

SPECIAL FORMS OF CYSTITIS

Interstitial cystitis (bladder pain syndrome) and malakoplakia

Clinicopathologic mechanisms • morphology • diagnostic reasoning

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Learning objectives

- Define bladder pain syndrome using the source-described clinical framework.
- Recognize cystoscopic and tissue findings in interstitial cystitis.
- Explain malakoplakia through bacterial persistence and defective phagocyte processing.
- Identify von Hanseman histiocytes and Michaelis–Gutmann bodies.
- Apply key diagnostic exclusions and morphologic discriminators.

Two distinctive inflammatory entities

Interstitial cystitis

- Clinical pain syndrome
- Cause remains unknown
- Often nonspecific histology
- Biopsy chiefly excludes CIS

Malakoplakia

- Distinctive chronic tissue reaction
- Chronic bacterial setting
- Defective phagocyte processing
- Characteristic histiocytic inclusions

Why these are “special” forms

Cystitis

A spectrum of bladder inflammation

Pain-dominant syndrome

Interstitial cystitis

Morphology-dominant reaction

Malakoplakia

The two subtypes are distinguished by different clinical and pathologic signatures.

The pathology question differs by entity

In suspected bladder pain syndrome

- Describe any tissue changes cautiously.
- Recognize histology as nonspecific.
- Exclude carcinoma in situ (CIS).

In suspected malakoplakia

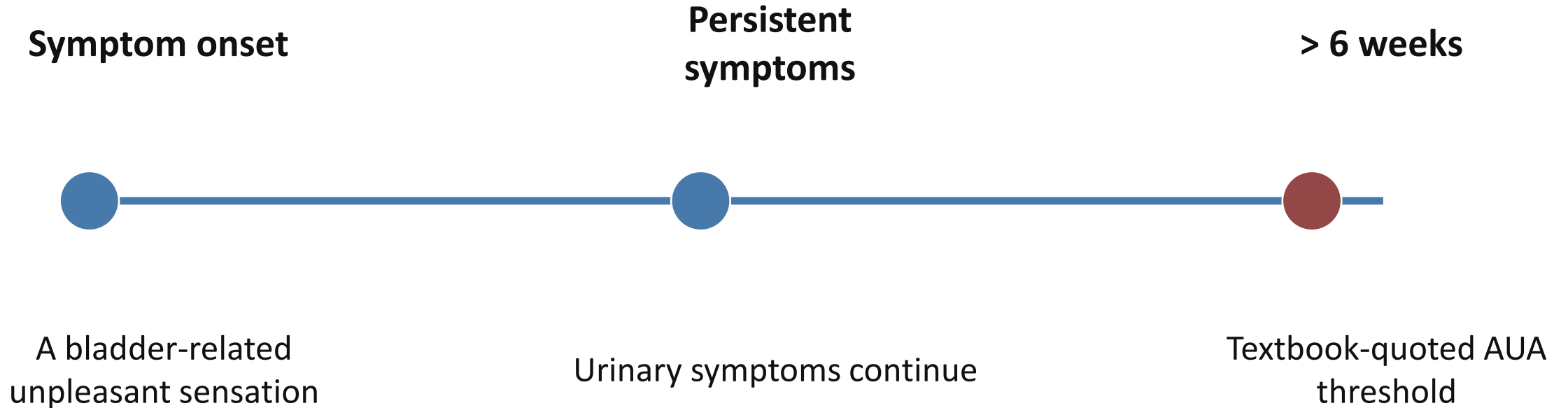
- Identify macrophage-rich inflammation.
- Seek distinctive cytoplasmic inclusions.
- Correlate with chronic bacterial context.

Bladder pain syndrome: Core definition

Bladder-related pain, pressure, or discomfort with associated urinary symptoms.

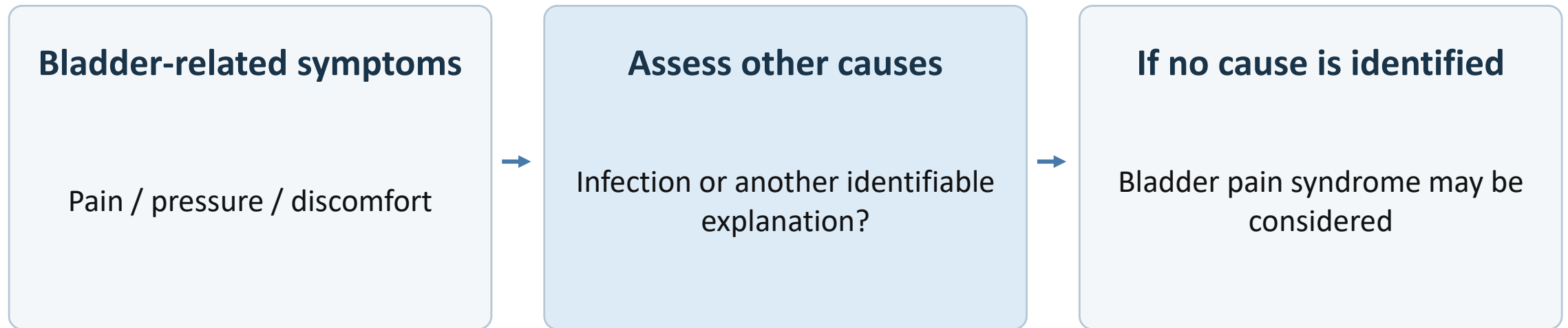
- Symptoms persist for more than six weeks.
- Infection and other identifiable causes must be absent.
- This is a clinical syndrome—not a specific histologic pattern.

The duration criterion matters



The threshold is part of the cited definition; Duration alone does not establish the diagnosis.

Exclusion is embedded in the definition



This diagram paraphrases the historical definition quoted; It is not a complete clinical guideline.

Epidemiologic context and uncertainty

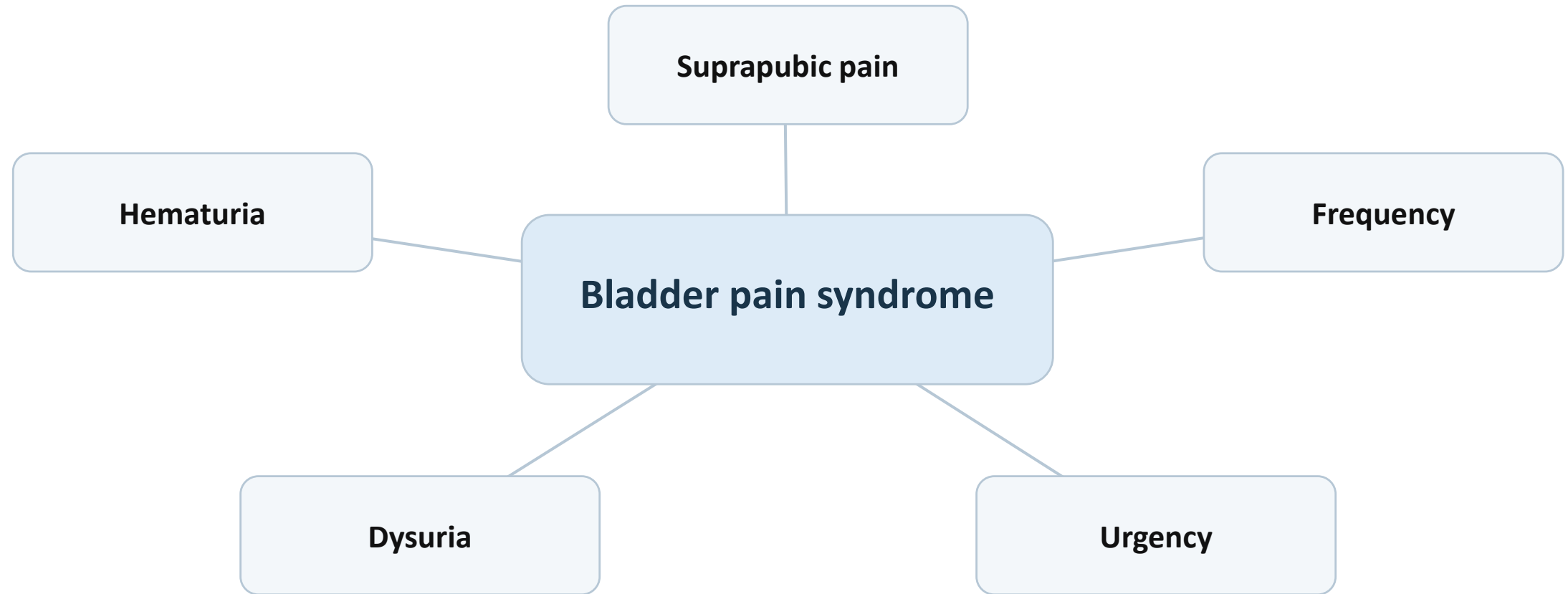
Observed distribution

- Occurs most frequently in females.
- The textbook does not give a prevalence estimate in this section.

