

Stress-Related Mucosal Disease

Etiology • Mechanisms • Morphology • Clinicopathologic correlation

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Learning objectives

After this lecture, distinguish:

- Clinical settings and pathogenesis of stress-related gastric mucosal injury
- Stress, Curling, and Cushing ulcer patterns
- Acute stress-ulcer morphology versus chronic peptic ulcer morphology
- Clinical consequences and alternative causes of gastric bleeding

Definition: Severe physiologic stress causes mucosal injury

Acute injury of the gastric mucosa associated with critical physiologic illness or trauma.

Injury spans shallow erosions to ulceration.

The major mechanistic theme is impaired local perfusion.

Physiologic stress is not everyday “stress”

Severe physiologic stress

Shock, sepsis, severe trauma

Extensive burns or intracranial disease

Major surgery or serious illness

Broader peptic-ulcer context

Psychological stress is listed as a PUD risk factor

Distinct from ICU stress-related mucosal disease

Avoid collapsing these entities into one

Settings linked to stress-related mucosal disease

Circulatory insults

Shock and sepsis can compromise gastric mucosal blood flow.

Tissue injury

Severe trauma and extensive burns create physiologic stress.

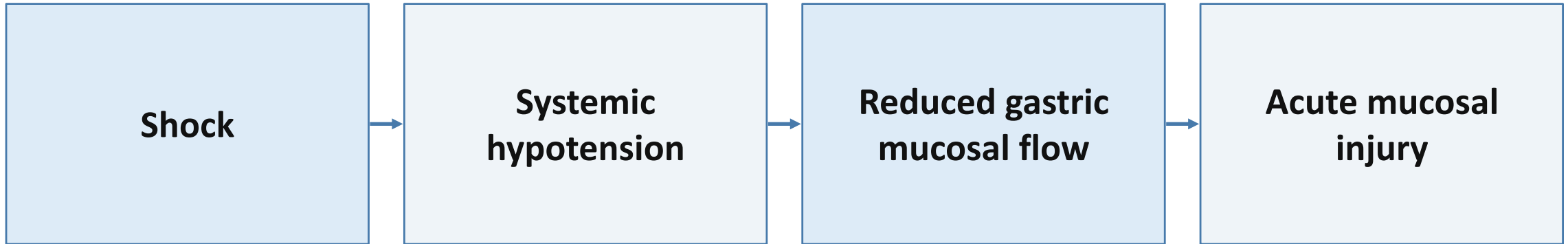
Neurologic illness

Intracranial disease has a distinctive acid-related mechanism.

Serious illness

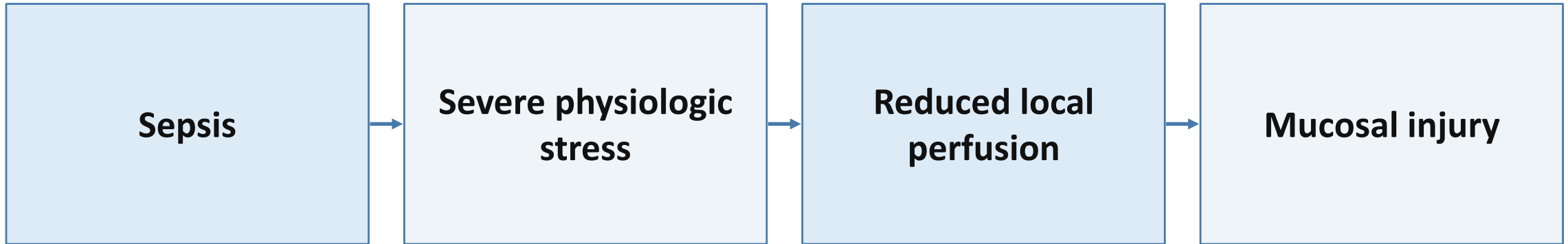
Major surgery and other severe medical diseases are associated.

Shock: A perfusion-centered pathway



Local ischemia is the central link between hemodynamic compromise and tissue damage.

Sepsis: When mucosal blood flow is compromised



Sepsis among the common settings for stress ulcers.

Severe trauma is a major setting

Key interpretive points:

- Severe trauma is associated with stress ulcers.
- Perfusion failure may accompany severe physiologic stress.
- Assess the injury in relation to the systemic clinical condition.

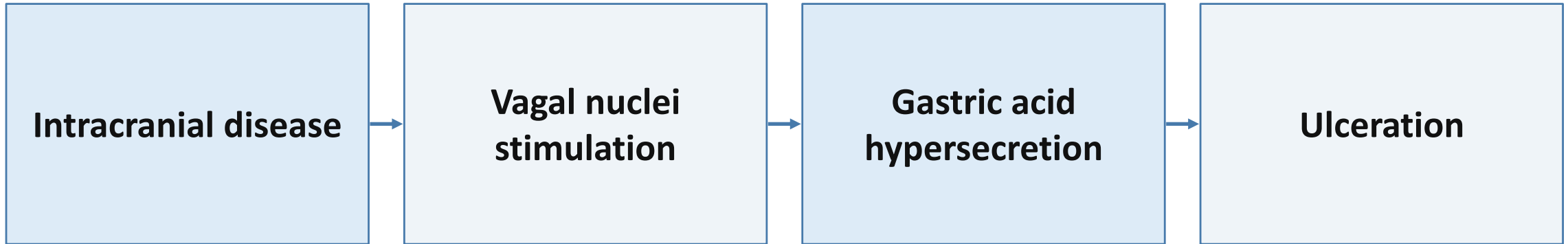
Severe burns: The Curling-ulcer association

Severe burns or trauma can be accompanied by ulcers in the stomach and proximal duodenum.

