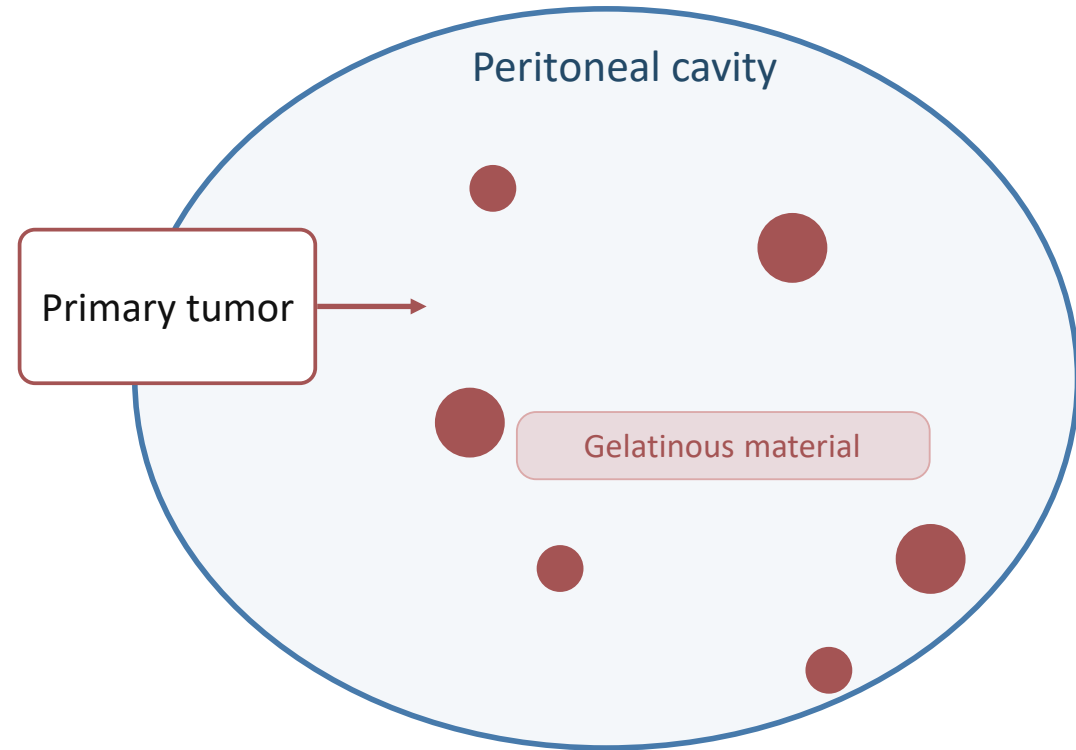
Schematic



Mucinous spread can fill the peritoneal space

- Mucus-secreting appendiceal or ovarian carcinomas may produce gelatinous neoplastic material.
- The resulting peritoneal accumulation is termed pseudomyxoma peritonei.
- The designation describes the characteristic cavity-filling presentation in the source.

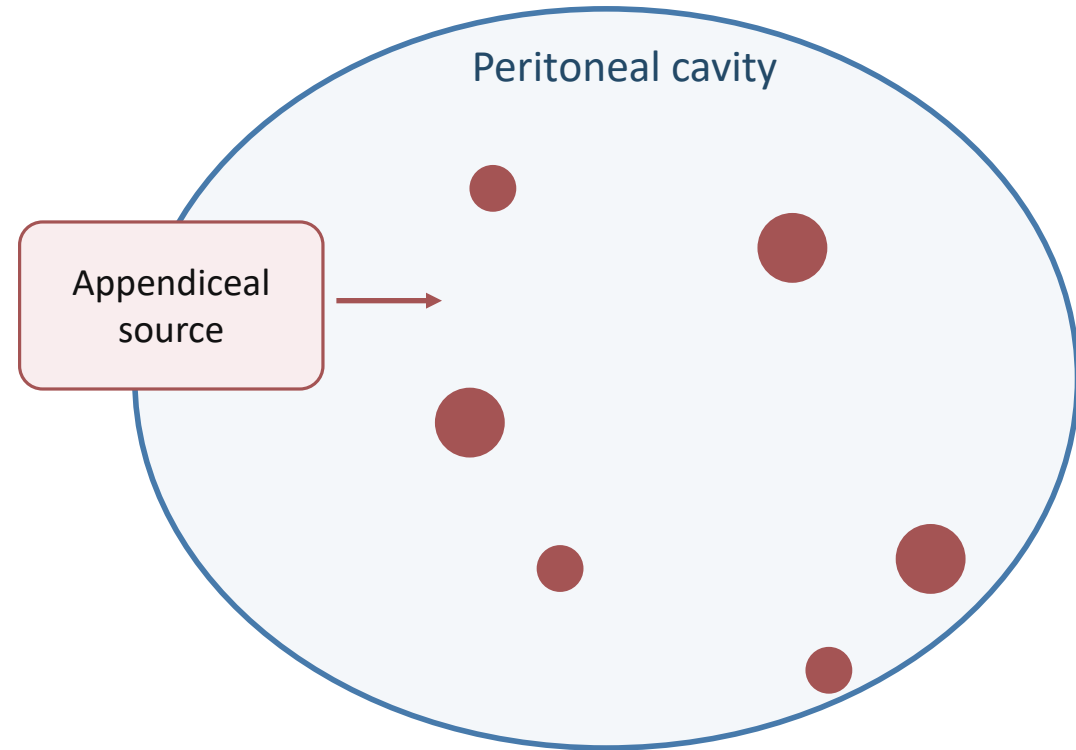
Schematic



Appendiceal carcinoma is a source of pseudomyxoma

- Mucus-secreting appendiceal carcinoma is a source example of pseudomyxoma peritonei.
- The relevant dissemination is peritoneal rather than principally nodal.
- Anatomic origin and resulting cavity pattern are distinct diagnostic questions.

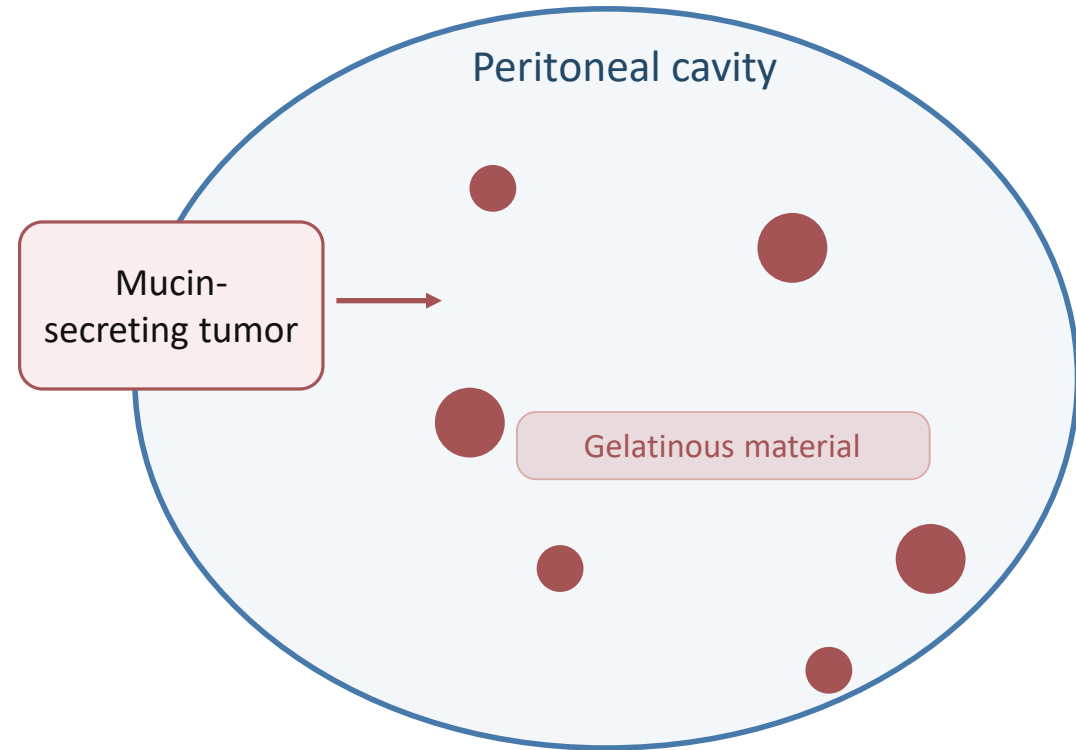
Schematic



Ovarian tumors may produce mucinous peritoneal spread

- Mucin-secreting ovarian carcinoma is another tumor type associated with peritoneal accumulation.
- Gelatinous material may coat or occupy the peritoneal compartment.
- Peritoneal distribution alone does not establish which organ contains the primary tumor.

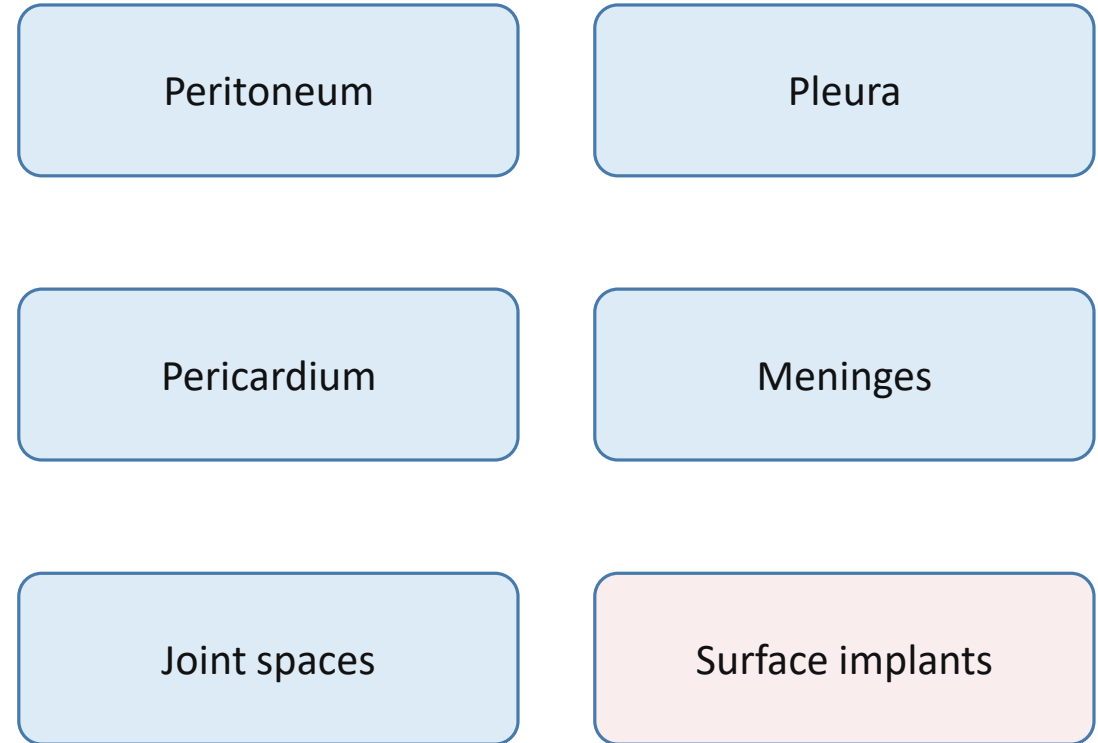
Schematic



Other cavities and surfaces can be seeded

- The pleural and pericardial spaces are possible sites of surface seeding.
- Meningeal surfaces may also receive disseminated tumor cells.
- Joint cavities are included' list of possible sites.