Etiologic interpretation

- Cause is described as unknown.
- Morphologic findings do not establish a unique mechanism.

Interstitial cystitis: Presenting pattern



Symptoms can coexist; The mixture alone is not pathognomonic.

The pain phenotype

Pain description

- Intermittent and sometimes severe.
- Usually localized to the suprapubic region.

How to interpret it

- Perceived as bladder-related.
- Must be assessed alongside lower urinary tract symptoms and exclusions.

Storage symptoms form part of the syndrome

Frequency

- Repeated need to void.
- Part of the syndrome's urinary symptom cluster.

Urgency

- Prominent symptom description.
- Not specific to this disorder in isolation.

Dysuria and hematuria require caution

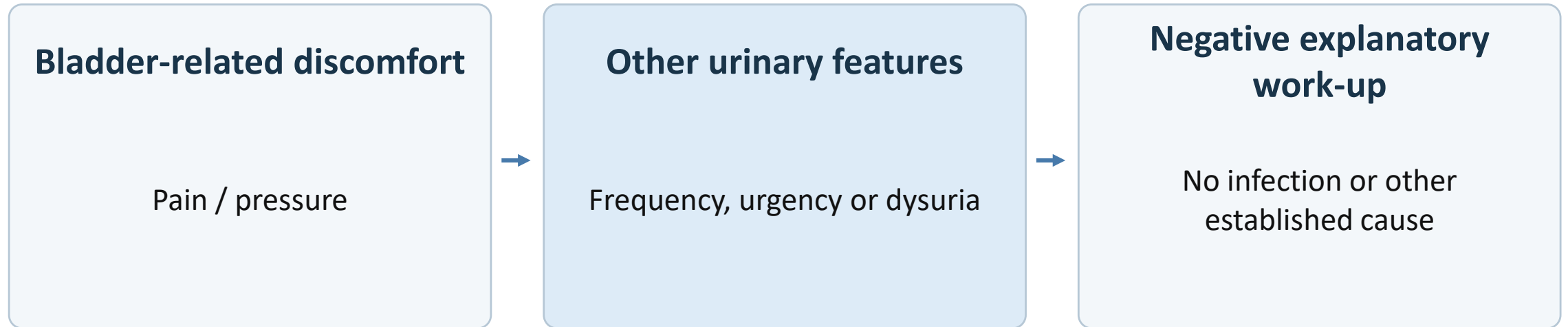
Source-described symptoms

- Dysuria can accompany the pain syndrome.
- Hematuria is also described.

Diagnostic implication

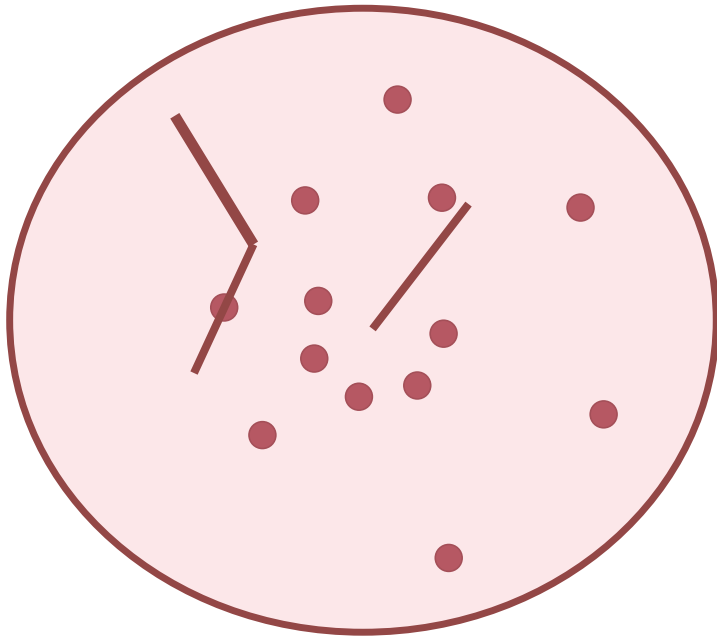
- Neither symptom independently identifies interstitial cystitis.
- Alternative causes remain important when evaluating the syndrome.

Clinical syndrome, not a single symptom



The combination supports a syndromic assessment; Individual symptoms are nonspecific.

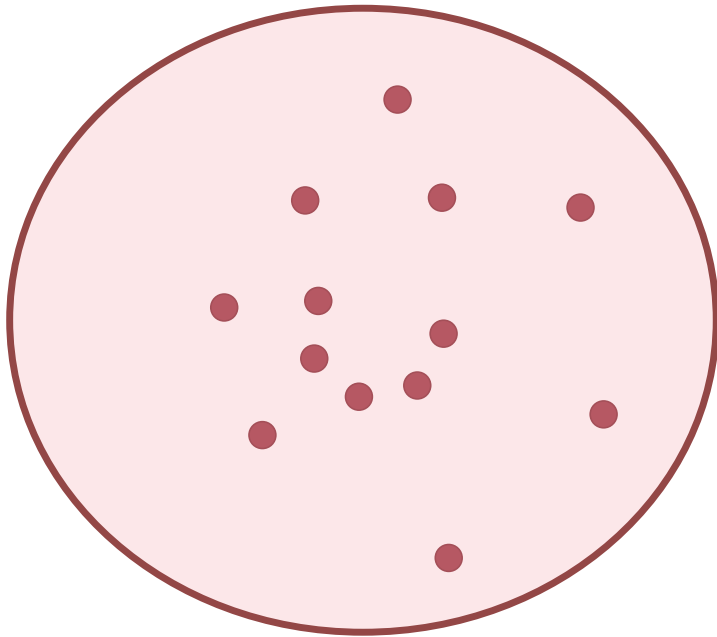
Cystoscopic appearances may be abnormal



Schematic — not a clinical or histologic specimen

- Mucosal fissures are described.
- Punctate mucosal hemorrhages are called glomerulations.
- The cystoscopic findings are not equivalent to a definitive histologic test.

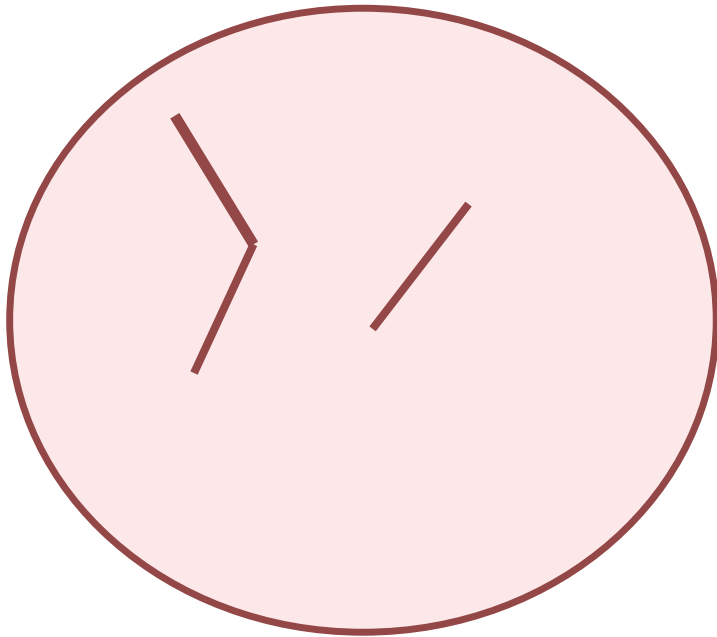
Glomerulations: Punctate hemorrhages



Schematic — not a clinical or histologic specimen

- Small, punctate mucosal hemorrhages.
- Described as a typical cystoscopic finding.
- Interpret within the wider symptom and exclusion context.