These lesions are termed Curling ulcers.

The eponym carries both an anatomic and clinical association.

Intracranial disease: A distinct pathway



Cushing ulcers are associated with intracranial disease; They also have greater perforation risk.

Major surgery and serious medical disease

Clinical context:

- Stress-related mucosal disease can follow major surgical procedures.
- Serious medical disease is an additional recognized setting.
- The common denominator is physiologic severity rather than a single diagnosis.

Different stressors, overlapping pathways

Shock / sepsis

Perfusion-related gastric injury is central.

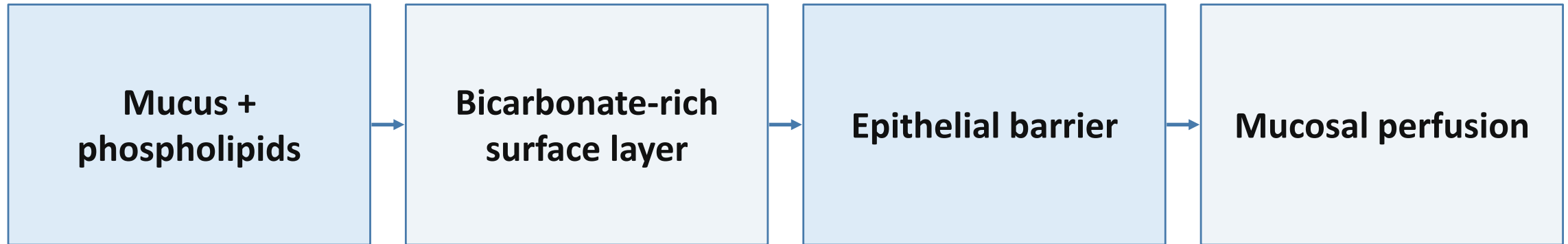
Burns / trauma

Severe injury accompanies stress-ulcer formation.

Intracranial disease

Vagal stimulation and increased acid have a distinct role.

Gastric defense is a layered system



These defenses collectively protect tissue despite highly acidic gastric contents.

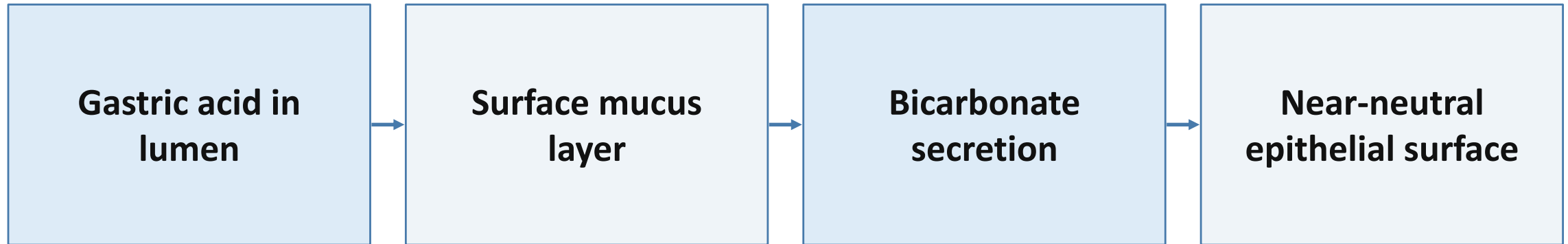
Mucus limits direct epithelial exposure

Foveolar-cell secretions form a mucus–phospholipid layer over the gastric mucosa.

Prevents food particles from contacting the epithelium directly.

Helps maintain a protected surface fluid compartment.

Bicarbonate creates a protective microenvironment



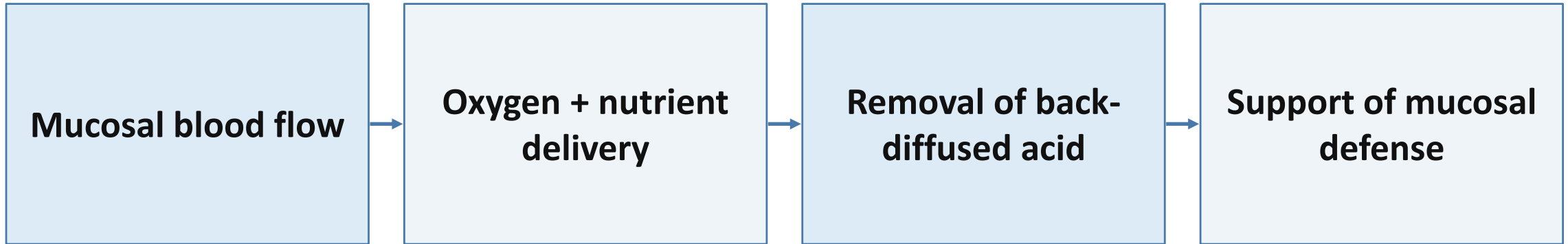
The protective pH gradient matters when acid approaches underlying tissue.

Surface epithelium: A physical barrier

The gastric epithelial sheet:

- Limits back diffusion of gastric acid.
- Prevents excessive movement of luminal material into the lamina propria.
- Protects the mucosa from luminal digestive enzymes.