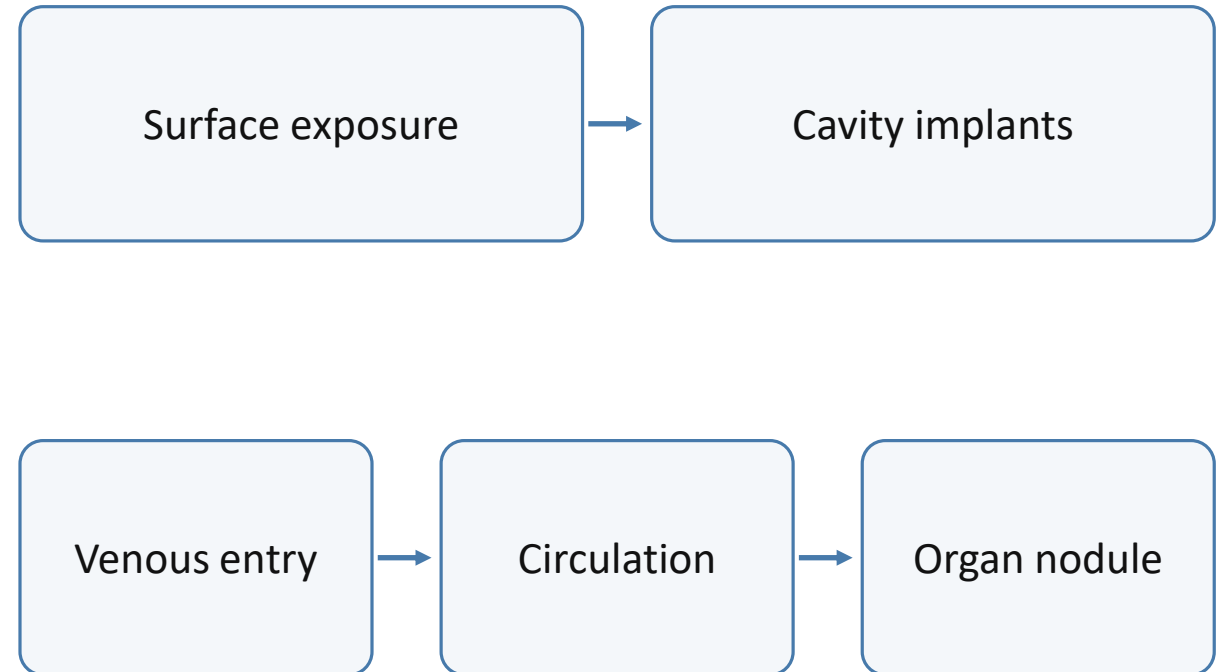
Schematic



Seeding is anatomically different from vascular spread

- Seeding primarily distributes tumor cells across a cavity and its surfaces.
- Blood-borne dissemination follows vascular pathways to capillary beds.
- Identical primary tumors can therefore produce different spatial patterns.

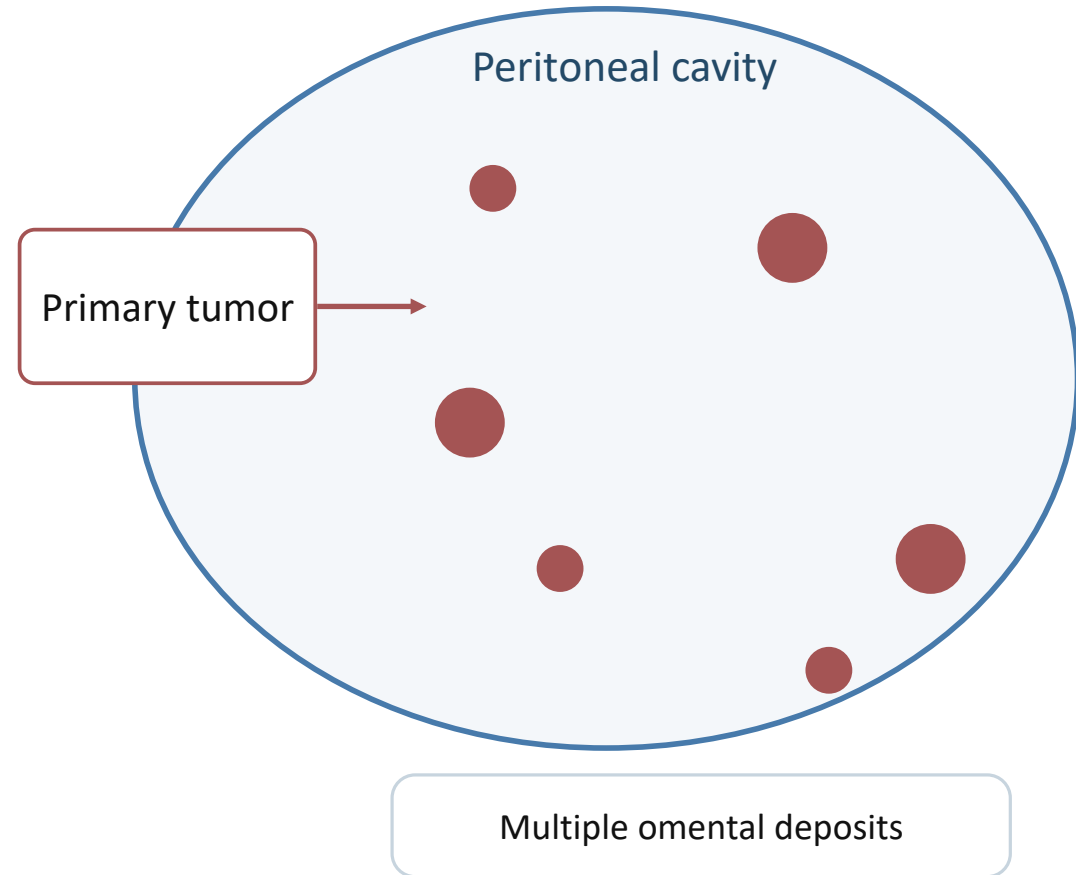
Schematic



Recognizing a cavity-seeding pattern

- Multiple separated serosal or omental deposits suggest transcoelomic dissemination.
- An extensive surface coating may obscure individual deposits.
- The pathway is inferred from the relationship between the primary site and implants.

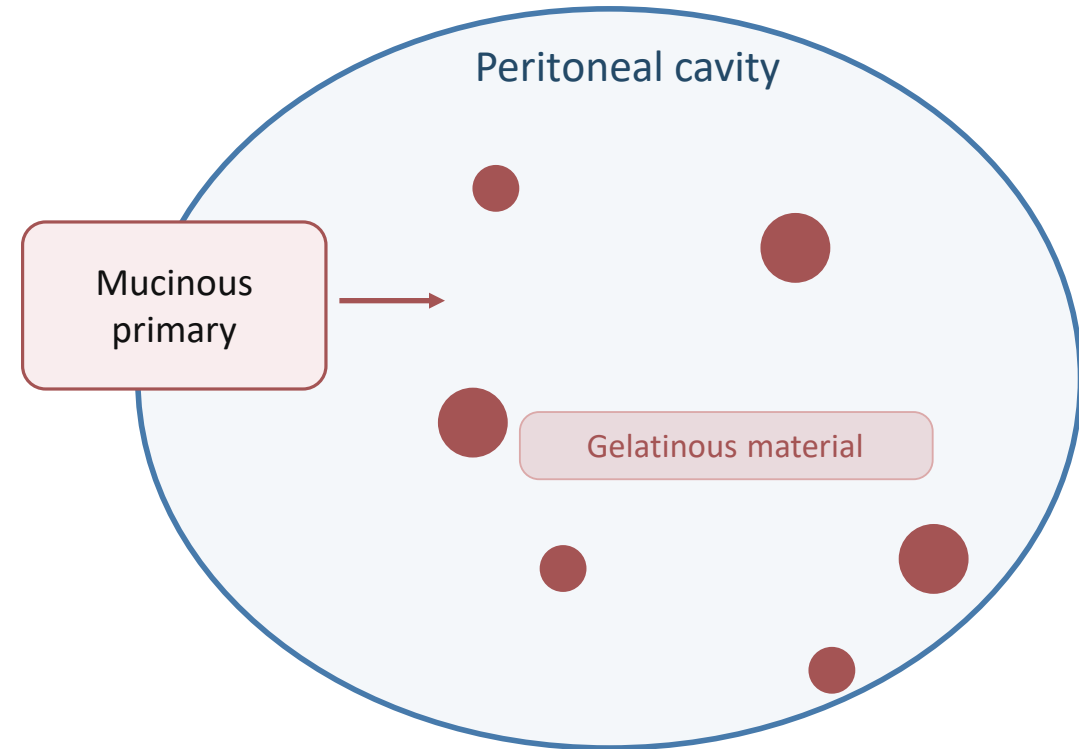
Schematic



Case: Nodules and gelatinous material in peritoneum

- Hypothetical teaching scenario: A patient has a mucin-secreting abdominal tumor.
- At exploration, multiple omental deposits coexist with gelatinous peritoneal material.
- Question: Which major dissemination route best explains this pattern?