Mucosal fissures: Another visual pattern



Schematic — not a clinical or histologic specimen

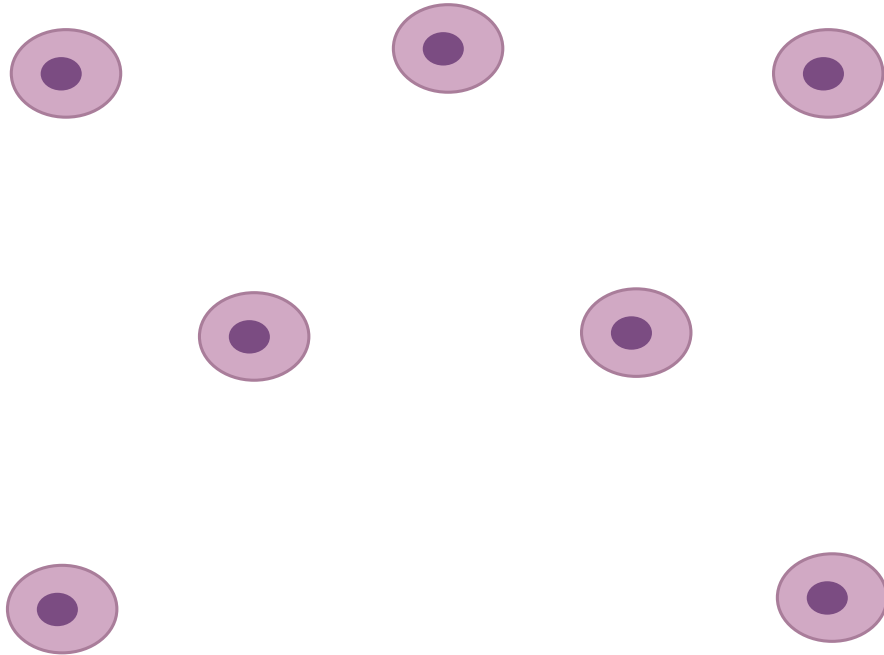
- Linear breaks in the mucosal surface may be seen.
- Fissures and glomerulations are visually distinct lesions.
- Cystoscopy depicts the mucosal surface; Biopsy samples tissue.

Histology is frequently nonspecific

There is no defining microscopic pattern in most cases.

- The source explicitly characterizes the microscopic pathology as nonspecific.
- A nonspecific biopsy cannot, by itself, prove the pain syndrome.
- Histology must be interpreted in clinical context.

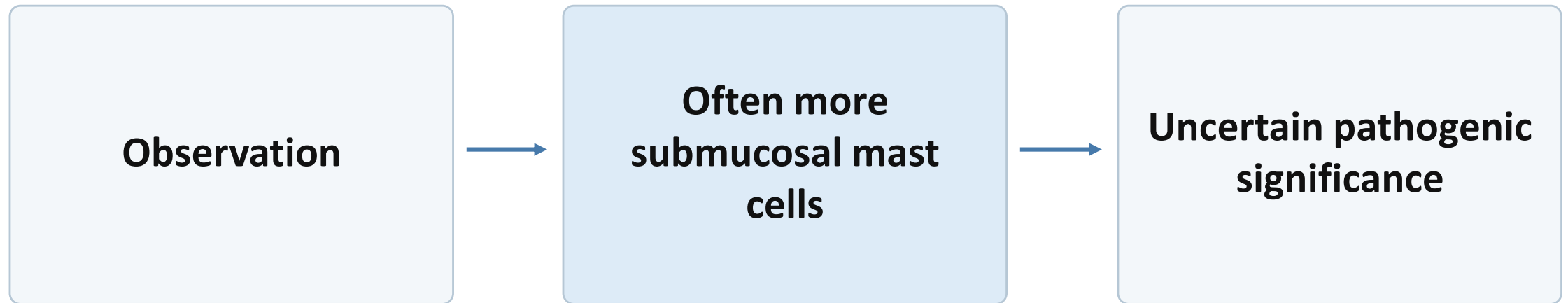
Mast cells may be increased



Schematic — not a clinical or histologic specimen

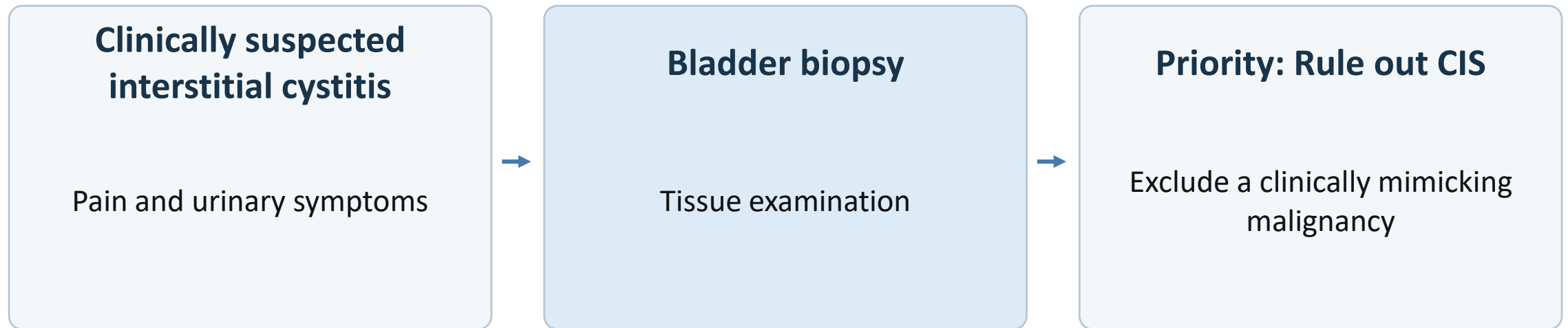
- Mast cells are often increased in the submucosa.
- The observation is described in the Robbins section.
- It is not presented as a stand-alone diagnostic criterion.

A finding is not automatically a mechanism



The text explicitly leaves the contribution of mast cells unresolved.

The main role of biopsy: Exclusion



This summarizes the stated primary purpose of biopsy, not a universal biopsy indication.

Carcinoma in situ is an important mimic

Bladder pain syndrome

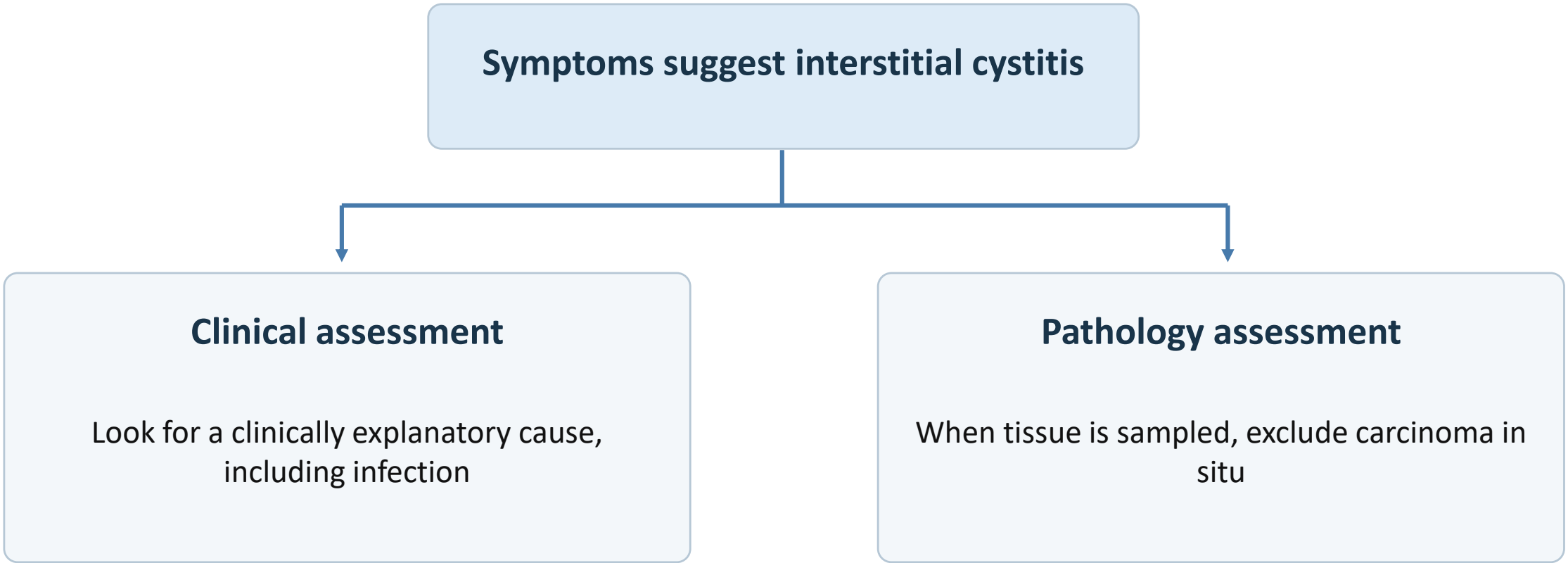
- Characteristic clinical complaint: Bladder-related pain plus urinary symptoms.
- Histology may be nonspecific.