Mucosal vasculature maintains tissue integrity



Perfusion protects the mucosa chemically and metabolically.

Epithelial renewal contributes to protection

Dynamic tissue maintenance:

- Surface foveolar cells are replaced over approximately 3–7 days.
- The barrier depends on ongoing epithelial replacement.
- Acute tissue injury and subsequent re-epithelialization are related processes.

Mucosal injury reflects a balance

Protective factors

Mucus, phospholipids, bicarbonate

Intact epithelial barrier

Adequate blood supply and renewal

Damaging influences

Luminal acid and enzymes

Ischemia or reduced oxygen delivery

Failure of local protective mechanisms

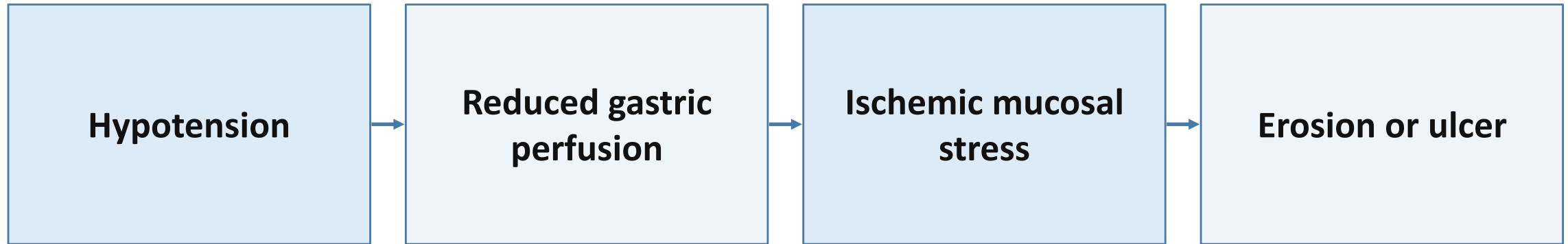
Local ischemia is the dominant mechanism

Stress-related gastric mucosal injury is most often related to local ischemia.

Systemic hypotension can limit gastric oxygen delivery.

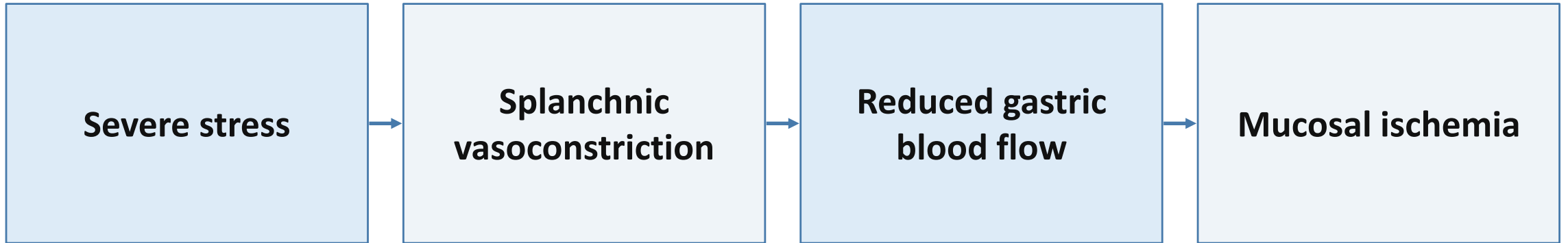
Stress-induced splanchnic vasoconstriction reduces local flow.

Systemic hypotension is one route to ischemia



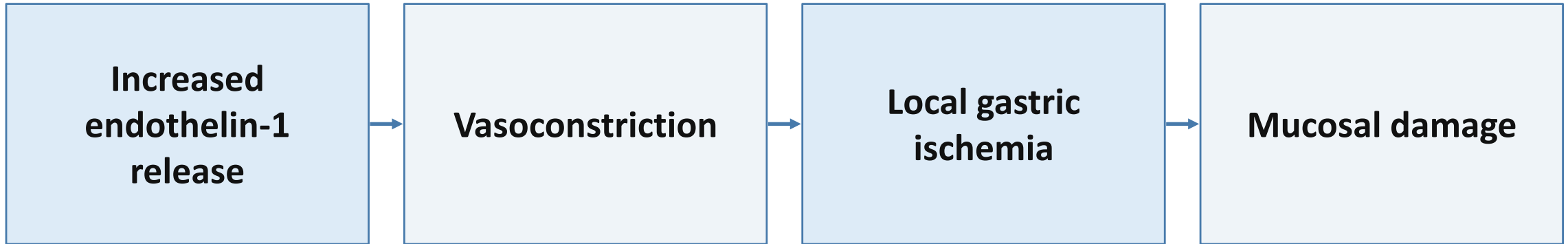
The stomach is vulnerable when its normally rich mucosal blood supply falls.

Splanchnic vasoconstriction is another route



Splanchnic vascular narrowing can compromise perfusion even when acid is not the primary initiating event.

Endothelin-1 may intensify perfusion injury



Upregulation and release of endothelin-1 as a contributor.