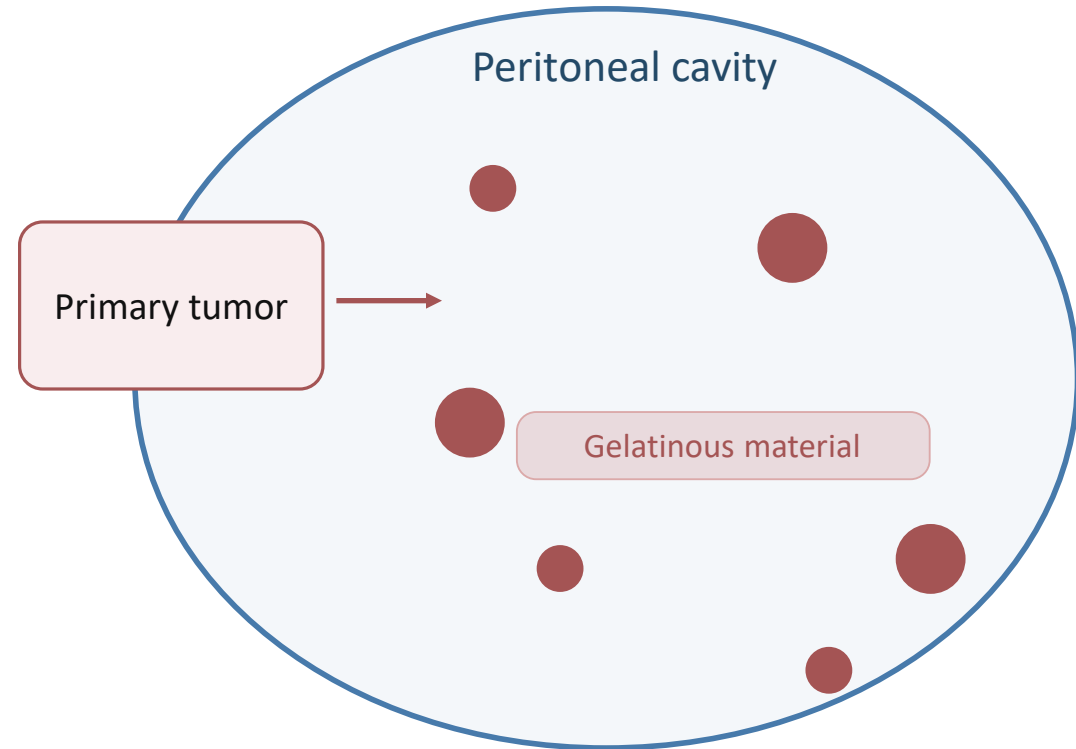
Schematic



Case interpretation: Direct cavity seeding

- The separated peritoneal and omental deposits indicate implantation on an open surface.
- The gelatinous material fits Robbins' account of pseudomyxoma peritonei.
- Appendiceal and ovarian mucinous carcinomas are the source examples described.

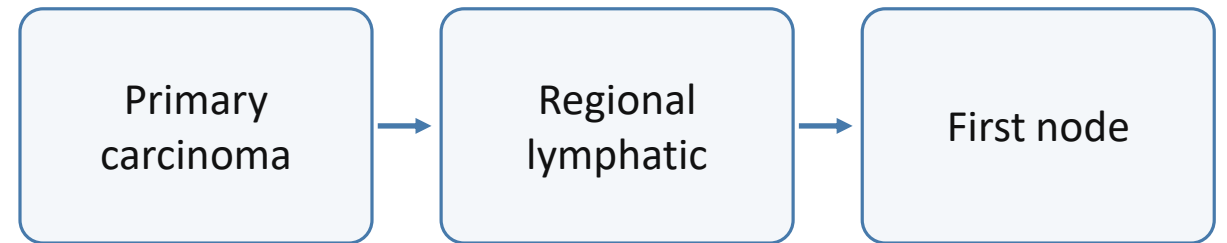
Schematic



Lymphatics commonly carry the first carcinoma deposits

- Lymphatic vessels are the most common pathway of initial carcinoma dissemination.
- This statement concerns preferential early routing, not an exclusive mode of spread.
- Sarcomas can also disseminate through regional lymphatics.

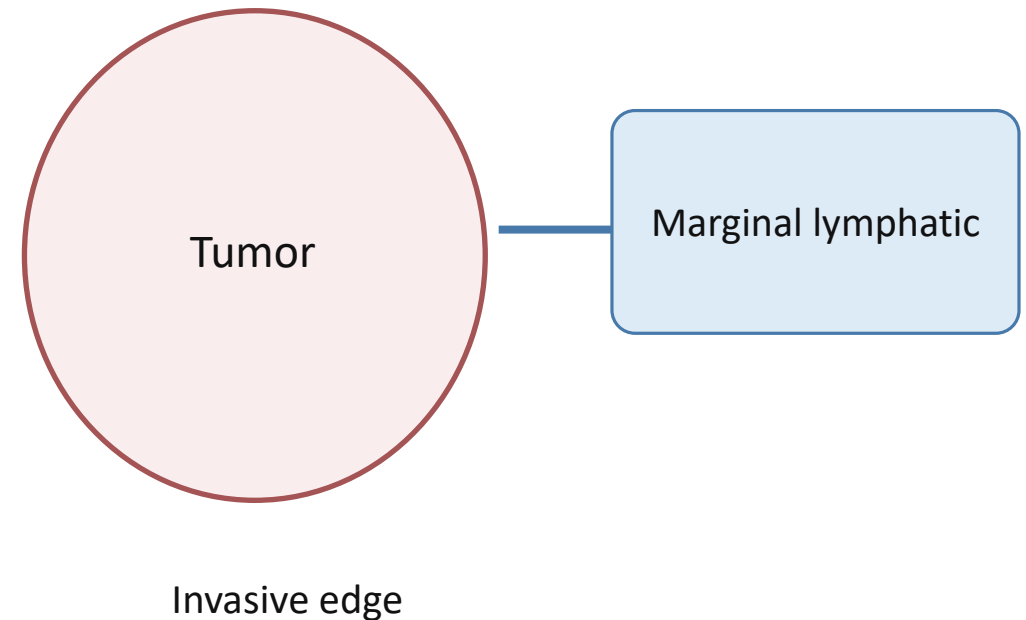
Schematic



Peritumoral vessels can mediate lymphatic spread

- The primary tumor mass need not have functional intratumoral lymphatic vessels.
- Functional lymphatic channels at the invasive tumor margins are sufficient for transit.
- Tumor cells therefore need not rely on a patent central intratumoral channel.

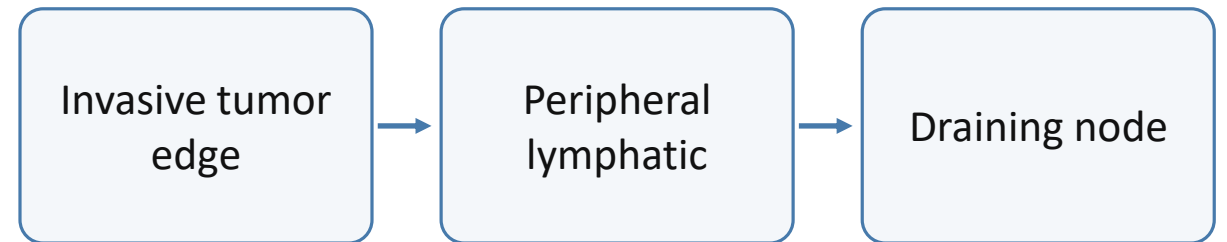
Schematic



The lymphatic route begins at the invasive edge

- Invading carcinoma reaches lymphatic vessels close to the advancing margin.
- Cells can then travel to the draining regional lymph node.
- The exact recipient node depends on native local drainage anatomy.

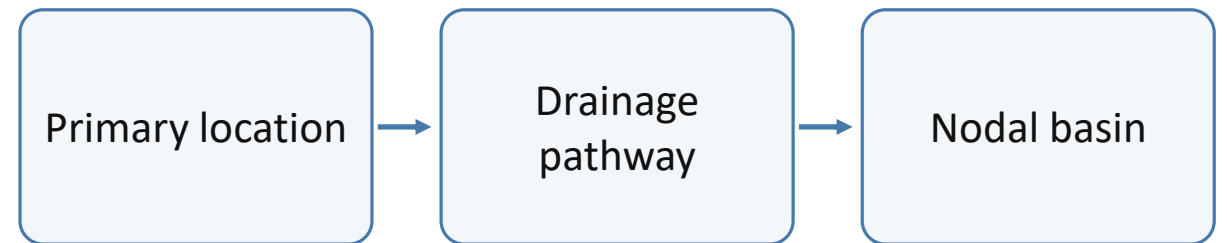
Schematic



Regional lymphatic drainage governs first nodal stations

- Metastatic cells generally follow the normal routes of lymphatic return.
- A tumor's anatomical location predicts likely first nodal basins.
- This principle explains organ-specific regional patterns without implying certainty.