Urothelial CIS

- Can present with a clinically similar symptom pattern.
- Requires exclusion when relevant by evaluating tissue morphology.

Avoid the diagnostic shortcut

Symptoms suggest interstitial cystitis



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graph TD; A[Symptoms suggest interstitial cystitis] --> B[Clinical assessment]; A --> C[Pathology assessment]; B --> D[Look for a clinically explanatory cause, including infection]; C --> E[When tissue is sampled, exclude carcinoma in situ];
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Clinical assessment

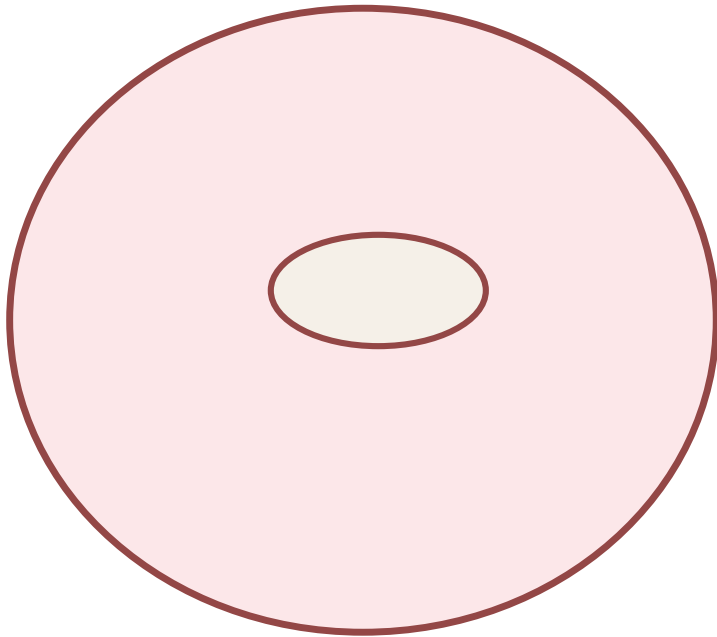
Look for a clinically explanatory cause,
including infection

Pathology assessment

When tissue is sampled, exclude carcinoma in
situ

A syndromic label must not replace appropriate exclusion of mimics.

Hunner ulcers identify a subset



Schematic — not a clinical or histologic specimen

- Some affected individuals develop chronic mucosal ulcers.
- These are termed Hunner ulcers in the source.
- Their presence distinguishes an ulcerative phenotype; Not all cases have them.

Classic ulcerative disease

Textbook terminology

- Hunner-associated cases are described as late, classic or ulcerative phase.

Interpretation limit

- The text says “some cases”; Do not imply that ulceration is inevitable.
- Avoid assuming that every patient follows one sequence.

Late wall injury may extend deeply

Mucosa: Chronic ulcer



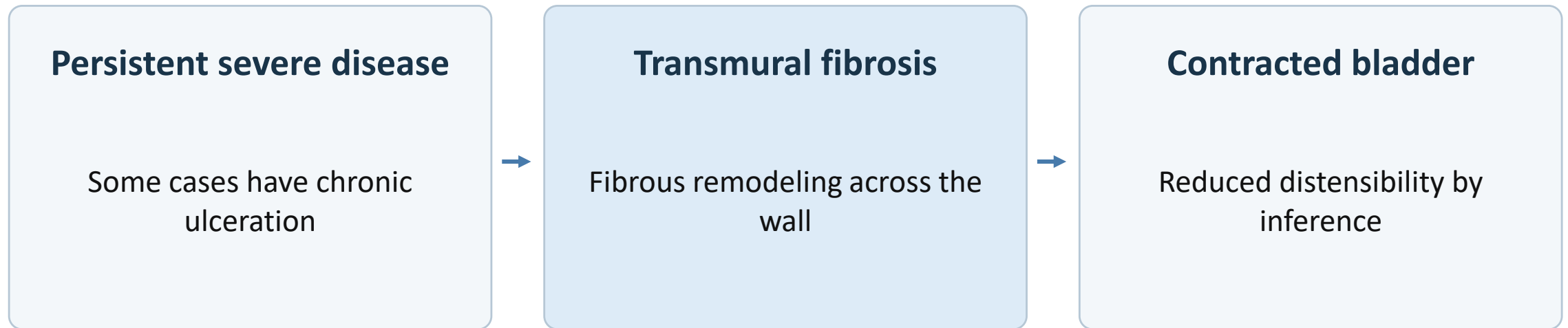
Wall: Progressive transmural fibrosis



Functional end result: Contraction

Schematic spatial pathway; “may” denotes a possible consequence, not inevitable progression.

A contracted bladder is a late consequence



Only the sequence to contracted bladder is stated directly; Reduced distensibility is explanatory inference.

Separate typical findings from late outcomes

Finding	Role in source	Interpretation
Glomerulations	Cystoscopic observation	Punctate hemorrhages
Hunner ulcers	Subset of patients	Classic ulcerative phenotype
Transmural fibrosis	Possible late change	May produce contracted bladder

Why treatment remains empiric

The source describes treatment as largely empiric.

- Underlying cause is not established.
- Histologic abnormalities are frequently nonspecific.
- No universal treatment algorithm is provided in this Robbins section.

Interstitial cystitis: Evidence boundaries

Grounded observations

- Bladder-related symptoms > six weeks.
- Typical cystoscopic patterns and possible ulcers.
- Mast-cell increase sometimes noted.

What not to overclaim

- A proven single etiology.
- Mast cells as diagnostic proof.
- Inevitable ulceration or contraction.

Case exercise: Painful bladder symptoms

Illustrative teaching vignette

An adult woman has prolonged bladder-related suprapubic discomfort, frequency and urgency. Investigation has not identified infection or another cause.

Clinical / pathologic question

Which diagnosis is suggested, and what important mimic must be considered if bladder tissue is examined?

Case reasoning: A syndrome plus an exclusion

Syndromic fit

Bladder-related discomfort with urinary symptoms lasting beyond the defined window.

Main uncertainty

A clinical pattern is not an etiologic or histologic proof.