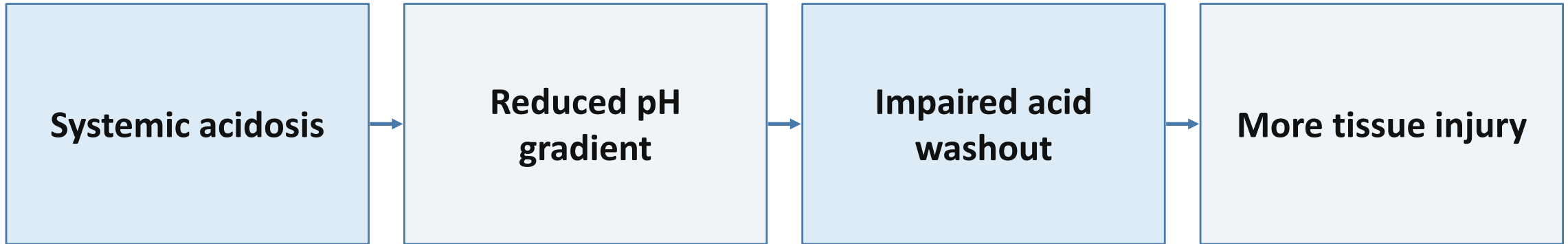
Ischemia undermines multiple defenses

The microcirculation is not merely a nutrient supply.

It delivers oxygen and supports epithelial metabolism.

It washes out gastric acid that has diffused into the lamina propria.

Systemic acidosis can amplify injury



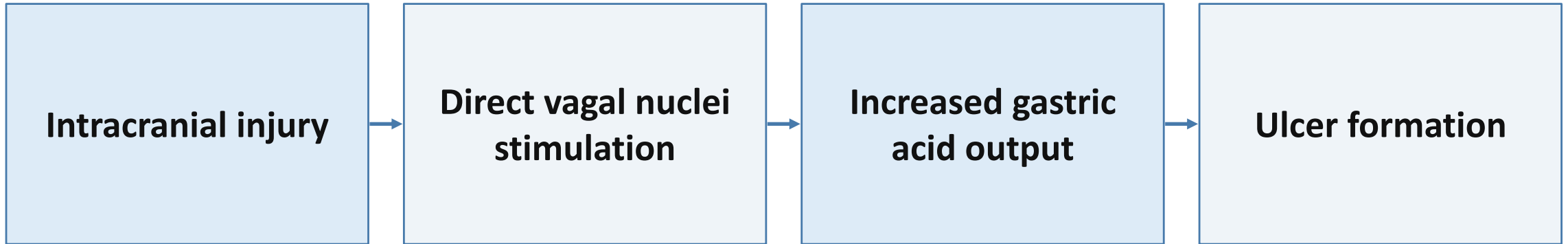
This as an additional contributing mechanism.

What is the pH-gradient hypothesis?

An acid washout mechanism:

- A pH gradient favors clearance of acid that back-diffuses into lamina propria.
- Systemic acidosis reduces this gradient.
- Consequently, local mucosal injury may be aggravated.

Intracranial injury changes the acid balance



This neurogenic pathway is described as the proposed basis of Cushing ulcers.

Two mechanistic emphases

Most stress-related injury

Local ischemia

Systemic hypotension or vasoconstriction

Endothelin-1 and acidosis may contribute

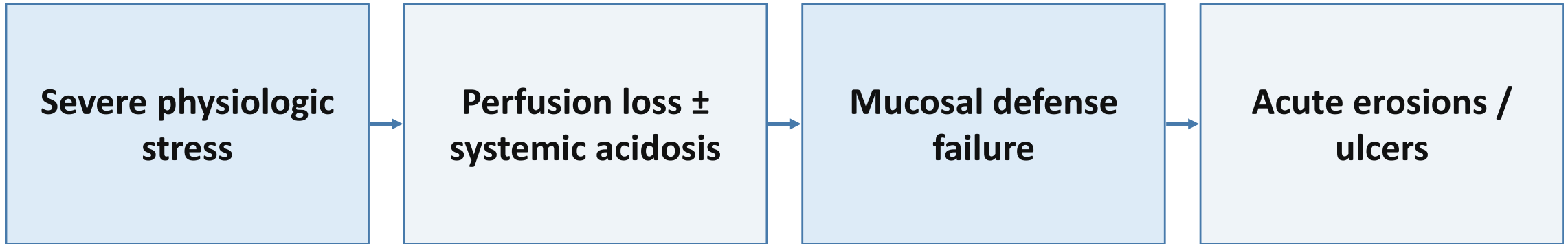
Cushing-associated injury

Intracranial disease

Vagal nuclei stimulation

Gastric acid hypersecretion

Integrated model: Stress ulcers have multiple inputs



Intracranial injury adds a distinctive acid-hypersecretion pathway.

Three clinically named ulcer patterns

Stress ulcers

Common with shock, sepsis, or severe trauma.

Curling ulcers

Stomach and proximal duodenum; Severe burns or trauma.

Cushing ulcers

Gastric, duodenal, or esophageal; Intracranial disease.

Stress ulcers: The general critical-illness pattern

Shock, sepsis, and severe trauma are common clinical settings.

Acute mucosal injury may be multifocal.

Profound systemic illness is the essential clinical clue.

Curling ulcers: Location plus severe injury

The eponym refers to ulcers in the proximal duodenum and stomach.

Observed in severe burns or trauma.

Anatomic location alone does not establish the clinical association.

Cushing ulcers: Intracranial pathology

Cushing ulcers may involve stomach, duodenum, and esophagus.

Occur in the setting of intracranial disease.

Compared with other stress ulcers, perforation risk is greater.