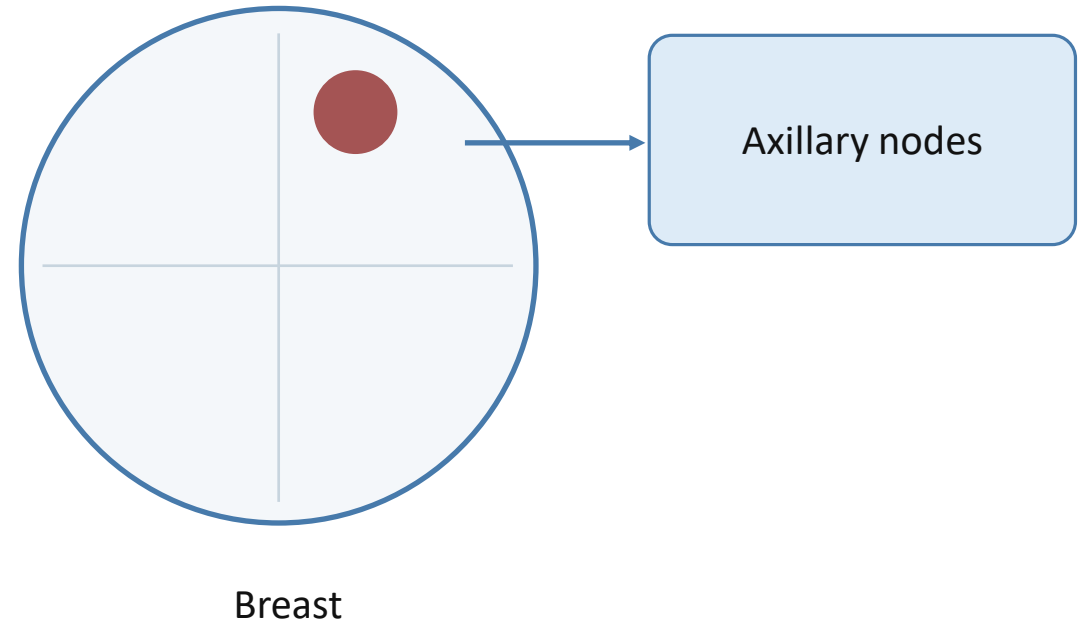
Schematic



Breast carcinoma: Upper outer quadrant to axilla

- Breast carcinomas often arise in the upper outer quadrants.
- The axillary nodes as the usual first regional destination.
- This pathway provides a clinically relevant nodal evaluation target.

Schematic

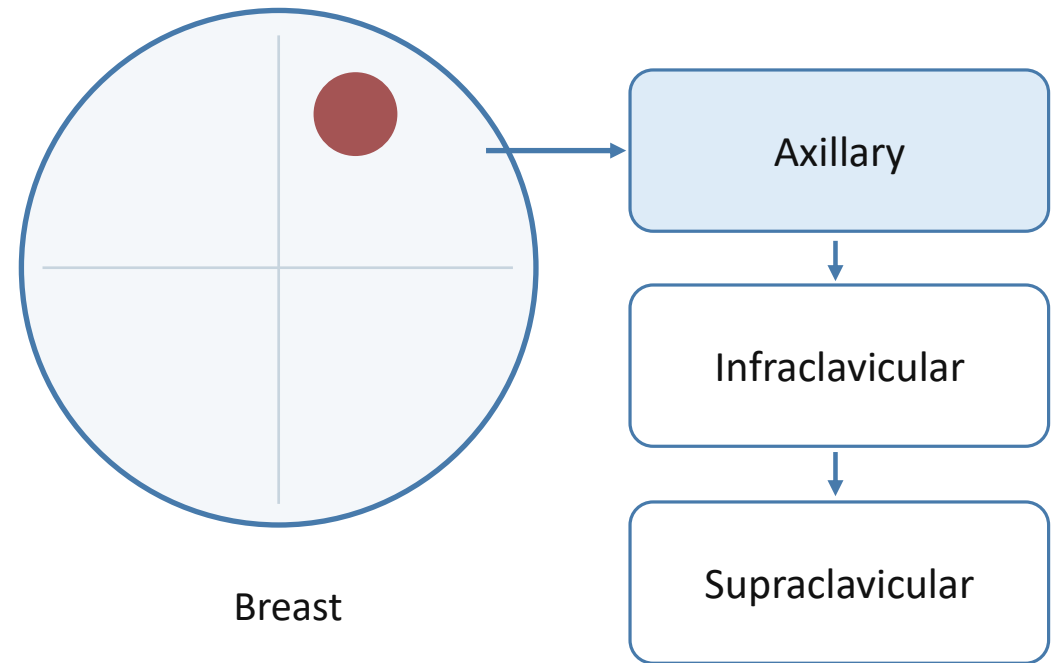


Simplified location and drainage schema

Breast carcinoma may advance to higher nodal stations

- Following axillary involvement, spread may reach infraclavicular nodes.
- Supraclavicular lymph nodes can be further along the drainage route.
- The diagram presents the sequence described, not obligatory progression in every patient.

Schematic

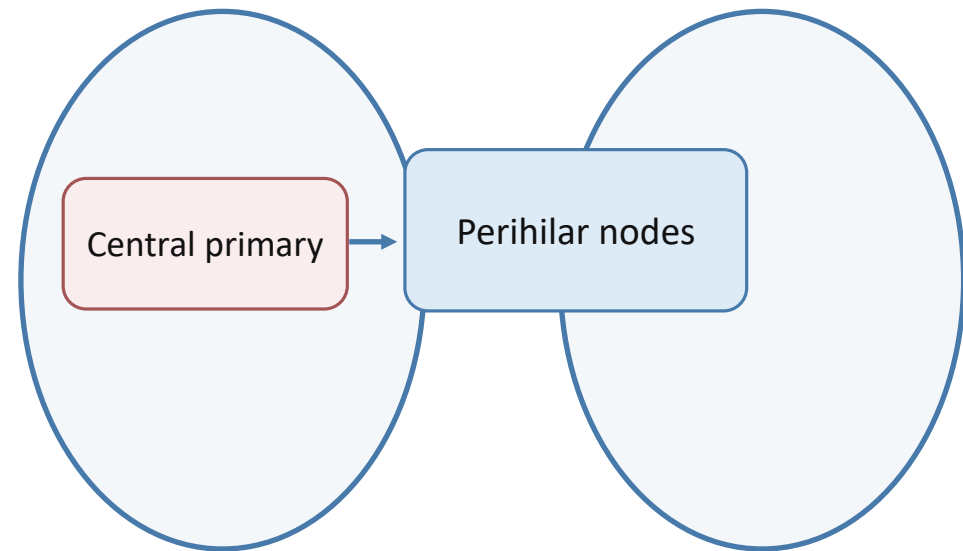


Simplified location and drainage schema

Central lung carcinoma: Perihilar nodes first

- Lung carcinomas arising in major respiratory passages drain first toward perihilar regions.
- Tracheobronchial nodes are specifically identified.
- Primary location helps explain nodal findings at the hilum.

Schematic

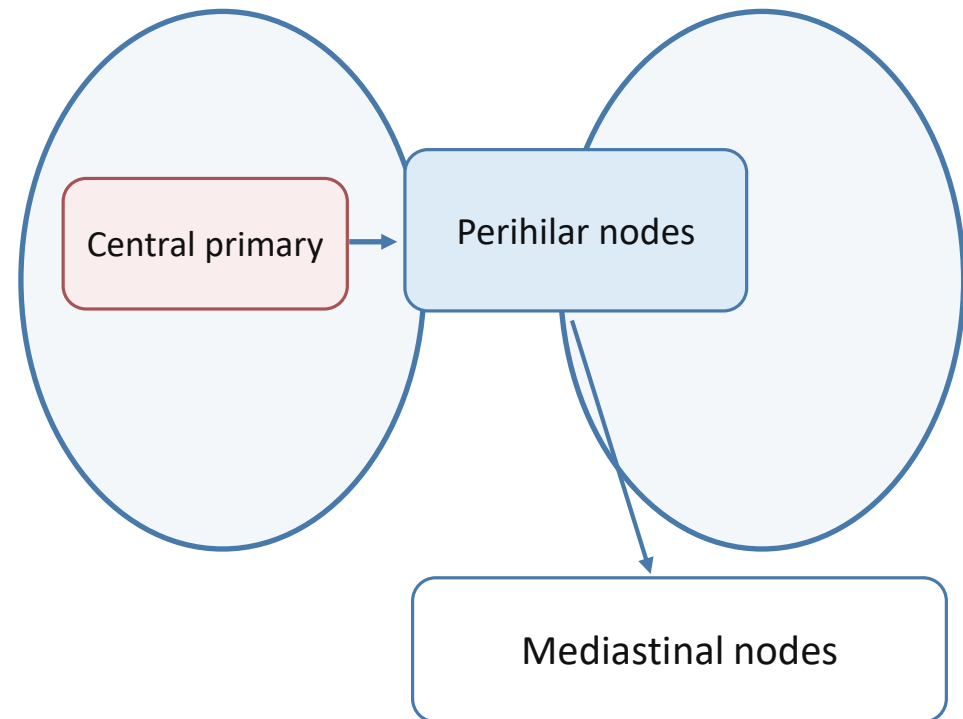


Simplified central lung and regional-node diagram

Mediastinal lymph nodes are part of the lung route

- Mediastinal nodes among early lymphatic destinations.
- Perihilar, tracheobronchial and mediastinal basins are anatomically linked.
- The actual involvement sequence may vary across tumors.

Schematic

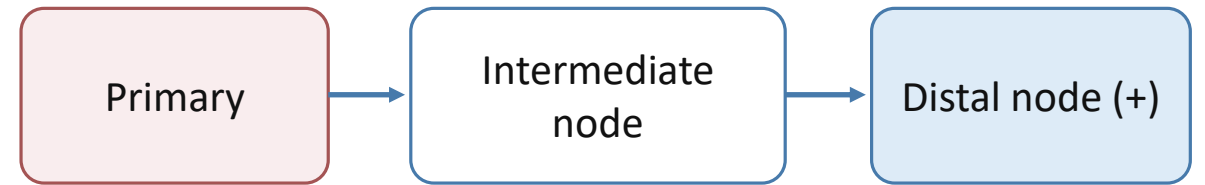


Simplified central lung and regional-node diagram

Skip metastasis: Local stations may be bypassed

- A distant regional node may contain tumor despite an apparently negative nearer station.
- This is termed skip metastasis.
- An uninterrupted, stepwise sequence should not be assumed from every specimen.

Schematic

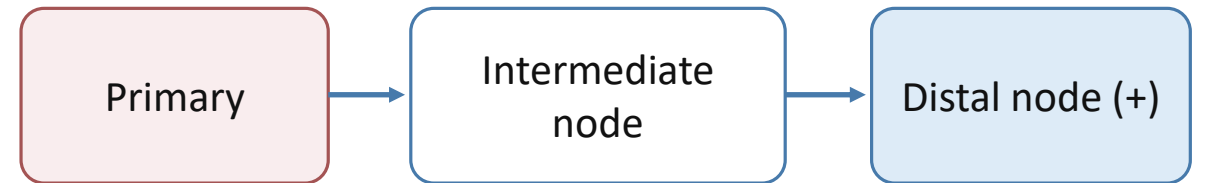


Apparent bypass of intermediate station

Why does an apparent skip occur?

