

Acute Tubular Injury / Necrosis

Pathogenesis • morphology • clinicopathologic course

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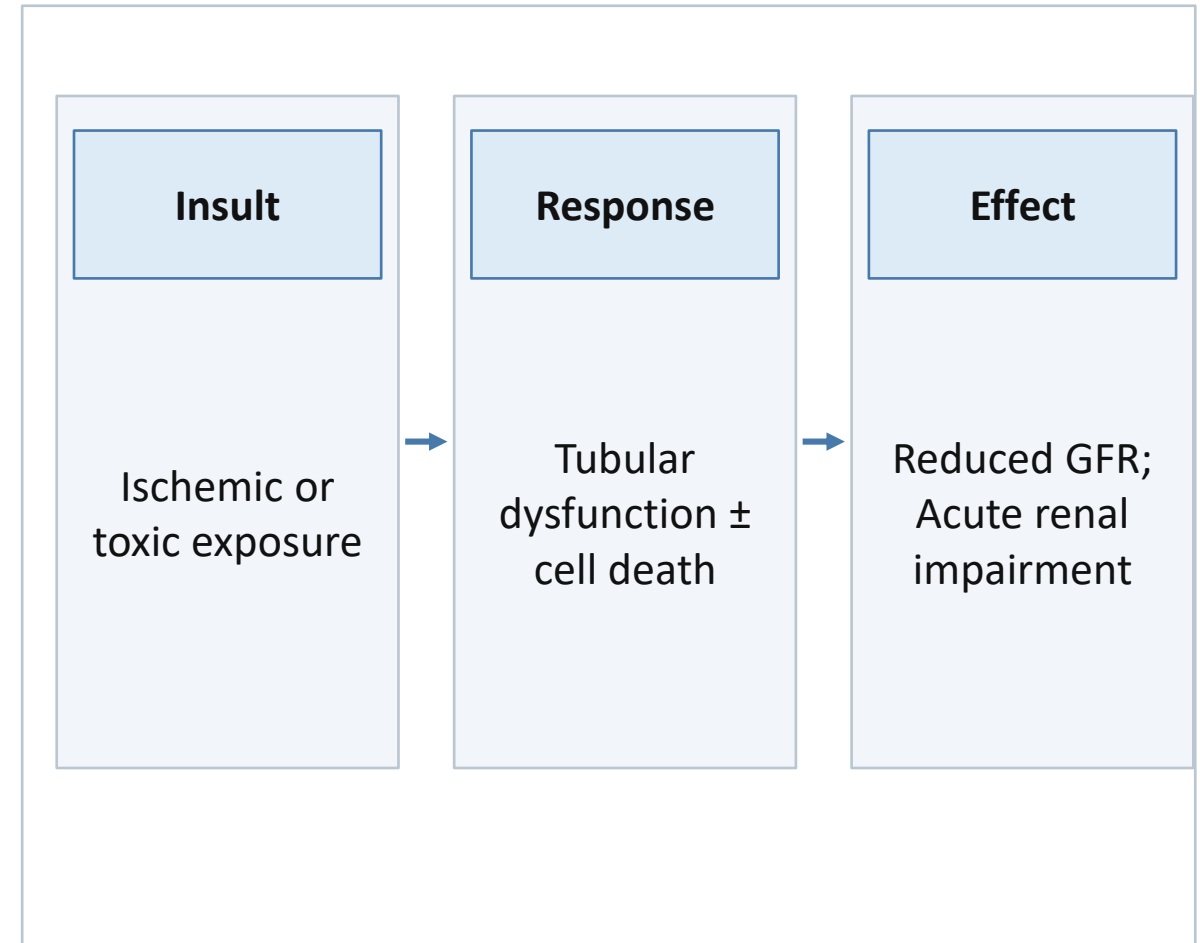
Learning objectives

- Distinguish ATI from the historical term acute tubular necrosis.
- Relate ischemic and toxic exposures to vulnerable nephron segments.
- Explain tubular, vascular and inflammatory contributors to decreased GFR.
- Recognize characteristic morphologic and clinical evolution.
- Connect epithelial regeneration with functional recovery.

ATI denotes a functional and structural injury spectrum

- Acute kidney injury occurs with tubular epithelial dysfunction.
- Necrosis is common but is not required for the diagnosis.
- Ischemia and toxins are the dominant initiating categories.