Names, contexts, and anatomic sites

Term	Clinical context	Typical sites
Stress ulcer	Shock; Sepsis; Severe trauma	Often gastric
Curling ulcer	Severe burns or trauma	Stomach; Proximal duodenum
Cushing ulcer	Intracranial disease	Stomach; Duodenum; Esophagus

Injury spans erosions and mucosal ulceration

Stress-related lesions range from shallow erosions to ulcers penetrating the mucosa.

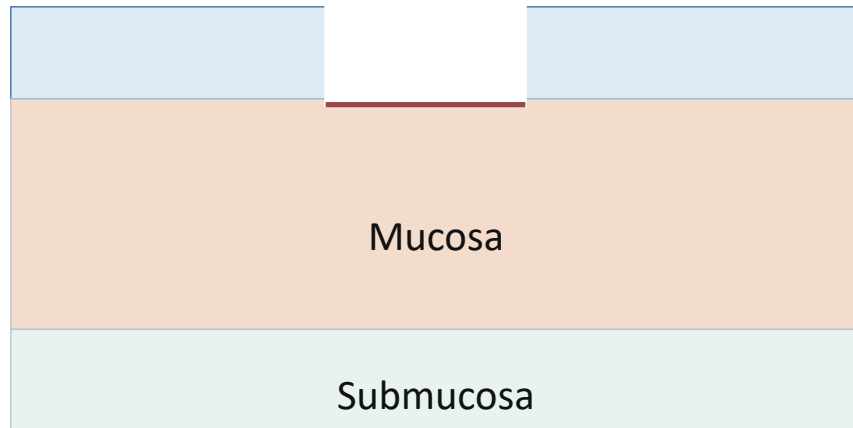
The lesions are benign description.

Extent and depth vary with injury severity.

Morphologic spectrum: Erosion to ulcer

Shallow erosion

Surface epithelium



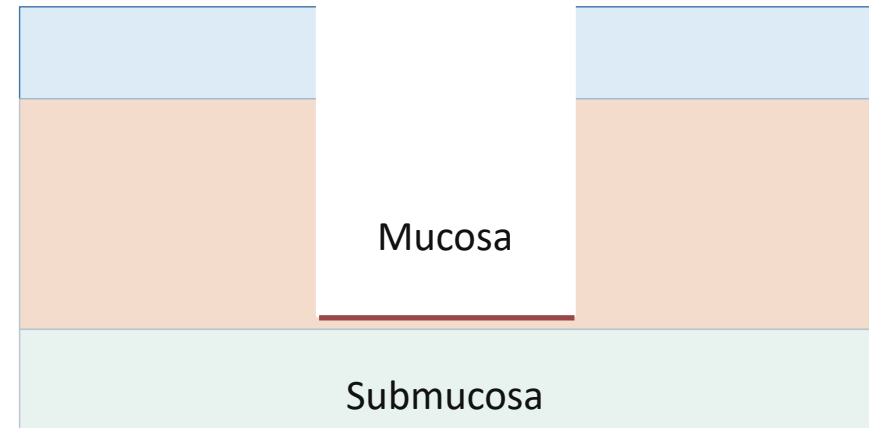
Mucosa

Submucosa

Superficial epithelial loss

Ulcer penetrating mucosa

Surface epithelium



Mucosa

Submucosa

Defect extends into the mucosa

Gross morphology: Usually small, rounded lesions

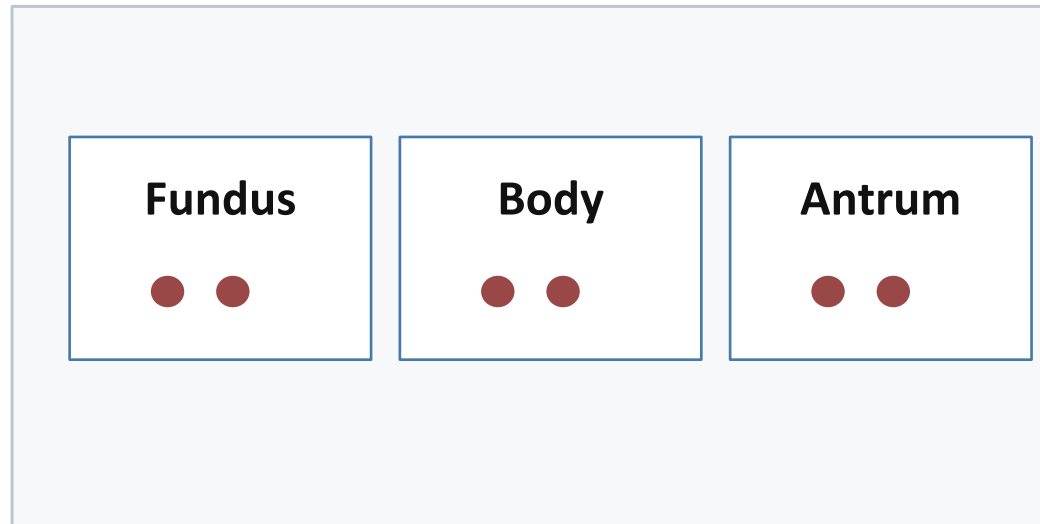
Acute stress ulcers are typically round and under 1 cm in diameter.

The gastric surface may contain multiple discrete defects.

Size and shape are descriptive—not an independent definitive diagnosis.