- Microscopic deposits in intermediate nodes may go undetected.
- Normal lymphatic drainage patterns vary between individuals.
- A negative intervening node does not establish that no cells passed through it.

Schematic



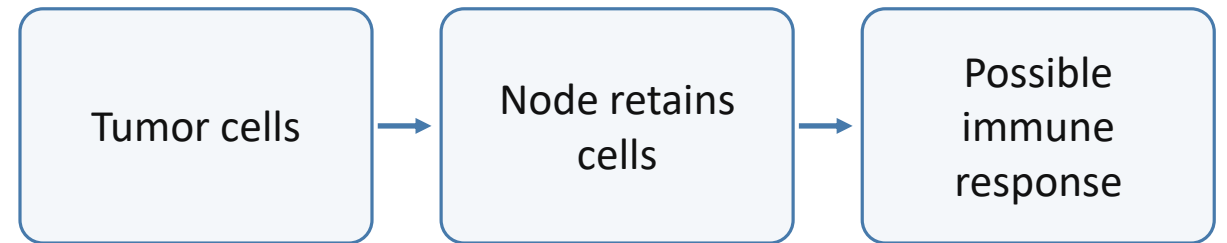
Occult microscopic deposit

Drainage variation

Regional nodes can temporarily impede spread

- A draining node may retain tumor cells and serve as a barrier for a time.
- Cells that arrest there may be destroyed through a tumor-specific immune response.
- This protective interpretation is presented as a possibility, not a guarantee.

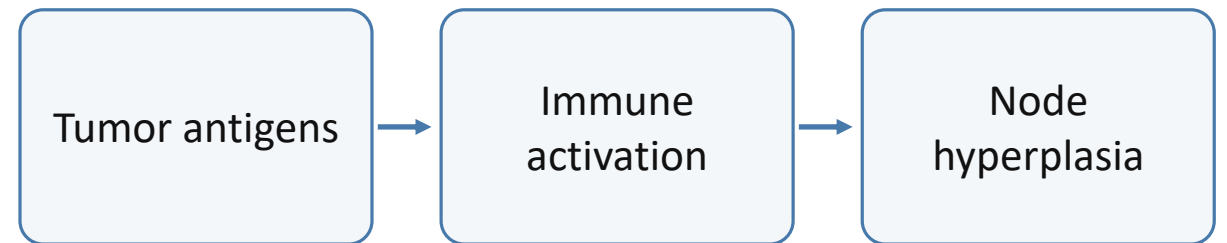
Schematic



An immune response can enlarge a draining node

- Tumor-derived antigens and immune activation can cause nodal hyperplasia.
- This reactive enlargement may occur without metastatic cells.
- Nodal enlargement alone is therefore not synonymous with malignant involvement.

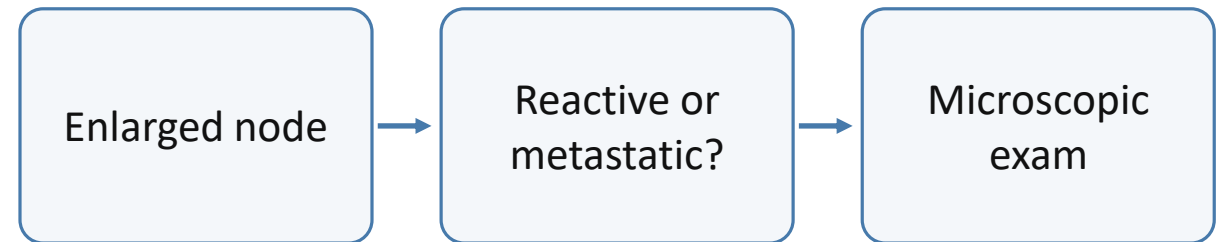
Schematic



A large node is not necessarily a positive node

- Reactive hyperplasia and metastatic deposits are different pathologic processes.
- Their distinction cannot be reliably made from size alone.
- Microscopic tissue examination establishes whether metastatic cells are present.

Schematic

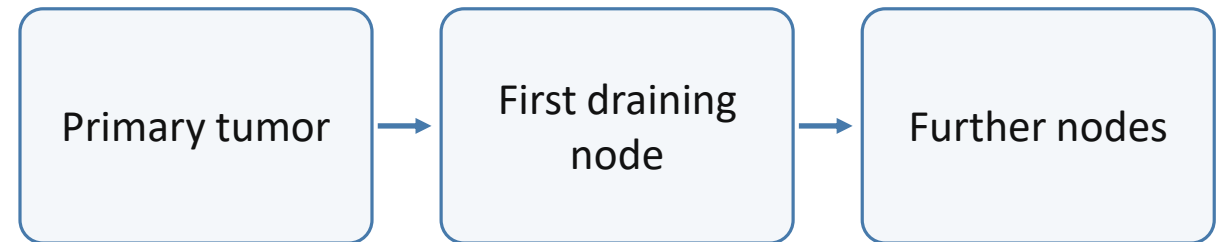


Node size cannot establish tumor involvement

Sentinel node: The first draining node

- A sentinel lymph node is the first node in a regional basin receiving lymph flow from the primary tumor.
- The definition is functional: It depends on the drainage pathway.
- The node is sampled to assess whether regional dissemination has occurred.

Schematic

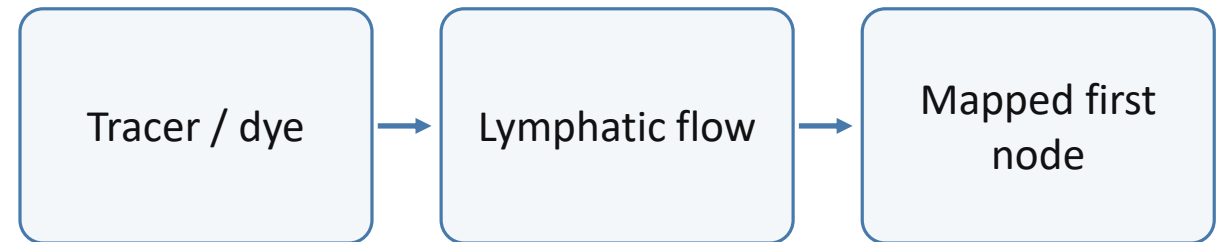


Definition depends on first lymphatic drainage

Mapping can identify the sentinel lymph node

- Radiolabeled tracer or colored dye can be injected near the tumor.
- The agent follows lymphatic drainage from the tumor region.
- Identification guides selective examination of the relevant node.

Schematic

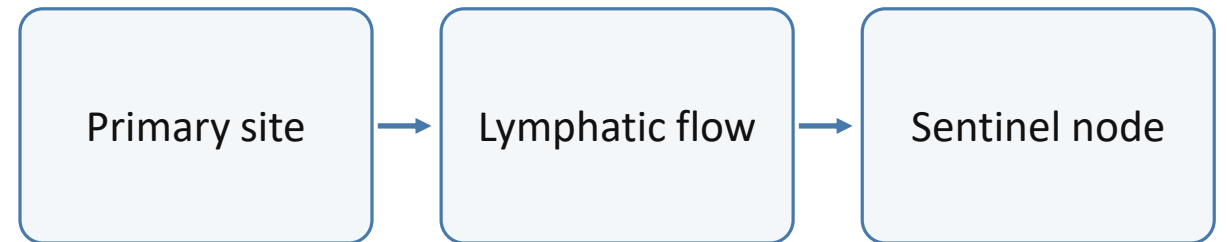


Definition depends on first lymphatic drainage

Sentinel mapping follows flow, not distance alone

- The sentinel node is the first recipient of lymph from the primary tumor.
- An anatomically nearest node is not always the functionally draining node.
- Altered or variable drainage helps explain the value of mapping.

Schematic

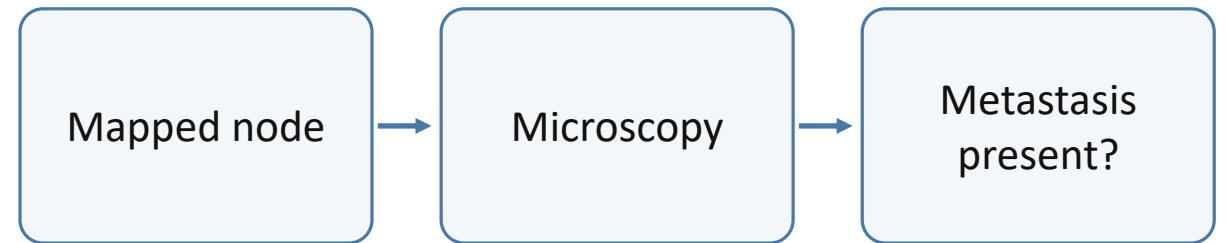


Definition depends on first lymphatic drainage

Microscopic sentinel-node assessment guides care

- Intraoperative frozen-section assessment is one described strategy for mapped nodes.
- Finding or excluding metastatic cells can influence the surgical plan.
- The educational principle is pathologic assessment; Practice details vary by cancer and setting.

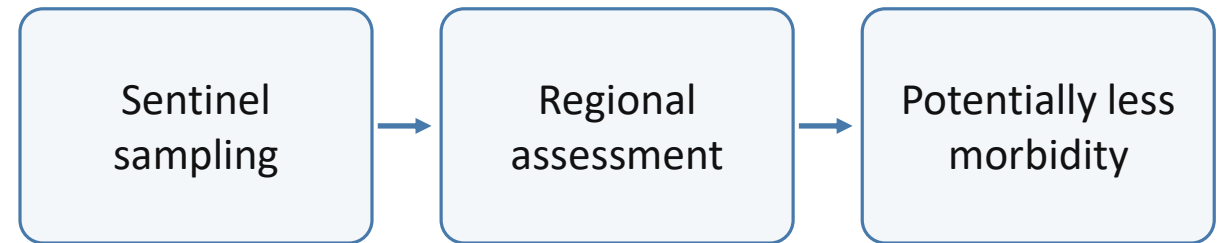
Schematic



Selective sentinel biopsy limits dissection morbidity

- Full axillary node dissection is associated with surgical morbidity.
- In appropriate breast cancer assessment, sentinel biopsy can reduce the need for extensive surgery.
- The aim is to retain regional staging information with less tissue removal.