Pathology priority

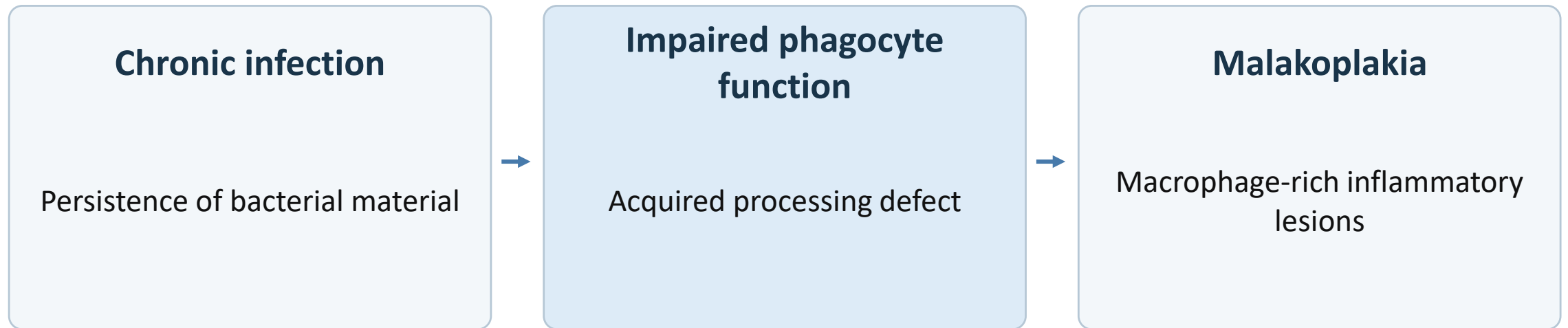
The biopsy role emphasized by Robbins is to rule out CIS.

Malakoplakia: A distinctive inflammatory reaction

A chronic macrophage-rich reaction associated with defective intracellular handling of bacterial material.

- Distinctive morphology contrasts with the nonspecific histology of interstitial cystitis.
- The pathogenic defect is believed to be acquired.
- Clinical context often includes persistent bacterial infection.

A chronic bacterial setting



Proposed explanatory pathway from the textbook; Not a demonstrated invariant sequence.

Organisms named in the source

Most frequent association

- Escherichia coli.
- Chronic bacterial infection is central to the described setting.

Occasional association

- Proteus species.
- The list is not an exhaustive microbiologic classification.

Immunosuppression increases association

Clinical context

- The condition occurs more frequently in immunosuppressed patients.
- Renal transplant recipients as an example.

Pathogenetic relation

- Impaired host handling of bacteria is consistent with the proposed lesion mechanism.
- Association does not prove the defect in every individual case.

Renal transplantation: A source example

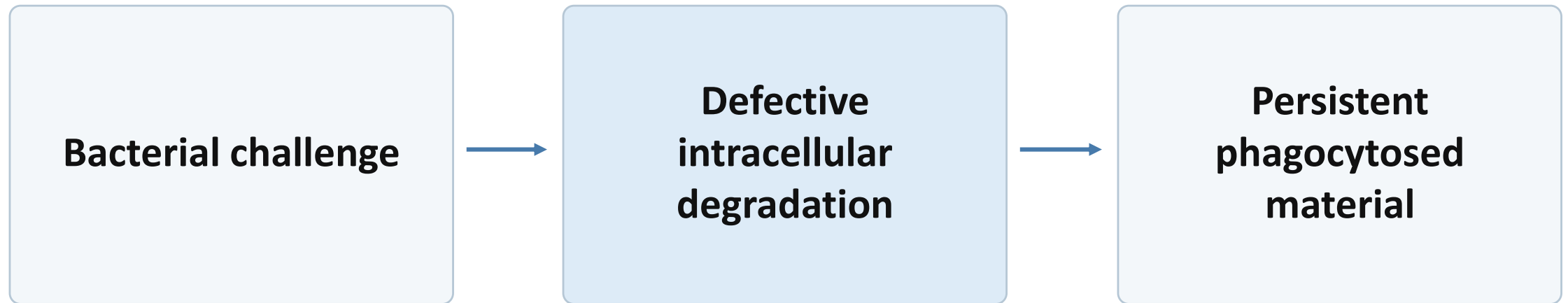
Illustrative teaching vignette

A renal transplant recipient with a chronic bacterial urinary tract setting develops unusual bladder mucosal plaques.

Clinical / pathologic question

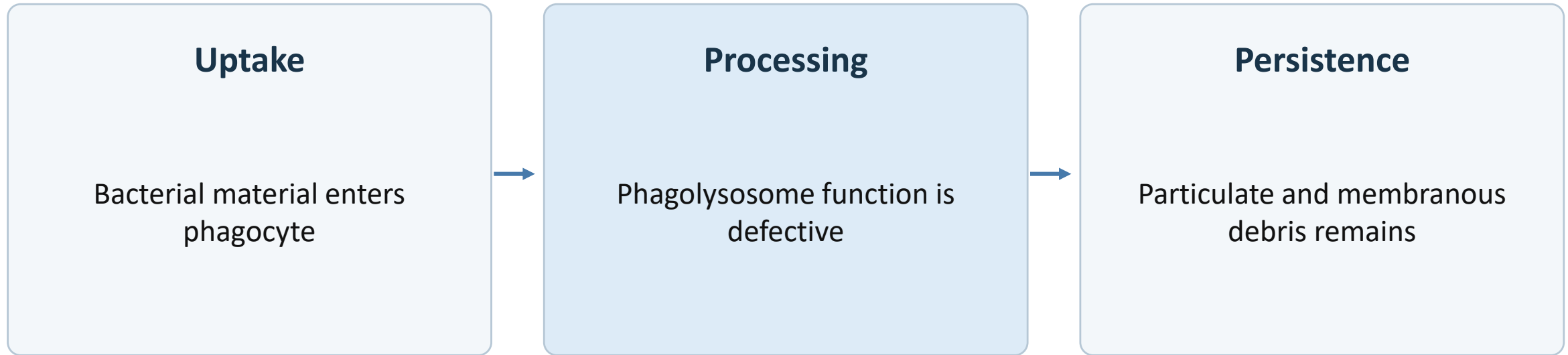
Which chronic inflammatory lesion should be included in the morphologic consideration?

Acquired defects in phagocyte function



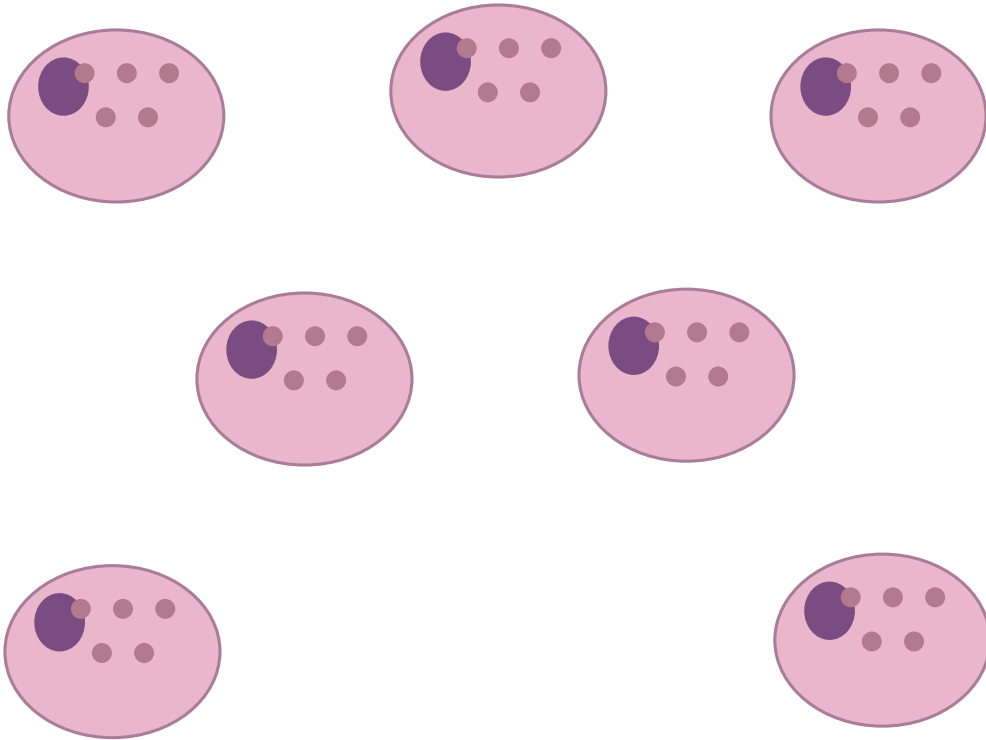
The causal explanation is described as apparent/proposed in the source, not as fully established for every case.

The phagolysosomal step matters



Proposed mechanism shown as an educational sequence; Not a quantitative model.