Three linked observations • schematic



Why “injury” is more precise than “necrosis”

- “Acute tubular necrosis” is the historical term.
- Reversible epithelial abnormalities may exist without overt necrosis.
- The term ATI avoids claiming morphology that may not be present.

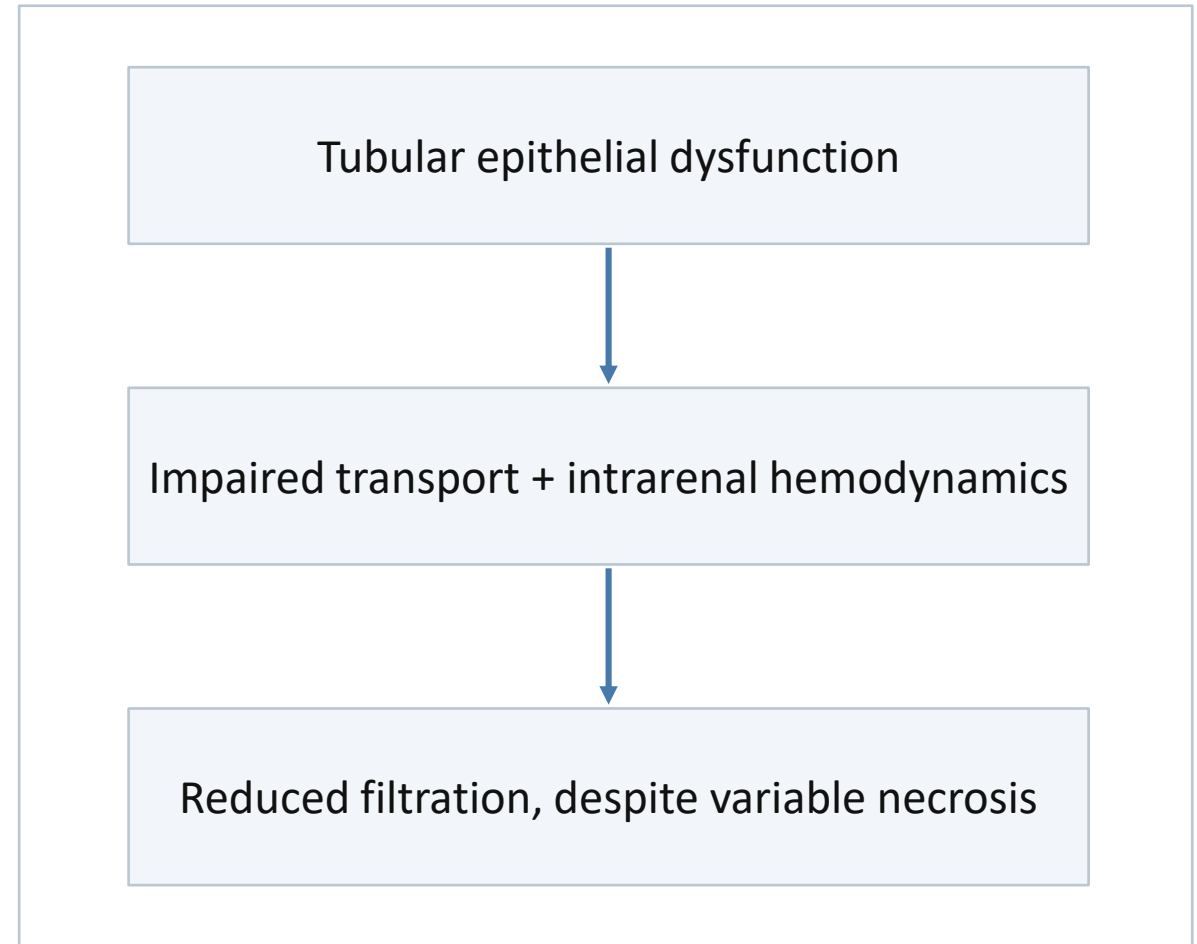
Comparison · conceptual

ATI	ATN
Preferred pathologic term	Historical designation
Includes sublethal injury	Implies epithelial necrosis
Necrosis not obligatory	Can be misleading when necrosis absent

Clinical dysfunction need not match tissue appearance

- Tubular injury can impair renal function even when necrosis is limited.
- The intensity of histologic abnormalities may not mirror clinical severity.
- Interpret tubular morphology in the clinical setting.