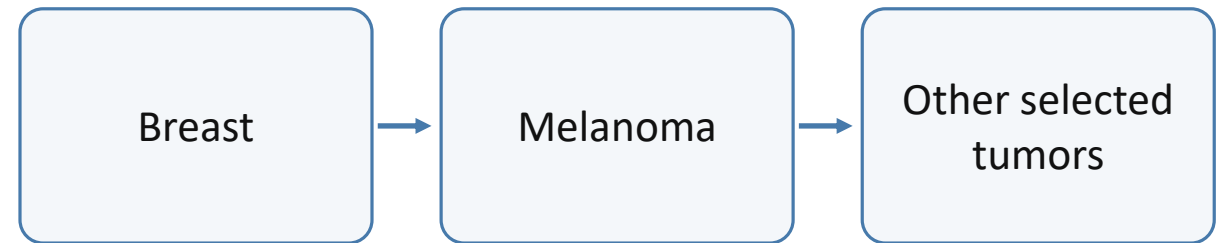
Schematic



Sentinel-node assessment is not restricted to breast

- Melanoma is another cancer for which sentinel-node examination has been used.
- Sentinel-node assessment has also been explored or used in colon cancer and other tumors.
- Use of sentinel-node sampling depends on the specific malignancy and clinical circumstances.

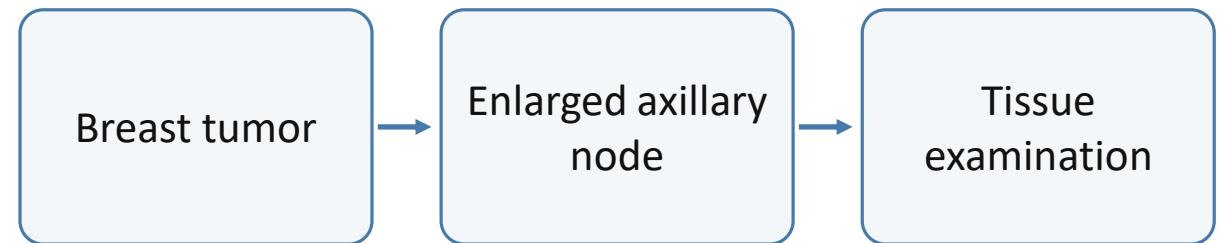
Schematic



Case: An enlarged node without visible tumor

- Hypothetical teaching scenario: A draining axillary node is enlarged near a breast carcinoma.
- A colleague interprets size alone as proof of metastasis.
- Question: What alternative pathologic process must be considered?

Schematic

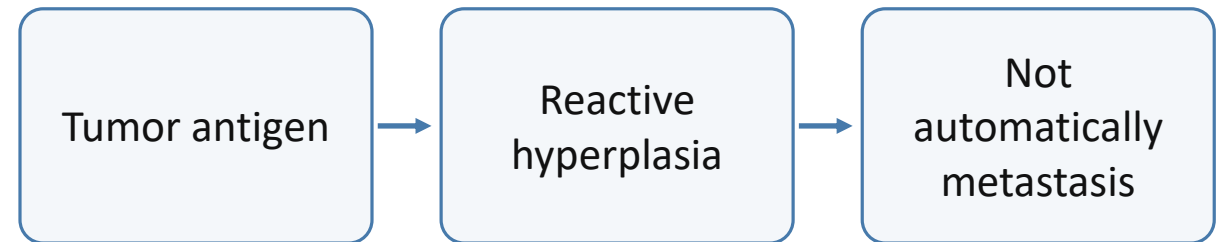


Node size cannot establish tumor involvement

Case interpretation: Histology resolves the ambiguity

- Immune stimulation by tumor antigens can cause reactive nodal hyperplasia.
- An enlarged node may be free of tumor deposits.
- Microscopic examination, not node dimensions alone, determines metastasis.

Schematic

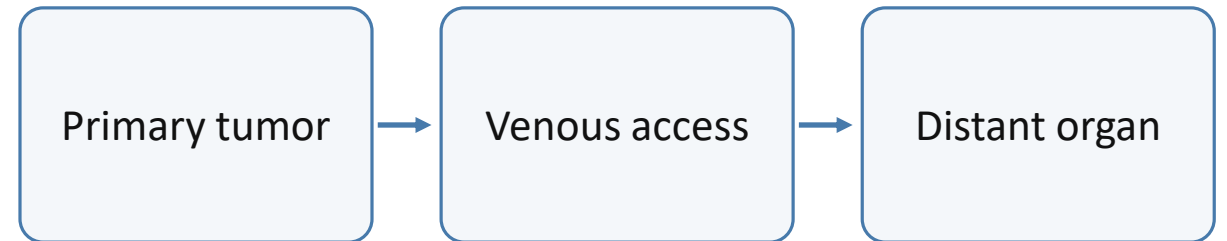


Node size cannot establish tumor involvement

Hematogenous spread is typical of sarcomas

- Sarcomas characteristically disseminate by vascular routes.
- Carcinomas also enter blood vessels and produce blood-borne metastases.
- Anatomic site and tumor behavior must be interpreted together.

Schematic



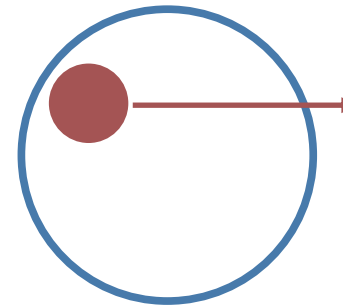
Direction shown follows the source pathway

Small-vessel invasion is a warning sign

- Histologic penetration of small vessels at the primary tumor suggests potential hematogenous spread.
- Robbins characterizes this finding as ominous.
- The finding concerns vascular invasion; It does not prove a distant metastasis is present.

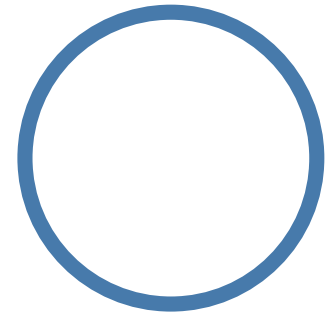
Schematic

Vascular invasion



Relatively accessible

Thick-walled artery



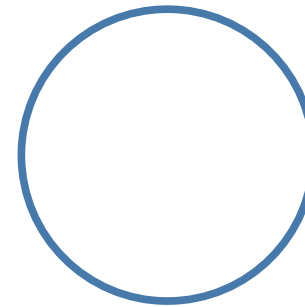
More resistant

Veins are penetrated more readily than arteries

- Involved vascular channels are usually small veins.
- Arteries have thicker walls and resist penetration more effectively.
- Vascular access thus reflects vessel-wall architecture as well as tumor invasion.

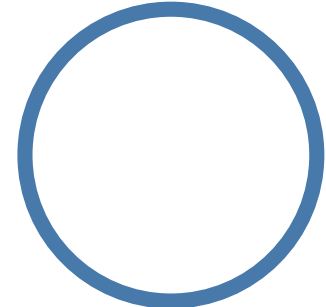
Schematic

Thin-walled small vein



Relatively accessible

Thick-walled artery

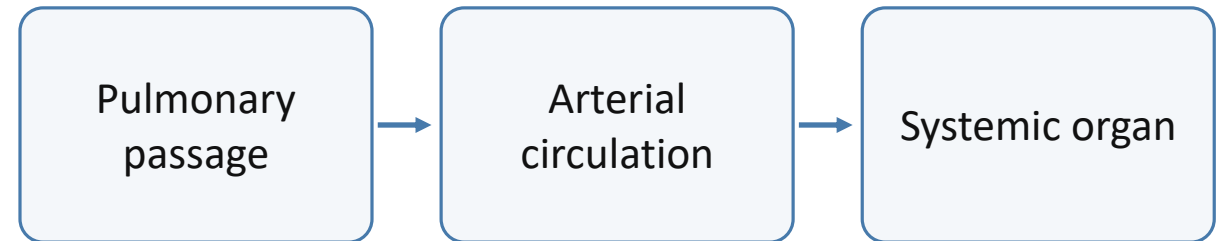


More resistant

Arterial dissemination can still occur

- Tumor cells may traverse pulmonary capillary beds or pulmonary arteriovenous shunts.
- Primary or metastatic lung cancers may release tumor emboli into arterial circulation.
- The arterial route represents a recognized exception to the usual venous entry pattern.

Schematic

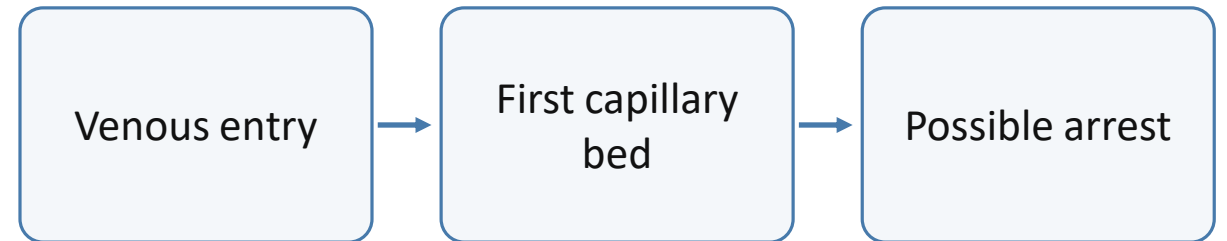


Direction shown follows the source pathway

Blood-borne cells often lodge at the first filter

- With venous invasion, tumor emboli may arrest in the first capillary bed encountered.
- The destination follows the vascular drainage pathway.
- Lung and liver capillary networks are common filtering sites.

Schematic

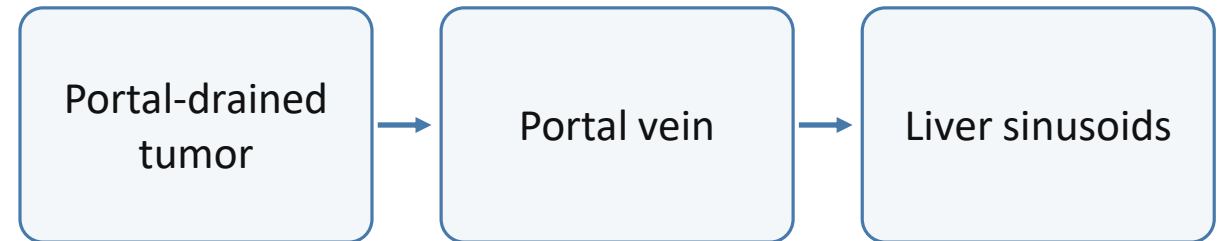


“First filter” is common, not universal

Portal drainage predicts liver metastasis

- Blood entering the portal vein passes through hepatic capillary beds.
- Tumor cells entering this circulation may be retained in the liver.
- The anatomy helps explain why liver metastases are common.