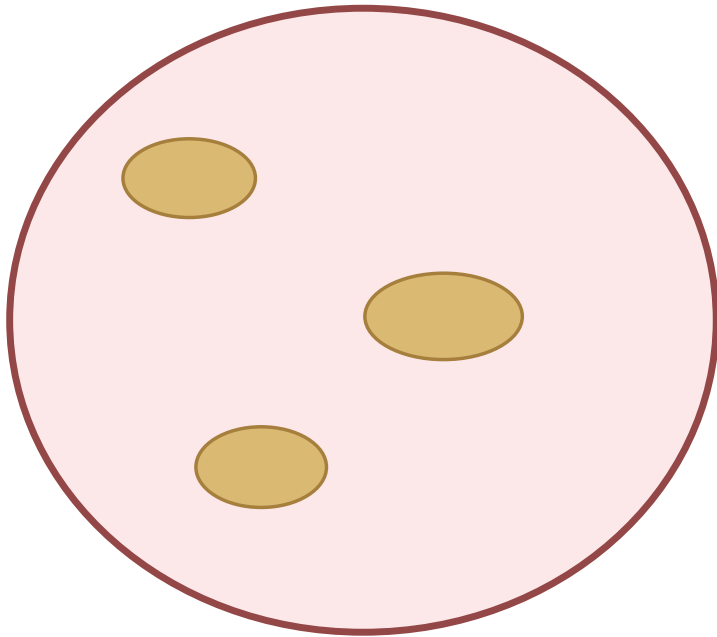
Debris accumulation explains the cytoplasm



Schematic — not a clinical or histologic specimen

- Macrophages contain numerous phagosomes.
- Phagosomes retain particulate and membranous bacterial debris.
- The result is abundant granular cytoplasm.

Gross malakoplakia: Yellow mucosal plaques



Schematic — not a clinical or histologic specimen

- Soft, slightly elevated mucosal plaques.
- Typically described as yellow or yellow-orange.
- A distinctive cystoscopic appearance.

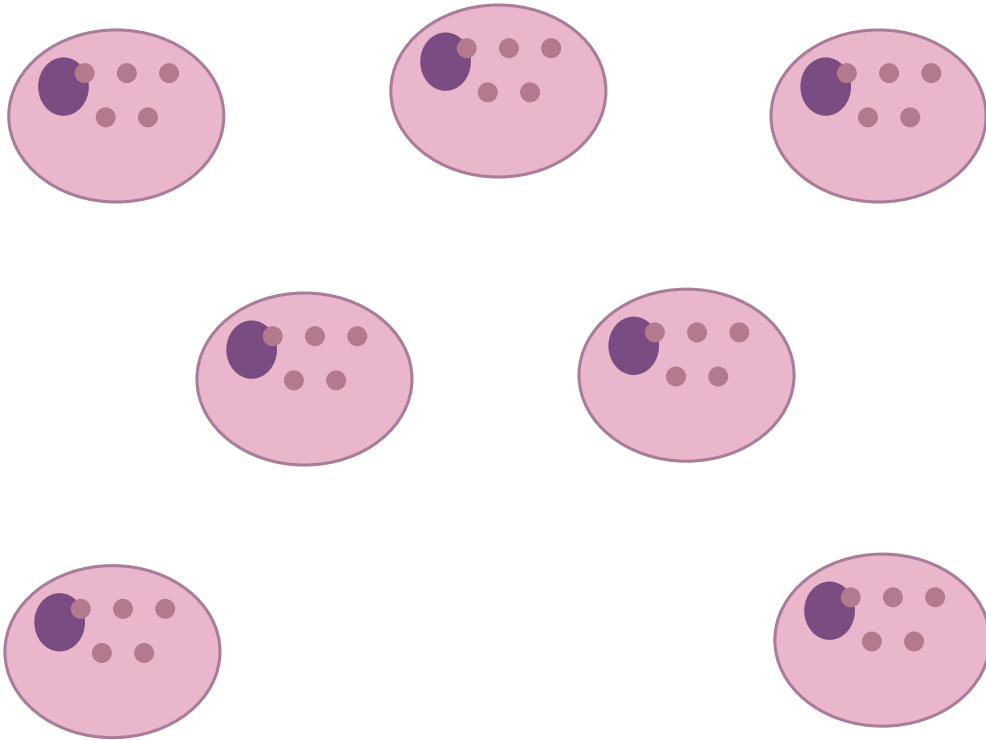
Plaque size and texture are descriptive

3–4 cm

Typical plaque diameter reported in the
source

- Soft surface, slightly raised contour.
- Color and plaque pattern support consideration of malakoplakia.
- Macroscopic appearance should be matched to the microscopic lesion.

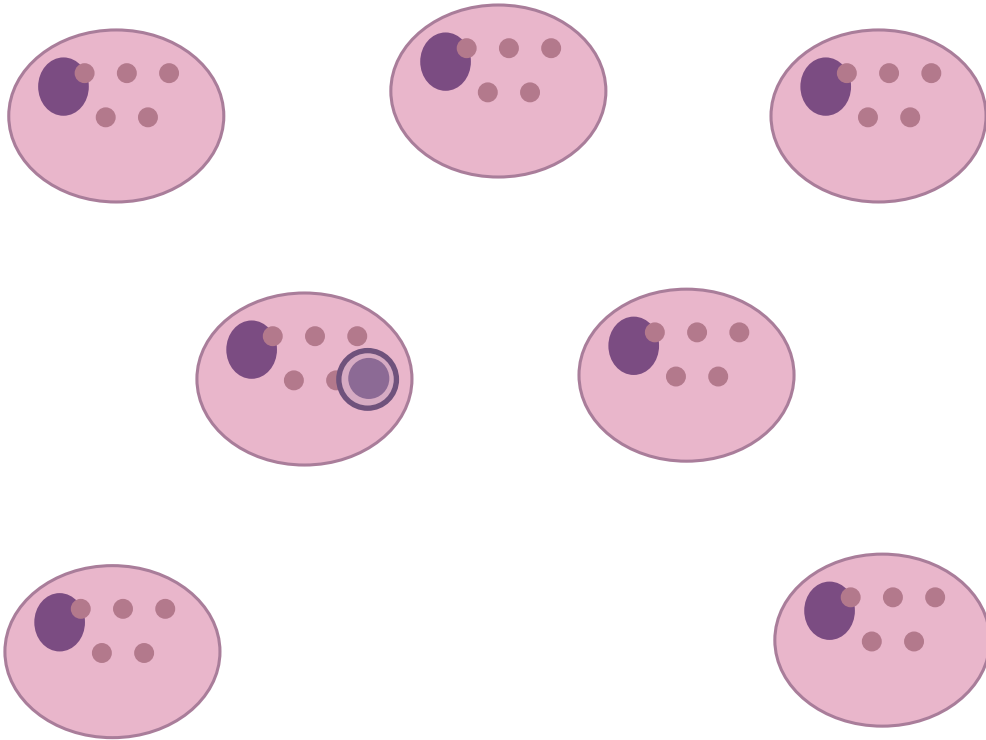
Histology: Aggregates of large macrophages



Schematic — not a clinical or histologic specimen

- Macrophages form conspicuous aggregates.
- Abundant granular or foamy cytoplasm creates the characteristic cellular background.
- The lesion is a distinctive chronic inflammatory reaction.

