

Acute Cholecystitis

Pathogenesis • morphology • clinical correlation

Calculous and acalculous patterns

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Learning objectives: Explain, recognize, distinguish

- Explain how cystic outflow obstruction initiates calculous inflammation.
- Describe the ischemic and stasis-related mechanisms of acalculous disease.
- Recognize gross, microscopic and clinical hallmarks of acute cholecystitis.
- Distinguish dangerous complications and the chronic counterpart.

The gallbladder stores and concentrates bile

Physiologic context

- Liver secretion may reach approximately 1 L of bile daily.
- Between meals, the gallbladder stores and concentrates bile.

Pathologic relevance

- Adult gallbladder capacity is approximately 50 mL.
- Stored bile is exposed to abrupt outflow obstruction and pressure changes.

Cholecystitis is a clinicopathologic spectrum

Acute

- Abrupt gallbladder inflammation.
- Frequently follows an impacted gallstone.

Chronic

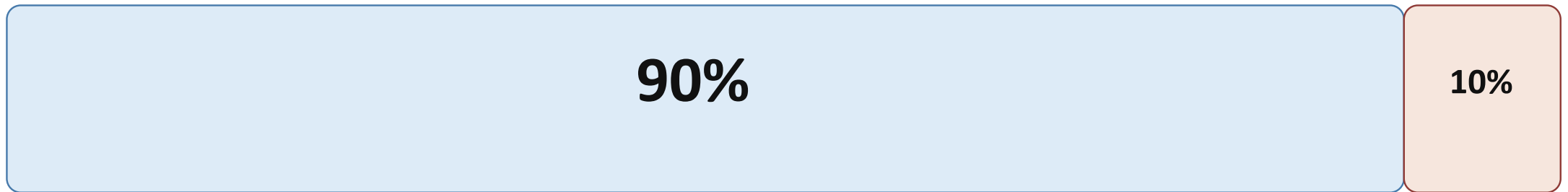
- Repeated or sustained wall inflammation.
- May occur without known acute attacks.

Acute on chronic

- Acute inflammation may supervene on chronic gallbladder disease.
- History and morphology may overlap.

Stone obstruction explains most acute attacks

Distribution of acute attacks

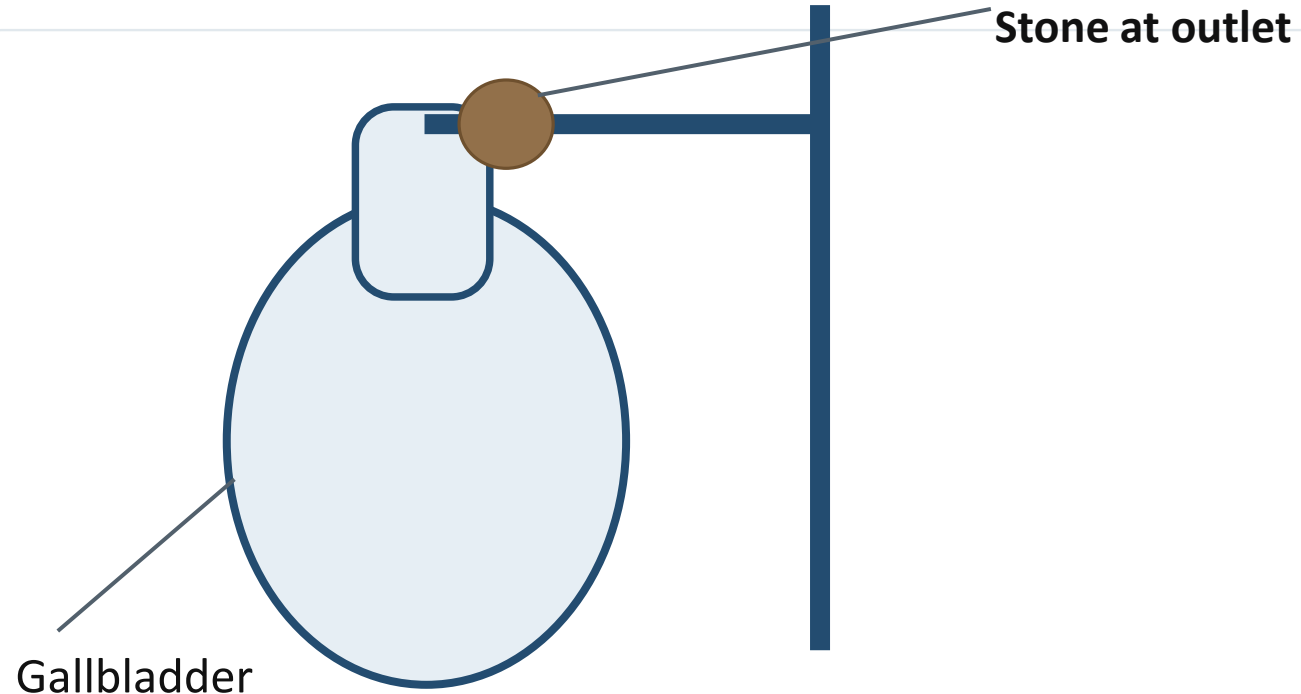


Stone obstruction / calculous

Acalculous

The groups describe triggering mechanisms, not different histologic appearances.