Schematic

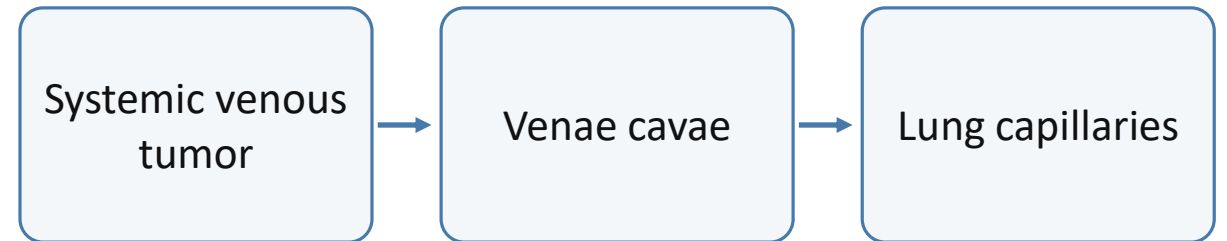


Direction shown follows the source pathway

Systemic venous return predicts lung metastasis

- Superior and inferior vena caval blood returns toward the pulmonary circulation.
- Tumor emboli can arrest within pulmonary capillary beds.
- The lungs are therefore another frequent site of hematogenous metastasis.

Schematic

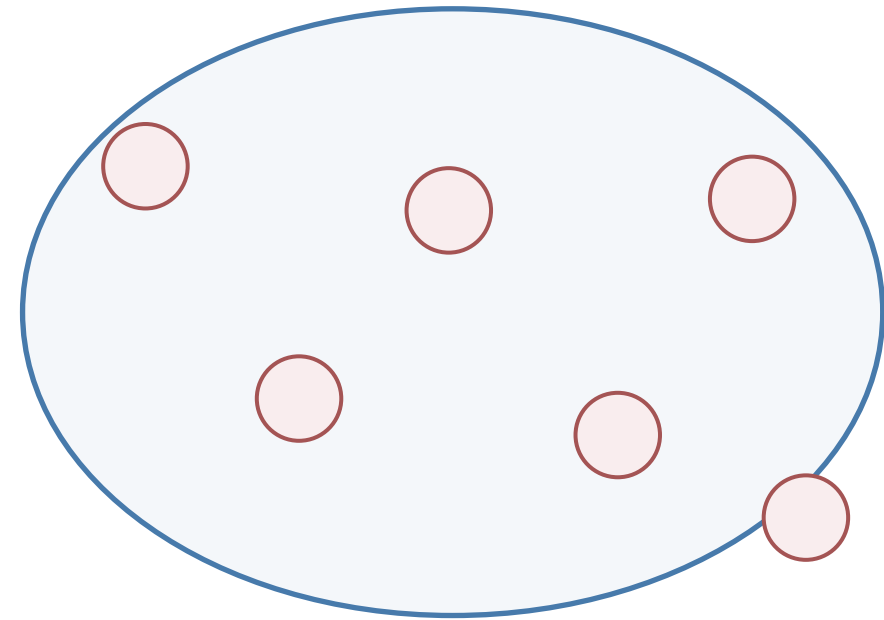


Direction shown follows the source pathway

Metastatic liver involvement may be multinodular

- Blood-borne dissemination may leave the liver studded with metastatic nodules.
- The gross distribution illustrates multiple secondary deposits.
- A multinodular distribution reflects separate metastatic deposits within one organ.

Schematic



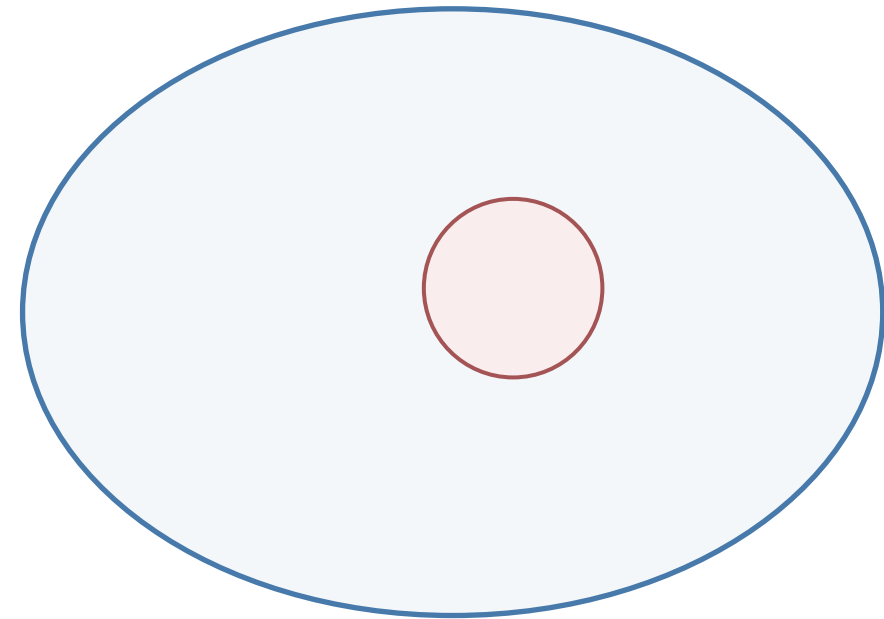
Multiple separate deposits

Distribution schematic; Not a specimen or photomicrograph

A pulmonary metastasis can form a discrete nodule

- Colonic adenocarcinoma can metastasize to the lung and form a secondary deposit.
- The secondary tumor forms a nodule within lung tissue.
- The example highlights a metastatic deposit away from the primary organ.

Schematic



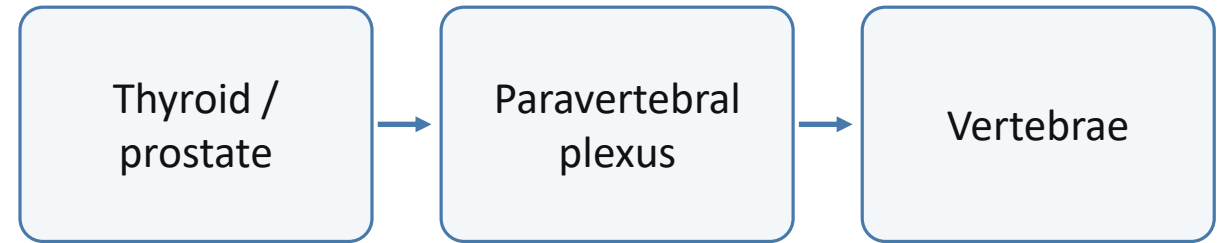
Single secondary nodule

Distribution schematic; Not a specimen or photomicrograph

Paravertebral veins provide a vertebral route

- Tumors close to the vertebral column may disseminate through the paravertebral plexus.
- Robbins gives thyroid and prostate carcinoma as examples.
- The resulting distant deposits may involve vertebrae.

Schematic

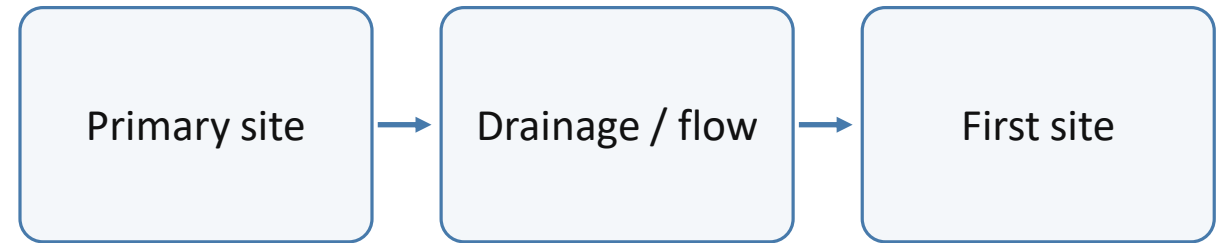


Venous route can bypass the usual lung/liver expectation

Drainage explains much—but not all—organ selection

- Venous routes provide a first anatomical prediction of organ deposition.
- Cancer-specific metastatic patterns exceed what simple drainage can explain.
- Anatomical drainage is only part of the explanation for tissue-specific deposits.

Schematic

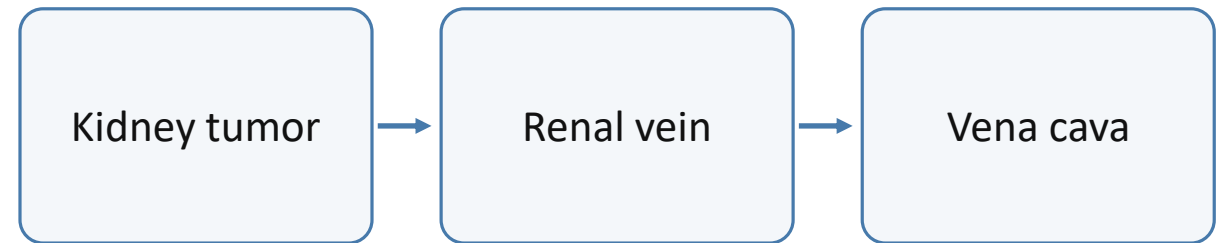


Flow alone does not predict every metastatic site

Renal cell carcinoma may extend into renal veins

- Renal cell carcinoma can invade small branches of the renal vein.
- Tumor may propagate along the renal vein as an intraluminal mass.
- This is a prominent example of tumor growing within a large venous channel.