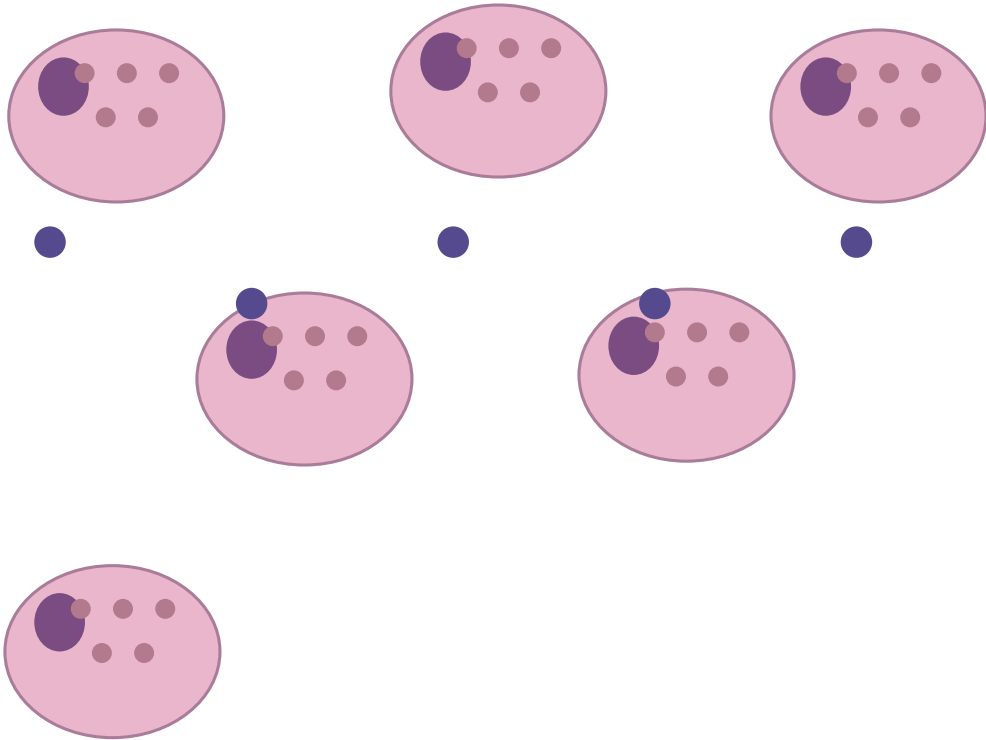
Von Hansemann histiocytes



Schematic — not a clinical or histologic specimen

- Name for the large characteristic lesional macrophages.
- Cells are rich in coarse granular cytoplasm.
- Recognition guides the search for Michaelis–Gutmann bodies.

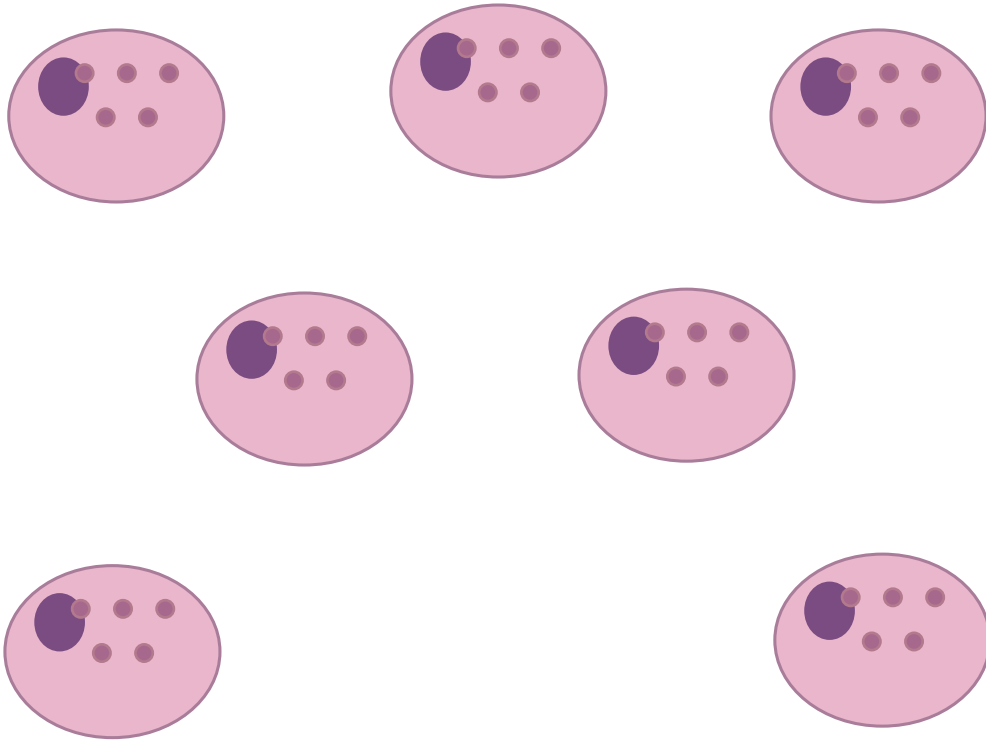
Accompanying inflammatory cells



Schematic — not a clinical or histologic specimen

- Occasional multinucleated giant cells may be present.
- Lymphocytes may accompany macrophage aggregates.
- The macrophage predominance is the defining cellular pattern.

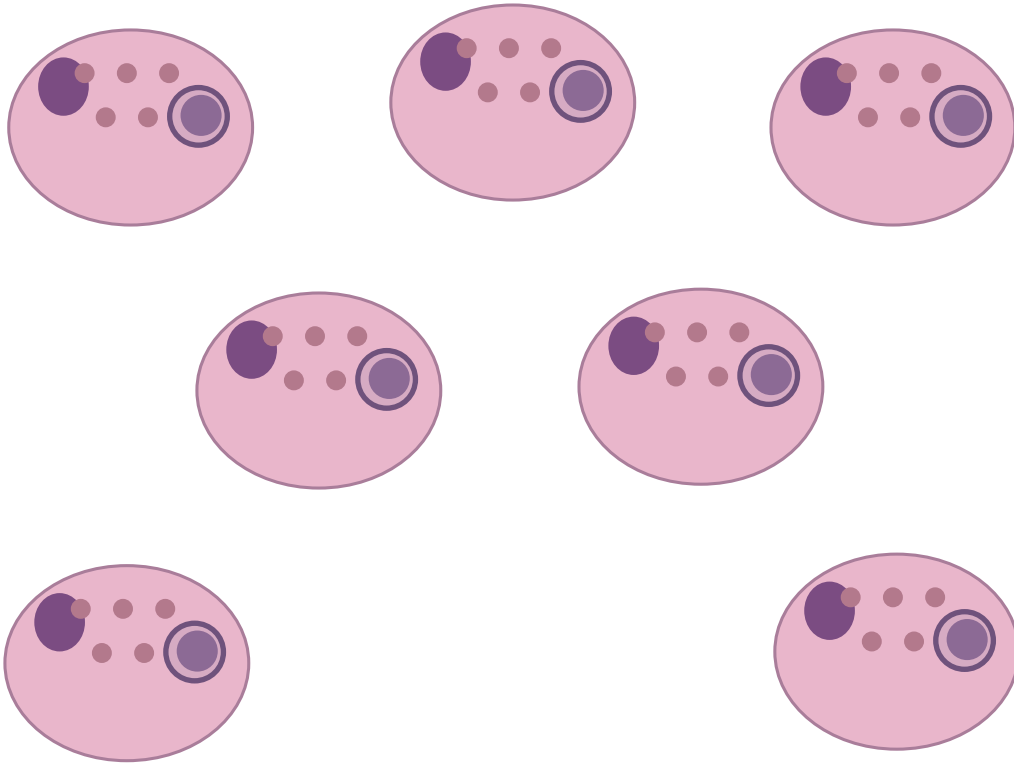
PAS-positive granular cytoplasm



Schematic — not a clinical or histologic specimen

- The source figure depicts granular PAS-positive macrophage cytoplasm.
- This aligns with accumulation of phagocytosed material.
- PAS positivity is descriptive; The defining inclusions are evaluated separately.