The cystic duct and neck are critical sites



Relevant anatomy

- Gallbladder lumen stores and concentrates bile.
- Neck continues into the cystic duct.
- Outflow obstruction initiates most acute attacks.

Biliary pain is not equivalent to acute inflammation

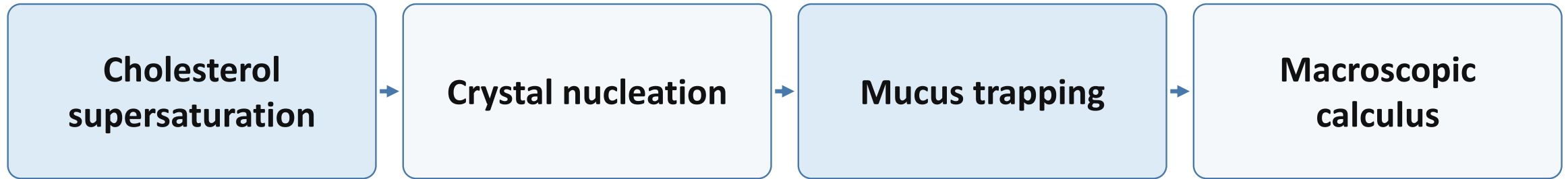
Symptomatic stones

- Gallbladder contraction pushes a calculus against the outlet.
- Pressure and pain may occur without established cholecystitis.

Acute cholecystitis

- Progressive right upper quadrant or epigastric pain.
- Pain characteristically persists beyond 6 hours.

Stone formation sets the upstream conditions

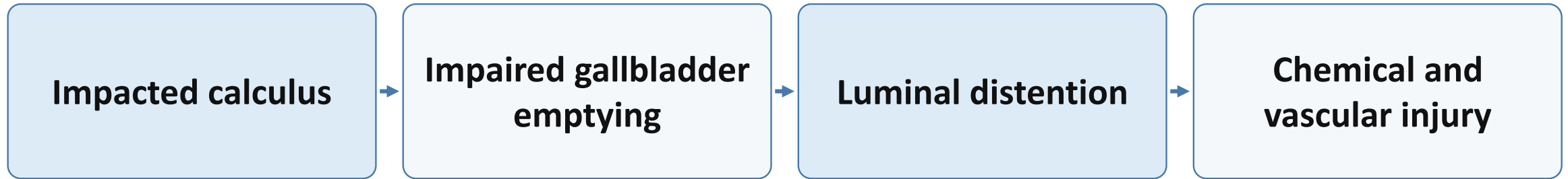


Hypomotility of the gallbladder further favors cholesterol stone formation.

Calculous cholecystitis is a major gallstone complication

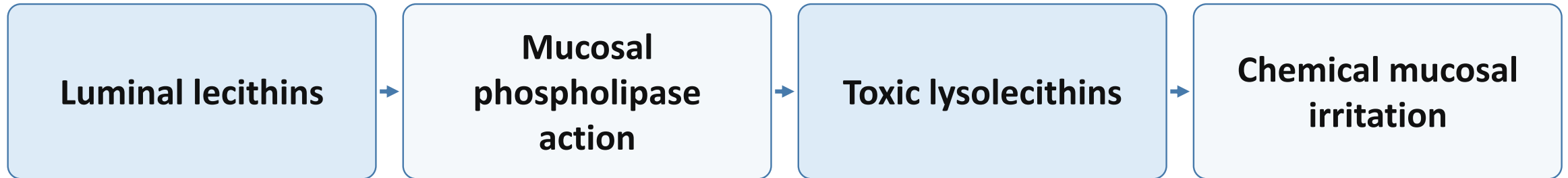
- It is described as the principal complication of gallstones.
- It is the commonest reason for emergency cholecystectomy in the source.
- Diabetes with symptomatic gallstones is an important clinical setting.

Calculous injury begins with outflow obstruction



This is initially an inflammatory response to the obstructed, distended organ.