Schematic

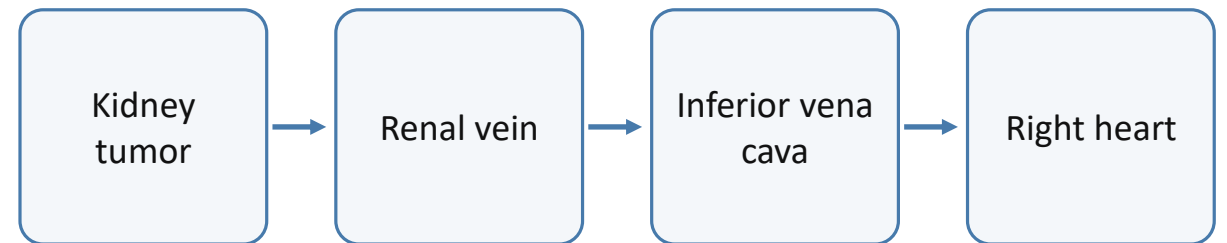


Contiguous intravascular tumor extension

Renal cell carcinoma may reach the right heart

- Continued venous extension can ascend through the inferior vena cava.
- An intraluminal tumor column may occasionally extend to the right side of the heart.
- The route is shown as direct intravascular extension, not as multiple distant nodules.

Schematic

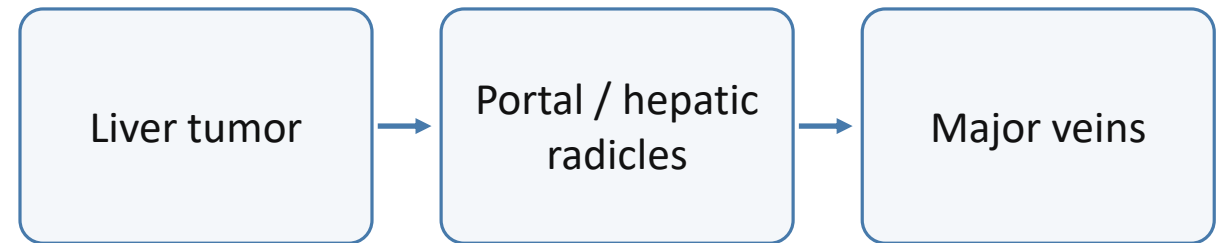


Contiguous intravascular tumor extension

Hepatocellular carcinoma can enter major veins

- Hepatocellular carcinoma can penetrate portal and hepatic venous radicles.
- Tumor may subsequently grow into larger venous channels.
- Intravascular expansion may be conspicuous even without widespread metastatic deposits.

Schematic



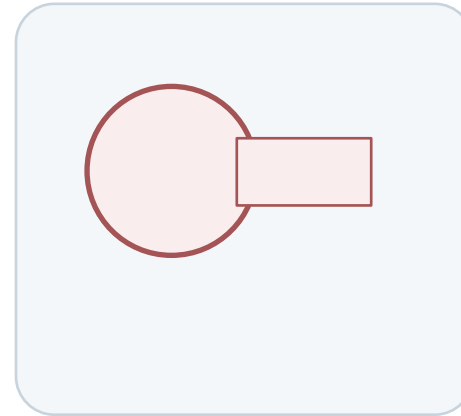
Intraluminal growth may be extensive

Venous tumor growth does not equal diffuse metastasis

- A continuous intravascular tumor column differs from separate distant metastatic foci.
- Striking growth within a vein can occur without widespread metastatic lesions.
- Always distinguish the route of extension from the final distribution of deposits.

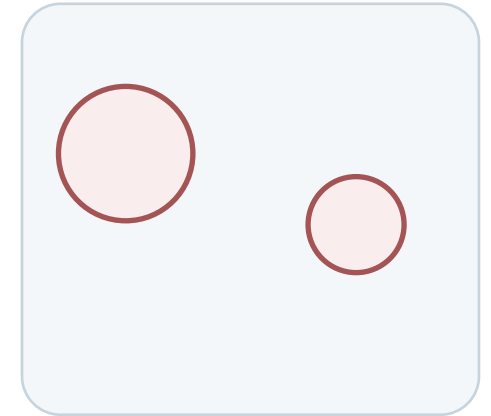
Schematic

Contiguous growth



Continuous column

Discontinuous deposit



Separate focus

Three routes compared at the specimen level

- Surface implants suggest a body-cavity route.
- Regional nodal deposits suggest lymphatic transport.
- Organ nodules following vascular paths suggest hematogenous spread.

Schematic

Serosa

Discontinuous implants

Regional node

Metastatic nodal cells

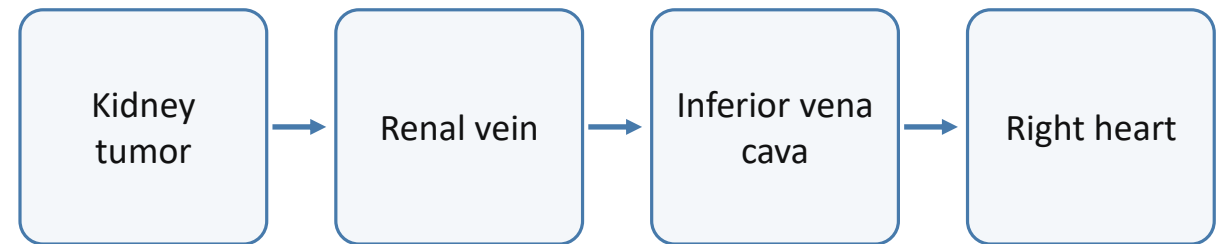
Blood-borne

Separate organ nodules

Integrative case: Renal mass with an IVC column

- Hypothetical teaching scenario: A renal tumor extends continuously into the renal vein and inferior vena cava.
- No separate organ deposits have been identified in the scenario.
- Question: Is this extension itself equivalent to proven widespread metastases?

Schematic

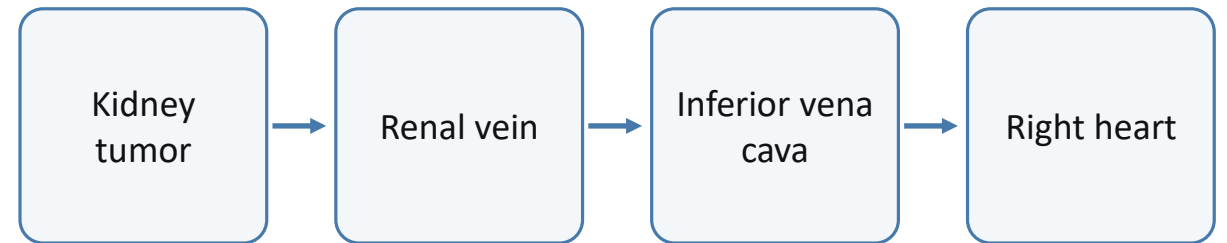


Contiguous intravascular tumor extension

Case interpretation: Separate two phenomena

- The venous column represents intravascular tumor growth.
- The finding demonstrates vascular invasion but not necessarily multiple distant deposits.
- The distinction parallels Robbins' description of renal and hepatic cancers.

Schematic



Contiguous intravascular tumor extension

Avoid five common pathway errors

- Equating contiguous local invasion with metastasis.
- Treating a route tendency as an exclusive rule.
- Assuming every lymphatic deposit follows visible stepwise order.
- Diagnosing nodal metastasis from size alone.
- Calling a continuous venous tumor column widespread metastatic disease.

Schematic

Route $\neq$ diagnosis

Find the deposit

Node size $\neq$ tumor

Use microscopy

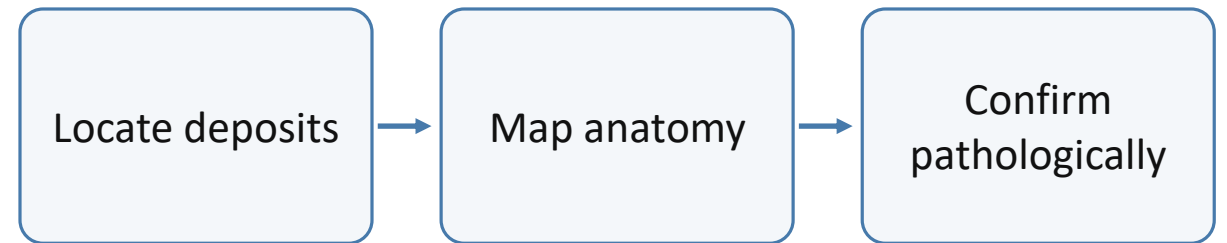
Venous column $\neq$ widespread
deposits

Assess continuity

A route-based diagnostic reasoning sequence

- Identify whether deposits are surface, nodal, vascular, or direct extensions.
- Map the observed distribution against native drainage anatomy.
- Interpret exceptions cautiously; Confirm tumor deposits pathologically where needed.
- Avoid using anatomic plausibility as a substitute for tissue evidence.

Schematic

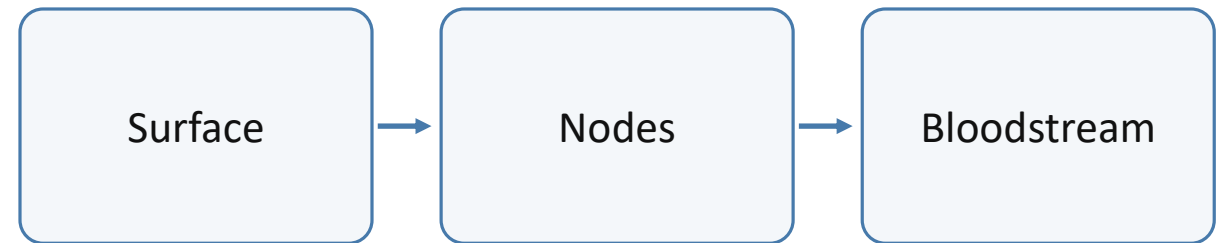


Mechanistic plausibility supports—but does not replace—evidence

Core conclusions

- Three main routes: Cavity seeding, lymphatic transport, and hematogenous spread.
- Peritoneal ovarian spread, breast/lung nodal drainage, and liver/lung blood filters are classic Robbins examples.
- Anatomic routes inform, but do not fully determine, cancer distribution.
- Pathologic confirmation matters especially for nodal enlargement and intravascular tumor.

Schematic



Three complementary routes of spread

Primary reference

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026).
- Chapter 7: Neoplasia; “Pathways of Spread,” pp. 243–244.
- Parent context: “Metastasis,” p. 242.
- Figures 7.12–7.14 cited descriptively; source image files were not supplied.