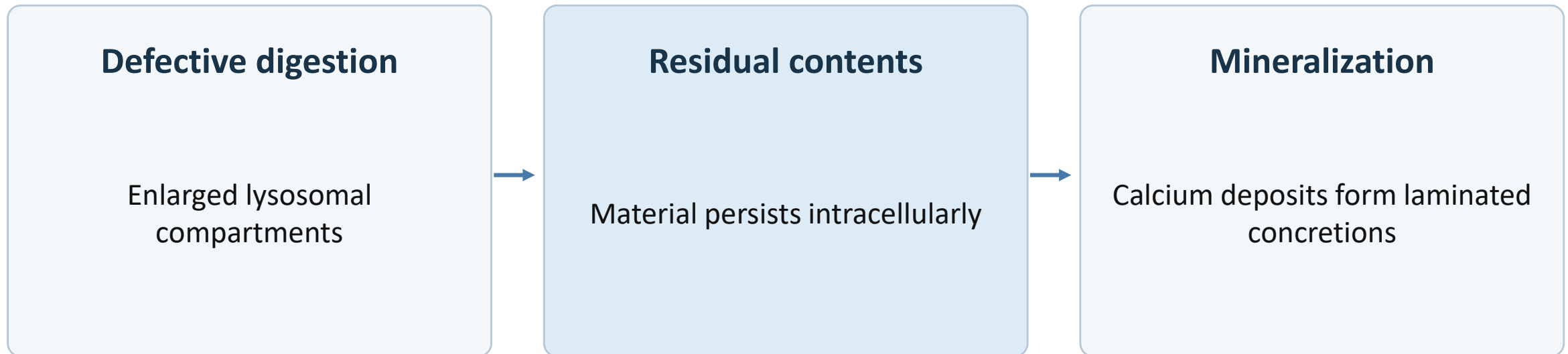
Michaelis–Gutmann bodies



Schematic — not a clinical or histologic specimen

- Characteristic rounded mineralized concretions.
- Typically present within the macrophages.
- May appear laminated or target-like in a schematic depiction.

How Michaelis–Gutmann bodies form



Proposed mechanism shown as an educational sequence; Not a quantitative model.

Microscopic recognition sequence

Macrophage-rich chronic inflammation

Large von Hanseman
histiocytes



Granular cytoplasm

Stored particulate /
membranous debris



Michaelis–Gutmann bodies

Characteristic mineralized
inclusions

Morphologic sequence for recognition, not a formal diagnostic scoring system.

Gross and microscopic features must align

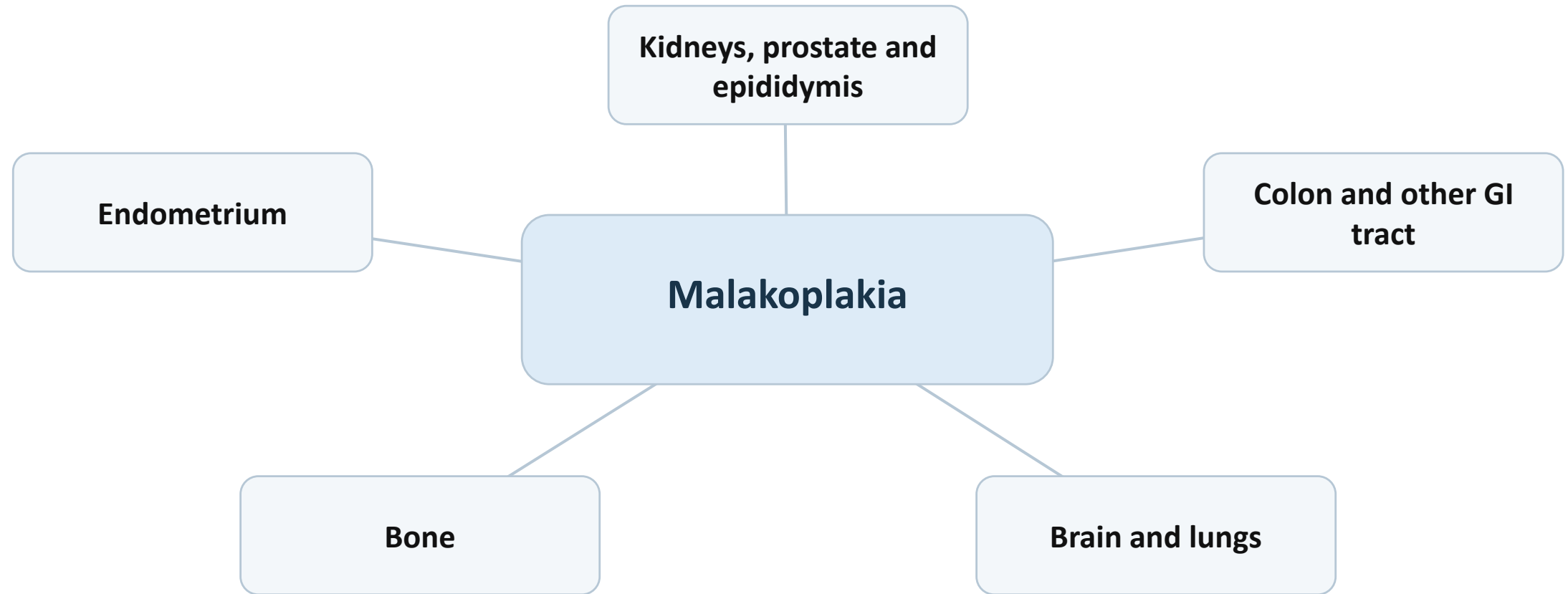
Cystoscopic lesion

- Soft, yellow-orange raised plaques.
- Typical size stated as approximately 3–4 cm.

Microscopic lesion

- Large macrophage aggregates with granular cytoplasm.
- Michaelis–Gutmann mineralized inclusions.

Malakoplakia is not limited to the bladder



Examples of other locations explicitly named.

Case exercise: Yellow plaques and inclusions

Illustrative teaching vignette

Cystoscopy shows soft yellow bladder plaques. Tissue sampling reveals aggregates of large macrophages with granular cytoplasm and intracytoplasmic laminated concretions.

Clinical / pathologic question

Name the condition, its characteristic cells, and the inclusions.

Case reasoning: Link cell injury to morphology

Clinical setting

Chronic bacterial context, especially E. Coli; Possible immunosuppression.

Cellular lesion

Macrophages have defective intracellular bacterial processing.

Diagnostic pattern

Granular histiocytes and mineralized Michaelis–Gutmann bodies.

Interstitial cystitis versus malakoplakia

Feature	Interstitial cystitis	Malakoplakia
Core phenotype	Bladder-related pain syndrome	Distinctive chronic inflammatory reaction
Cause / association	Unknown etiology	Chronic bacteria; impaired phagocytes
Tissue pattern	Usually nonspecific	Histiocytes and mineralized inclusions
Critical clue	Exclude CIS on biopsy	Michaelis–Gutmann bodies

A practical pattern-recognition pathway

What dominates the clinical/pathologic picture?

Clinical assessment

Pain syndrome + negative explanatory work-up → consider bladder pain syndrome

Pathology assessment

Yellow plaques + histiocytes + inclusions → consider malakoplakia

Always integrate symptoms, morphology and clinical context; This is a teaching schematic.

Three common interpretation pitfalls

Pitfall	Why it is incorrect	Safer inference
Mast cells prove IC	Pathogenic meaning uncertain	Descriptive observation only
All IC has Hunner ulcers	Source says some cases	Specify ulcerative subset
Macrophages alone prove malakoplakia	Macrophages are nonspecific	Seek Michaelis–Gutmann bodies

Applied discrimination: Three statements

Identify the only statement supported by Robbins.

A. In suspected bladder pain syndrome, biopsy chiefly establishes a unique inflammatory pattern.

B. Von Hanseemann histiocytes accumulate partly degraded bacterial material.

C. Hunner ulcers occur in all bladder pain syndrome cases.

Applied discrimination: Interpretation

**Statement A —
unsupported**

Microscopic abnormalities in IC are generally nonspecific; Biopsy chiefly excludes CIS.

Statement B — supported

Defective phagolysosome processing leaves bacterial debris in the histiocyte cytoplasm.

**Statement C —
unsupported**

Only some IC cases develop Hunner ulcers.

Synthesis: Two different diagnostic logics

Interstitial cystitis

- Syndrome first, exclusions essential.
- Histology often nonspecific.
- CIS is the critical tissue mimic.

Malakoplakia

- Tissue pattern is strongly informative.
- Look for granular macrophages.
- Seek characteristic mineralized inclusions.

Primary reference and visual provenance

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026). Chapter 21, pp. 869–870.
- Topic scope: “Special Forms of Cystitis”; contextual distinction from adjacent “Acute and Chronic Cystitis”.
- All anatomical and microscopic diagrams in this deck are original, native PowerPoint schematics—not actual clinical or histologic specimens.