Phospholipases convert lecithins into lysolecithins



The toxin-producing reaction is part of the stated chemical-injury mechanism.

A protective mucus layer normally limits bile injury

Intact barrier

- Glycoprotein mucus separates epithelial cells from concentrated bile.
- The mucosal surface is normally protected.

Barrier disruption

- Acute inflammation damages the protective mucus layer.
- The epithelium becomes directly exposed to bile salts.

Bile salts become harmful when the barrier is lost

1 Glycoprotein mucosal protection is disrupted.



2 Bile salts come into direct contact with epithelium.



3 Detergent action worsens epithelial injury.

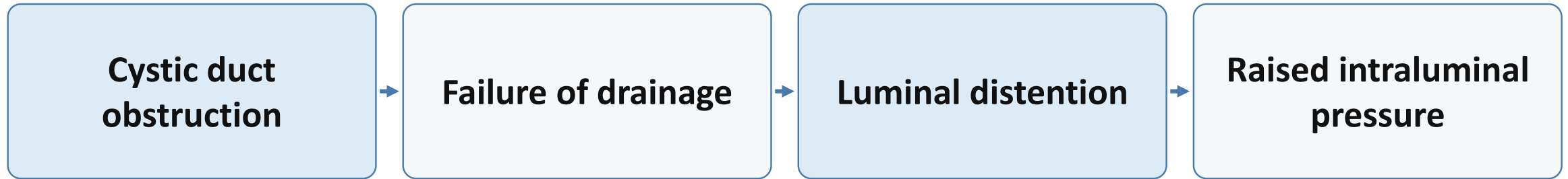


4 Chemical injury reinforces local inflammation.

Prostaglandins contribute to mural inflammation

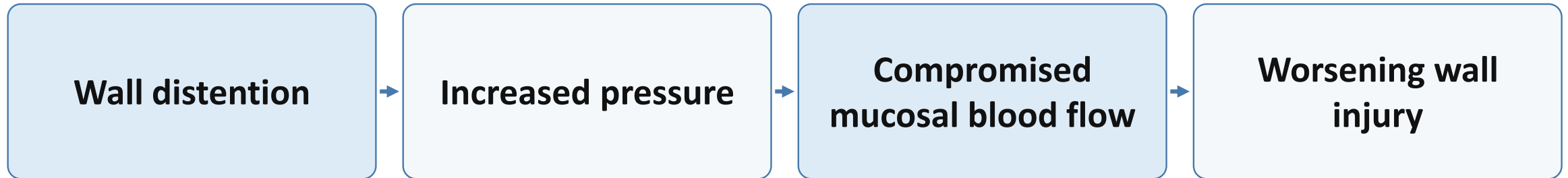
- Distended gallbladder tissue releases inflammatory prostaglandins.
- Their activity contributes to mucosal and mural inflammation.
- The response is not explained solely by bacterial contamination.

Distention increases intraluminal pressure



Progressive pressure increases the threat to gallbladder-wall perfusion.

Pressure-related vascular compromise injures mucosa



The mechanical and chemical pathways are concurrent rather than mutually exclusive.

Calculous pathogenesis is multifactorial

Chemical

- Lysolecithins are injurious.
- Bile salts act directly after mucus loss.

Inflammatory

- Prostaglandins enhance mucosal and mural reactions.
- Irritation initially need not involve bacteria.

Vascular

- Distention elevates pressure.
- Mucosal blood flow becomes compromised.

Initial injury may be sterile

Early phase

- Obstruction causes chemical irritation and ischemic stress.
- A bacterial cause is not required at onset.

Subsequent course

- Bacterial infection may be superimposed.
- Superinfection can intensify the inflammatory process.