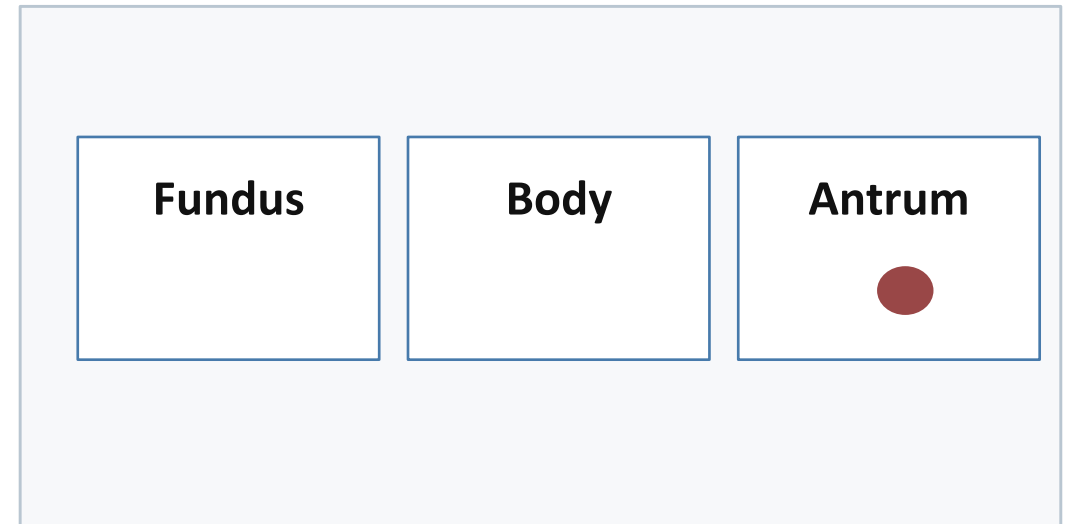
Spatial pattern is an important diagnostic clue

Acute stress ulcers



Often multiple, across the stomach

Chronic peptic ulcer disease



Commonly solitary; Gastric antral tendency

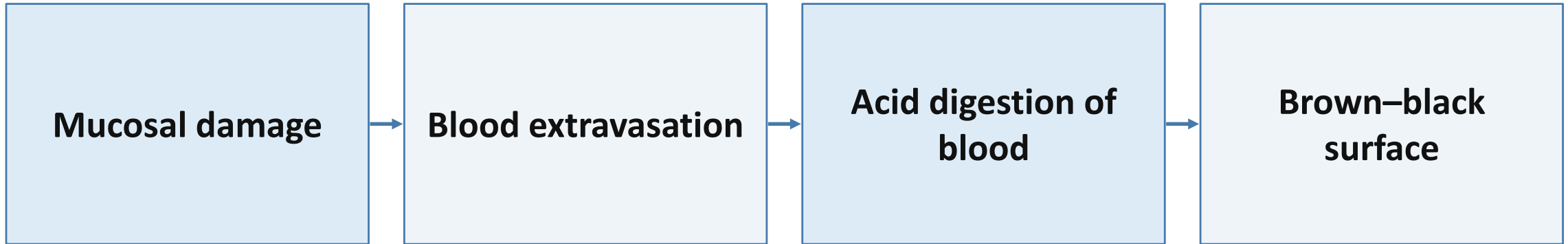
Brown–black ulcer bases reflect altered blood

Acid digestion of extravasated blood can stain an ulcer base brown to black.

This color has a mechanistic explanation.

The appearance should be interpreted in its clinical context.

From vascular compromise to dark ulcer base



The ulcer color relates to blood exposed to the acidic gastric environment.

Microscopy: Sharply defined acute defects

The stress-ulcer boundary is sharply demarcated.

Adjacent mucosa may remain relatively normal.

This spatial pattern contrasts with the chronicity of conventional peptic ulcer disease.

Adjacent mucosa can appear relatively normal

A distinction worth reporting:

- Acute stress ulcers can have an abrupt transition to surrounding mucosa.
- Morphology must be integrated with the critical-illness setting.
- Chronically scarred background tissue is not the characteristic pattern.

Stress ulcer versus chronic peptic ulcer: Healing signature

Acute stress ulcer

Sharp demarcation

Relative preservation of adjacent mucosa

Chronic scarring and thickened vessels
absent

Chronic peptic ulcer

Usually solitary and chronic

Granulation tissue and fibrous scar

Often thickened larger vessels

Serositis may accompany an acute stress ulcer

Serosal inflammation is possible in stress-related ulceration.

It is not present in every lesion.

The condition can be more than a surface-only abnormality.

Absence of fibrosis helps indicate acute injury

Conspicuous scarring is not typical of acute stress ulcers.

Scarring is a hallmark of chronic peptic ulcers.

Histologic chronicity should not be inferred solely from ulcer depth.

Absence of thickened vessels is another clue

Chronic peptic-ulcer-type vascular wall thickening is conspicuously absent.