Superinfection changes the inflammatory burden

1 Initial chemically mediated inflammation develops.



2 Infection may become superimposed later.

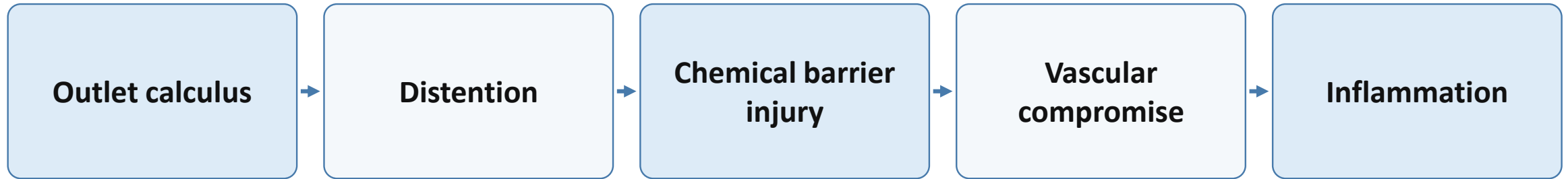


3 Suppurative exudate may accumulate in the lumen.



4 Sepsis becomes a possible complication.

Calculous disease: The complete causal chain

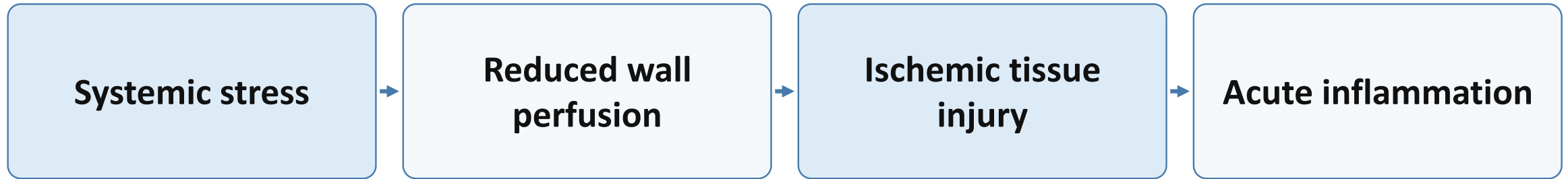


Secondary bacteria may aggravate this chain, but are not mandatory to initiate it.

Acalculous cholecystitis occurs without stones

- Approximately 10% of acute attacks occur without gallstones.
- Disease arises most often in patients severely ill for another reason.
- The dominant proposed mechanism is ischemic gallbladder injury.

Acalculous cholecystitis is fundamentally ischemic



This summarizes the proposed predominant mechanism, not a universal exclusive pathway.

The cystic artery has limited collateral protection

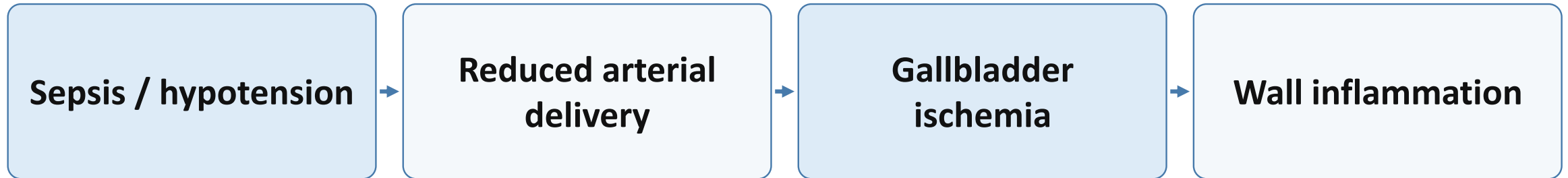
Anatomic property

- The cystic artery functions as an end artery.
- The source describes no collateral circulation.

Clinical implication

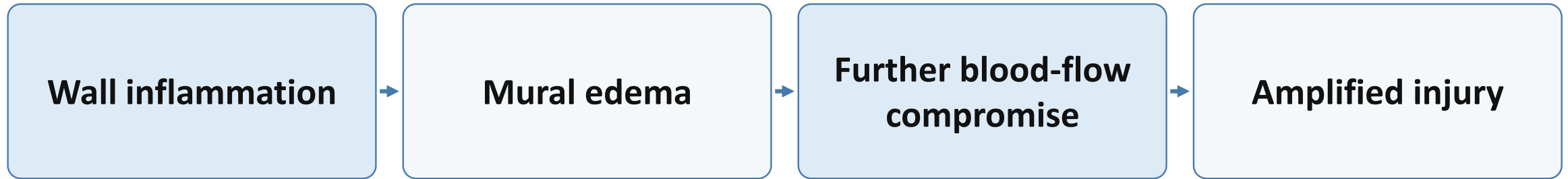
- Reduced perfusion can rapidly compromise the wall.
- Systemic hypotension therefore increases vulnerability.

Sepsis and hypotension undermine wall perfusion



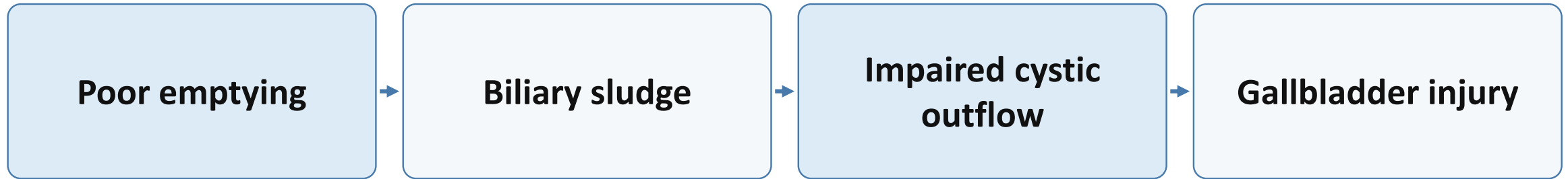
Sepsis with hypotension and multiorgan dysfunction is a source-listed risk context.

Mural edema can worsen ischemic compromise



The sequence is a simplified causal loop: Edema and inflammation can aggravate vascular compromise.

Stasis provides a second acalculous mechanism



Sludge can obstruct the cystic duct even in the absence of a macroscopic stone.

Acalculous obstruction may involve three materials

Microcrystals

- Cholesterol crystals accumulate as sludge.
- The material is not a typical macroscopic gallstone.

Viscous bile

- Concentrated, thick bile contributes to stasis.
- Impaired drainage sustains retention.

Mucus

- Mucus joins the stagnant luminal contents.
- Outflow compromise may occur without stones.

Acalculous injury is a reinforcing process

1

Critical illness promotes ischemia or biliary stasis.



2

Stasis and sludge impede emptying.



3

Inflammation and edema further impair perfusion.



4

The acutely inflamed wall may become necrotic.

Sepsis with organ failure is a major risk setting

- Sepsis and hypotension are recognized risk factors.
- Multisystem organ failure may coexist.
- Gallbladder symptoms may be masked by the primary illness.

Trauma and extensive burns increase vulnerability

- Major trauma and burns are established risk contexts.
- Systemic physiologic stress can coexist with vascular compromise.
- An acalculous attack may be overlooked during intensive care.

Immunosuppression and diabetes matter

Immunosuppression

- Listed as a risk factor for acute acalculous inflammation.
- Overlapping illness may obscure manifestations.

Diabetes mellitus

- A risk factor for acalculous episodes.
- Also highlighted in symptomatic calculous disease.

Rare primary infections can be acalculous

- Some episodes are caused by primary bacterial infection.
- The source names Salmonella Typhi and staphylococci as examples.
- These are unusual mechanisms, not the general explanation for acalculous attacks.

More indolent acalculous disease has other contexts

Vascular causes

- Systemic vasculitis.
- Severe atherosclerotic ischemic disease in older patients.

Infectious / biliary contexts

- AIDS-associated disease, often linked in the source to Cryptosporidium.
- Ascending biliary tract infection.

Calculous versus acalculous: Different triggers

Calculous

- Obstructing stone in neck or cystic duct.
- Toxic bile exposure and pressure-induced vascular compromise.
- Acute pain often clinically conspicuous.

Acalculous

- Absence of a gallstone.
- Ischemia and biliary stasis are prominent.
- Often develops amid severe illness.

Acute cholecystitis enlarges and distends the organ

- The gallbladder is usually enlarged and tense.
- The serosal surface may appear unusually congested or discolored.
- Macroscopic appearance depends on the severity of injury.

Serosal discoloration reflects hemorrhagic injury

Reported colors

- Bright red or blotchy violaceous regions.
- Severe injury may yield a green-black appearance.

Structural explanation

- Subserosal hemorrhages contribute to discoloration.
- Progression to green-black necrosis marks gangrenous disease.

The serosa may develop fibrinous exudate

Mural inflammation



Serosal reaction



Fibrinous coating



**Fibrinopurulence if
severe**

Exudate is a pathologic surface finding, distinct from luminal pus.

Inflamed gallbladder contents become turbid

- Bile may appear cloudy or turbid rather than clear.
- Fibrin, pus and hemorrhage can mix with luminal bile.
- Additional stones are common in calculous cases.

A calculus may remain impacted at the outlet

Location

- Gallbladder neck.
- Cystic duct.

Meaning

- Persistent obstruction explains luminal distention.
- The finding distinguishes the calculous form from acalculous morphology.

Empyema means a lumen dominated by pus

Gallbladder empyema = virtually pure pus within the lumen

- A suppurative complication of acute inflammation.
- Not synonymous with uncomplicated biliary stasis.

Mild acute disease shows edema and hyperemia

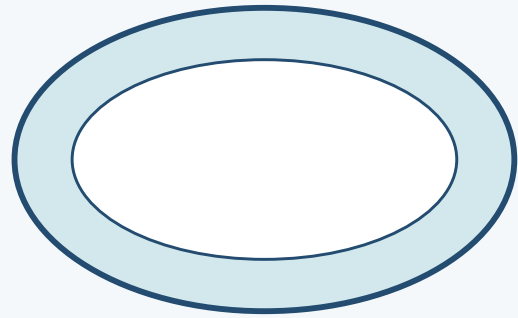
Gross findings

- Thickening of the gallbladder wall.
- Edematous, hyperemic appearance.