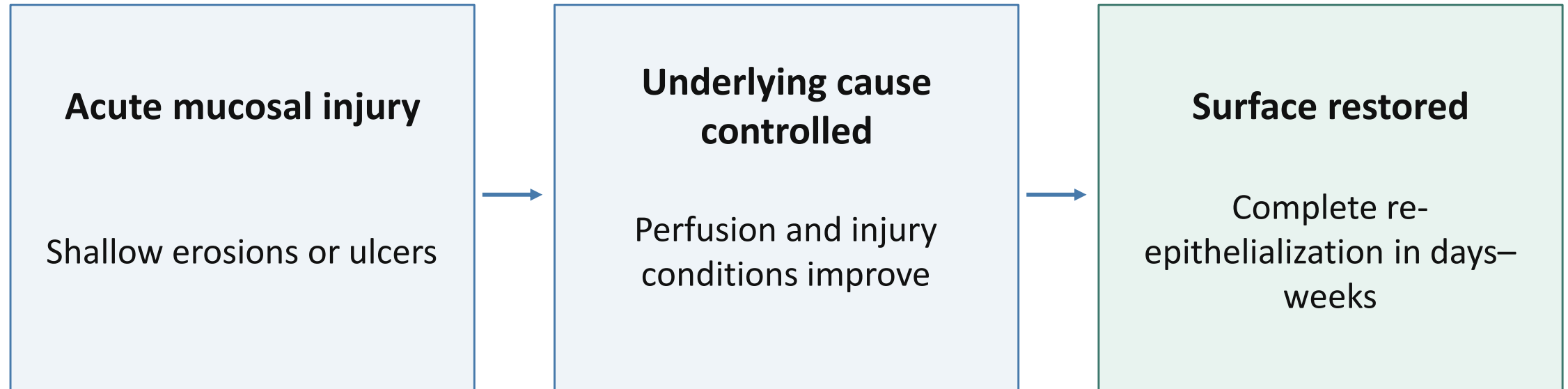
Chronic peptic ulcers can contain thickened larger vessels within scar.

The distinction reflects the duration and tissue response.

Morphologic distinctions: Acute stress vs chronic peptic

Feature	Acute stress ulcer	Chronic peptic ulcer
Number	Often multiple	Usually solitary
Distribution	Across the stomach	Often antrum / proximal duodenum
Edge	Sharp demarcation	Punched-out defect
Background	Relatively normal adjacent mucosa	Frequently chronic gastritis
Chronic scar	Absent	Characteristic
Thickened vessels	Absent	Can occur in ulcer base

Healing can restore the surface epithelium



Recovery follows treatment of the stressor; Prophylaxis alone does not eliminate the cause.

Microscopic mucosal damage is common in critical illness

Most intensive-care patients have histologic evidence of gastric mucosal damage.

Histologic injury does not equate to major hemorrhage.

The severe bleeding subgroup is much smaller.

Clinically important bleeding is substantially less common

That 1%–4% of intensive-care patients require transfusion.

This is a textbook figure for clinically consequential bleeding.

It should not be mistaken for the prevalence of any microscopic injury.

Frequency and severity are different measures

Histologic involvement

Common in critical illness

Can be detected without overt bleeding

Represents mucosal injury

Clinically important bleeding

Much less frequent

Transfusion required in 1%–4%

Represents a clinical consequence

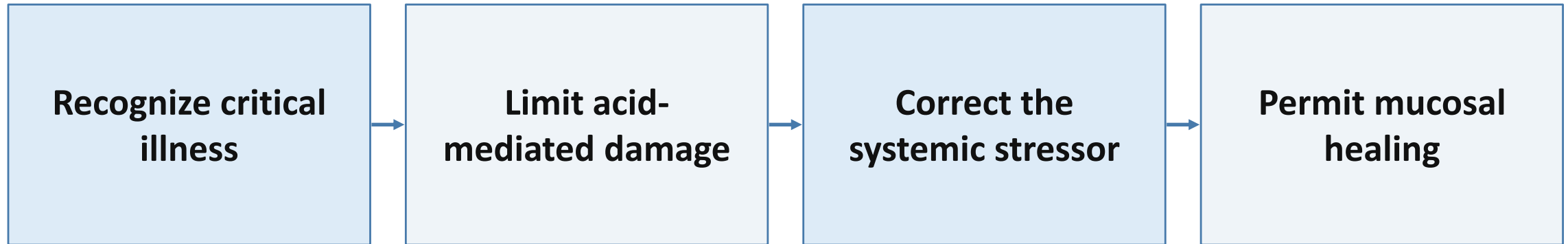
Perforation is an uncommon complication

Perforation and other complications are rarer than bleeding.

Cushing ulcers carry relatively greater perforation risk.

Relative risk does not mean that perforation is common.

Clinical strategy addresses mechanism and context



Correction of the underlying condition as most effective.

Acid suppression is used prophylactically

Proton pump inhibitors are frequently used to blunt stress ulceration.

This is a statement of textbook practice, not a patient-specific prescribing guideline.

Risk and necessity are determined clinically.

Treating the underlying condition is central

Correction of the precipitating severe illness is the most effective approach.

An ischemic mechanism cannot be corrected by acid suppression alone.

As physiologic injury resolves, complete re-epithelialization may follow.

Not every acute gastric bleed is a stress ulcer

Dieulafoy lesion

Abnormal submucosal arteriole erodes through surface epithelium.