Microscopic correlates

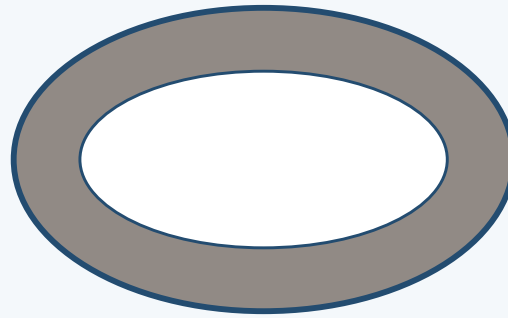
- Interstitial edema and vascular congestion.
- Early erosion of the mucosal lining.

Gangrenous cholecystitis is necrotizing injury



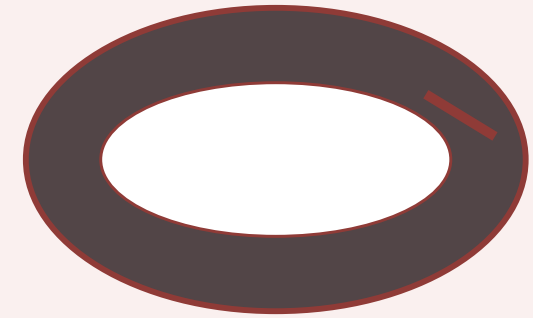
Mild

Edematous, hyperemic wall



Severe

Green-black wall necrosis

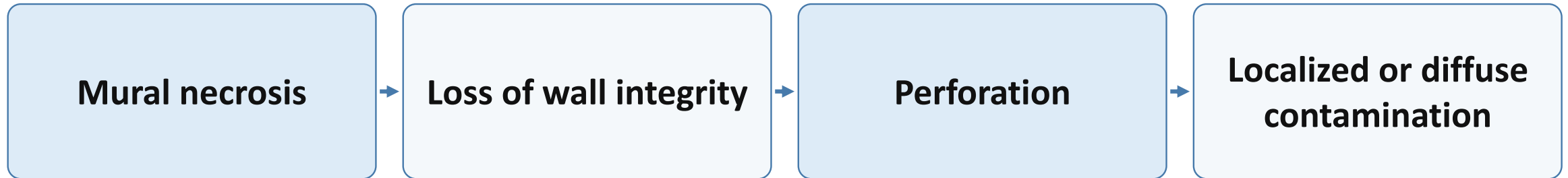


Complicated

Potential perforation

Schematic progression: Actual pathology varies by severity and case.

Perforation follows destructive wall injury



Complications include local abscess or diffuse peritonitis.

Gas-forming infection may cause emphysematous disease

Etiologic organisms cited

- Clostridia.
- Coliform bacteria.

Pathologic consequence

- Organisms can generate gas in the inflamed gallbladder.
- This is a severe infectious variant, not typical early sterile injury.

Early histology shows vascular and epithelial injury

1 Vascular congestion in the gallbladder wall.



2 Interstitial mural edema.



3 Erosion of the mucosal surface.



4 Variable superimposed suppurative inflammation.

Early neutrophils may be less prominent than expected

- Typically sparse neutrophils in early acute disease.
- A striking neutrophilic infiltrate may appear with superimposed infection.
- Early morphological interpretation requires the vascular and epithelial context.

Stone presence is the main morphological discriminator

Shared acute findings

- Edema, congestion and erosion.
- Serosal exudation and possible necrosis.
- Turbid luminal contents if advanced.

Specific distinction

- An obstructing gallstone is identified in calculous disease.
- Acalculous attacks lack such a stone; Otherwise the lesions overlap.

Pain usually persists beyond six hours

- Pain becomes progressive in the right upper quadrant or epigastrium.
- Persistence beyond 6 hours is characteristic in the source.
- Prior gallbladder-related painful episodes are common but not obligatory.

Fever and gastrointestinal symptoms often accompany pain

Constitutional

- Mild fever.
- Sweating and tachycardia.

Appetite

- Anorexia may occur.
- An attack can begin suddenly.

Gastrointestinal

- Nausea.
- Vomiting.

Jaundice suggests additional ductal obstruction

Typical acute cholecystitis

- Most affected patients are not jaundiced.
- Inflammation often remains centered on the gallbladder.