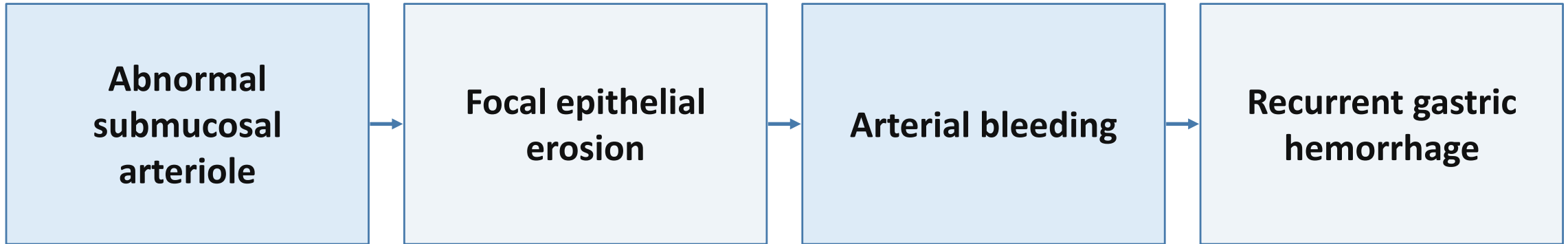
GAVE

Ectatic antral vessels produce patterned mucosal erythema.

Coagulopathy

Systemic bleeding disorders can mimic stress lesions.

Dieulafoy lesion: A focal arterial cause



Typically near the lesser curvature by the gastroesophageal junction.

Dieulafoy bleeding can be disproportionately large

Important features:

- Usually located near the gastroesophageal junction on the lesser curvature.
- Bleeding may be recurrent and copious despite a small mucosal defect.
- Nonsteroidal anti-inflammatory drugs may increase bleeding risk.

GAVE: Longitudinal erythematous stripes

Gastric antral vascular ectasia produces alternating red and pale mucosal stripes.

Endoscopic pattern is called “watermelon stomach.”

Red stripes reflect ectatic mucosal vessels.

GAVE histology identifies the vascular substrate

Reactive gastropathy with dilated capillaries containing fibrin thrombi.

Vascular ectasia explains the endoscopic erythema.

The antral localization is an important anatomic clue.

GAVE has clinical associations beyond acute stress

The Robbins description notes:

- GAVE is most often idiopathic.
- It may be associated with cirrhosis or systemic sclerosis.
- Recurrent bleeding can lead to occult blood and iron deficiency anemia.

A systemic coagulopathy can mimic stress ulceration

Coagulopathy may produce gastric lesions resembling stress ulcers.

The bleeding mechanism may be systemic rather than limited to local ulcer biology.

Clinical context is necessary for interpretation.

Upper GI bleeding: Differentiating clues

Condition	Clue	Pathologic mechanism
Stress ulcers	Severe physiologic stress; Often multiple	Ischemic mucosal injury
Dieulafoy lesion	Focal lesion near lesser curvature / GEJ	Abnormal submucosal arteriole
GAVE	Striped antral erythema; Chronic blood loss	Ectatic mucosal capillaries
Coagulopathy	Systemic hemostatic disturbance	Bleeding with ulcer-like damage

Case: Shock and multiple small gastric lesions

A critically ill patient in shock has several small, sharply delimited gastric ulcers with dark bases.

Interpretation

- Which hemodynamic process best explains the injury?
- Which gross findings favor acute stress ulceration?

Case resolution: Perfusion failure with acute morphology

Shock → systemic hypotension → gastric mucosal ischemia.

Multiple discrete ulcers and dark bases support acute stress injury.

Dark coloration is consistent with acid-altered extravasated blood.

Case: Intracranial disease and ulceration

A patient with intracranial disease develops gastric and duodenal ulceration.

Interpretation

- Name the eponym and the proposed neurogenic mechanism.
- Which major complication has relatively greater risk?

Case resolution: Cushing ulcers

Intracranial injury can stimulate vagal nuclei and increase gastric acid secretion.

The corresponding ulcers are termed Cushing ulcers.

They have an increased risk of perforation.

Case: Severe burns and proximal duodenal ulcers

Following extensive burns, a patient develops ulcers in the stomach and proximal duodenum.

Interpretation

- Which eponym is supported by the setting and sites?
- Why is the injury categorized as stress-related?

Case resolution: Curling ulcers

Burn-associated lesions in the stomach and proximal duodenum are Curling ulcers.

The patient has severe physiologic stress rather than an isolated acid disorder.

Clinical association is essential for the eponym.

Case: Antral stripes and chronic blood loss

Endoscopy shows alternating erythematous and pale longitudinal stripes in the antrum; The patient has iron deficiency anemia.

Interpretation

- Which vascular lesion is most consistent with this pattern?
- What are its characteristic microscopic findings?

Case resolution: Gastric antral vascular ectasia

GAVE produces the “watermelon stomach” pattern.

Ectatic mucosal vessels with fibrin-containing thrombi are characteristic.

Recurrent bleeding can cause iron deficiency anemia.

Final synthesis: Mechanism predicts morphology

The reasoning sequence:

- Severe physiologic stress is linked predominantly to local ischemia.
- Acute multifocal erosions and ulcers differ from scarred chronic peptic ulcers.
- Bleeding can be clinically important; Perforation is less common.
- Recovery depends fundamentally on correction of the precipitating condition.

Rapid review: Recognize the pattern

Observation	Interpretation
Shock with multiple small ulcers	Acute stress-related mucosal disease
Major burns + proximal duodenal ulcer	Curling ulcer
Intracranial disease + ulcers	Cushing ulcer
Antral longitudinal red stripes	Gastric antral vascular ectasia
Focal lesser-curvature arterial bleeding	Dieulafoy lesion

Primary textbook reference

Robbins, Cotran & Kumar

Pathologic Basis of Disease

11th edition (2026)

Chapter 17 — The Gastrointestinal Tract

Stress-Related Mucosal Disease; related stomach and peptic ulcer sections