Concerning additional finding

- Hyperbilirubinemia raises suspicion of common bile duct obstruction.
- Assess the biliary tree beyond the cystic duct.

Laboratory changes provide supportive clues

- Mild to moderate leukocytosis may accompany acute disease.
- Serum alkaline phosphatase can be modestly elevated.
- Neither finding alone identifies the triggering mechanism.

Clinical severity ranges from mild to urgent

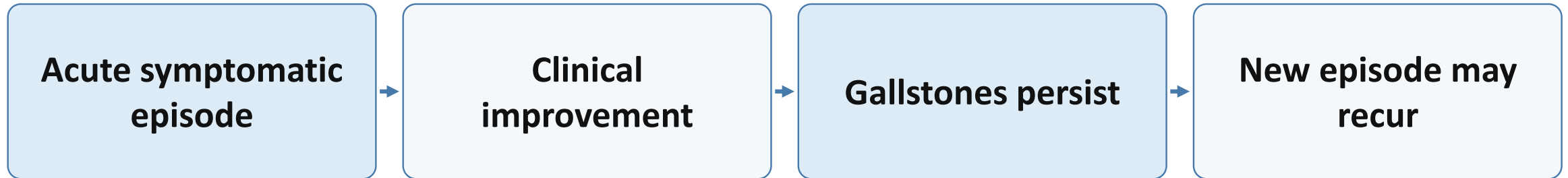
Relatively mild course

- Some attacks resolve without intervention.
- Symptoms may decrease over the following days.

Progressive disease

- A substantial minority worsen instead of resolving.
- Severe progression can demand immediate surgical attention.

Symptom resolution does not eliminate recurrence

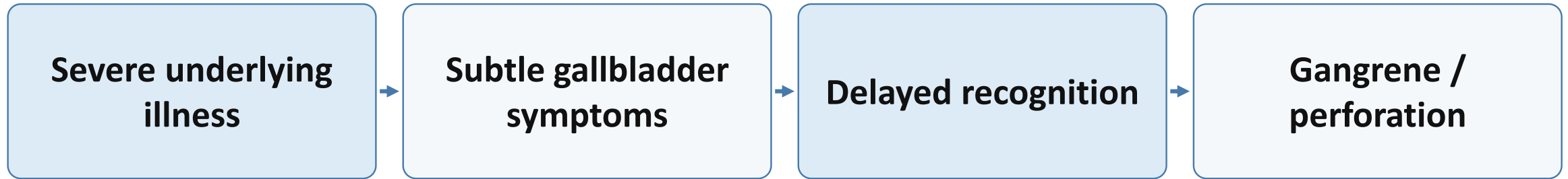


Recurrence is common when patients recover without surgery.

Acalculous presentations can be clinically silent

- Symptoms may evolve insidiously rather than abruptly.
- Critical illness may obscure gallbladder-related complaints.
- A higher proportion have no localizing gallbladder symptoms.

Delayed recognition threatens the acalculous patient



The source stresses the much higher complication rate in acalculous disease.

Bacterial superinfection can spread beyond gallbladder

Acute cholecystitis



Bacterial superinfection



Cholangitis or sepsis

Systemic deterioration may accompany spread or superinfection.

Perforation has localized and diffuse outcomes

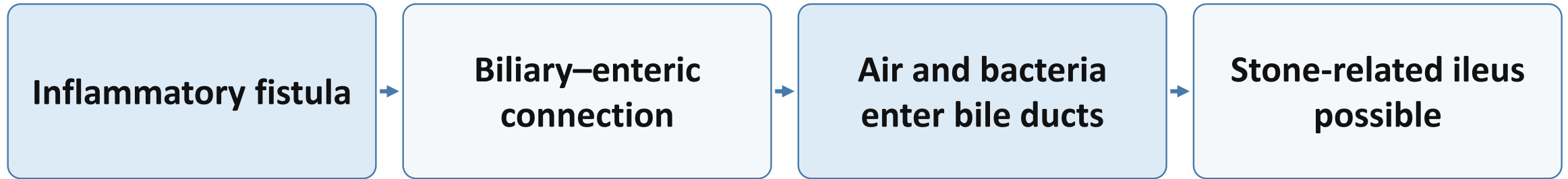
Contained injury

- Gallbladder perforation.
- Local abscess formation.

Uncontained rupture

- Spillage into the peritoneal cavity.
- Diffuse peritonitis.

Biliary-enteric fistula links gallbladder to bowel



A gallstone may pass into bowel through a fistula and obstruct intestine.

Acute gallbladder disease can destabilize other organs

Cardiopulmonary

- Preexisting cardiac illness may worsen.
- Pulmonary decompensation is possible.

Renal

- Acute illness may worsen renal function.
- Multiorgan dysfunction increases risk.

Hepatic

- Liver disease may decompensate.
- Sepsis and biliary obstruction add burden.

Chronic cholecystitis supplies important context

- Chronic disease can follow recurrent acute attacks.
- It also develops without a documented history of acute attacks.
- It is associated with cholelithiasis in more than 90% of cases.

Chronic disease is not simply persistent acute edema

Acute-dominant pattern

- Edema, congestion, mucosal erosions.
- Fibrinous or fibrinopurulent exudate.

Chronic-dominant pattern

- Fibrosis and mononuclear inflammation.
- Wall thickening, adhesions and epithelial outpouchings.

Acute and chronic cholecystitis: Contrast

Feature	Acute	Chronic
Pain	Progressive; >6 h typical	Recurrent steady RUQ/epigastric
Pathology	Edema / acute injury $\pm$ necrosis	Variable fibrosis and mononuclear cells
Outlet stone	Commonly obstructs neck/duct	Outflow obstruction not prerequisite
Systemic illness	Fever and leukocytosis possible	Less striking manifestations

Case 1: Progressive pain with an impacted stone

ILLUSTRATIVE CLINICAL VIGNETTE

- An adult has sustained right upper quadrant pain for over 6 hours.
- Nausea and low-grade fever accompany the attack.
- A stone is found lodged at the gallbladder neck.

What initiates inflammation, and is early bacterial infection required?

Case 1: The first injury is chemical and vascular

Trigger

- Cystic outlet stone prevents emptying.
- Gallbladder distention impairs mucosal perfusion.

Mechanism

- Lysolecithins and bile salts cause chemical injury.
- Bacterial superinfection may occur subsequently.

Case 2: An ICU patient without localizing pain

ILLUSTRATIVE CLINICAL VIGNETTE

- A critically ill patient has sepsis, hypotension and organ failure.
- No gallstone is identified.
- Clinical findings referable to the gallbladder are minimal.

Which form is likely, and what complication must be anticipated?

Case 2: Suspect ischemic acalculous injury

Reasoning

- Acalculous attacks occur with severe systemic illness.
- End-arterial circulation makes the wall ischemia-prone.

Urgency

- The onset may be insidious and occult.
- Gangrene and perforation are particularly concerning.

Case 3: A dark gallbladder wall and pus

ILLUSTRATIVE CLINICAL VIGNETTE

- An enlarged gallbladder appears green-black at surgery.
- The lumen contains abundant purulent material.
- The wall contains focal areas of perforation.

Identify the three pathological complications represented.

Case 3: Identify the complications precisely

Gangrene

- Green-black wall necrosis.
- Severe tissue destruction.

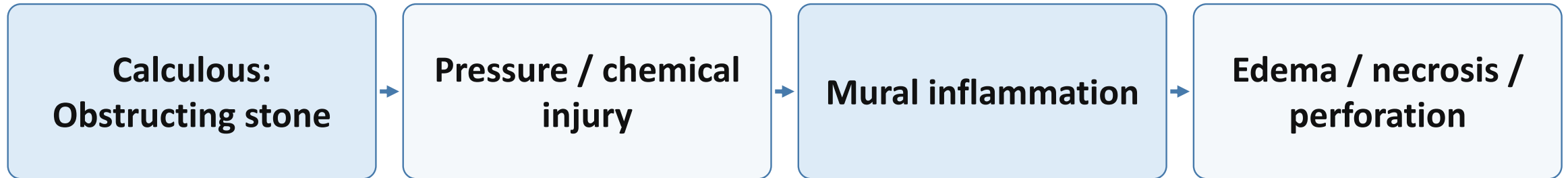
Empyema

- Virtually pure pus in the lumen.
- Suppurative complication.

Perforation

- Loss of wall integrity.
- May form abscess or peritonitis.

The two etiologic pathways converge on wall injury



Acalculous disease reaches overlapping damage through ischemia and stasis rather than a large obstructing stone.

Four diagnostic concepts to retain

- Calculous attacks start with cystic outflow obstruction in most cases.
- Acalculous disease preferentially affects severely ill patients and is ischemia-prone.
- Gross and microscopic inflammation overlap; Stones distinguish the two etiologies.
- Gangrene, empyema, perforation and systemic infection signal dangerous progression.

Primary teaching reference

Robbins, Cotran & Kumar: Pathologic Basis of Disease

- 11th edition (2026).
- Gallbladder — cholecystitis and related complications.