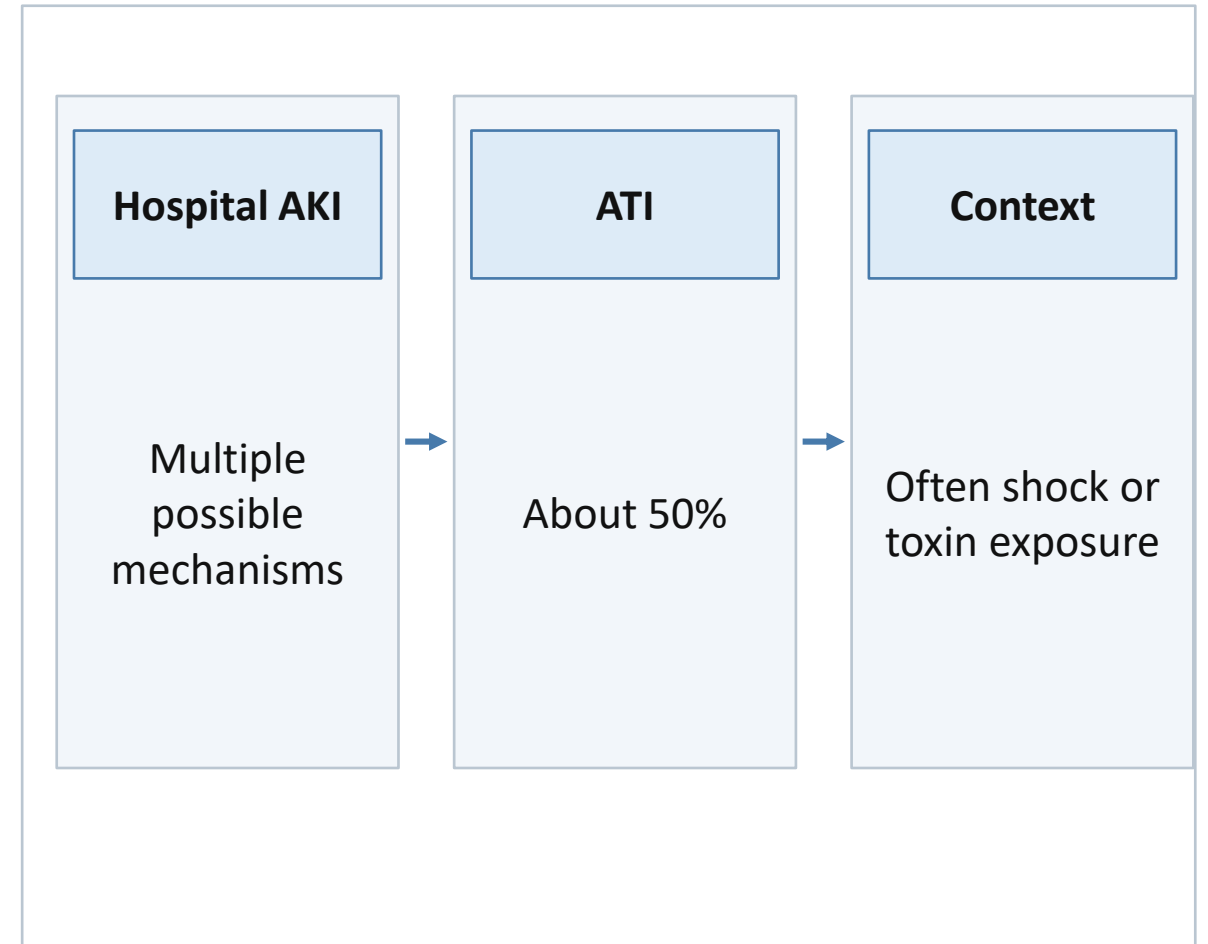
Mechanistic sequence • schematic



ATI is a major cause of hospitalized AKI

- ATI as the most common cause of acute kidney injury.
- It accounts for approximately half of hospitalized AKI cases in the source.
- The etiologic setting helps identify the relevant mechanism.

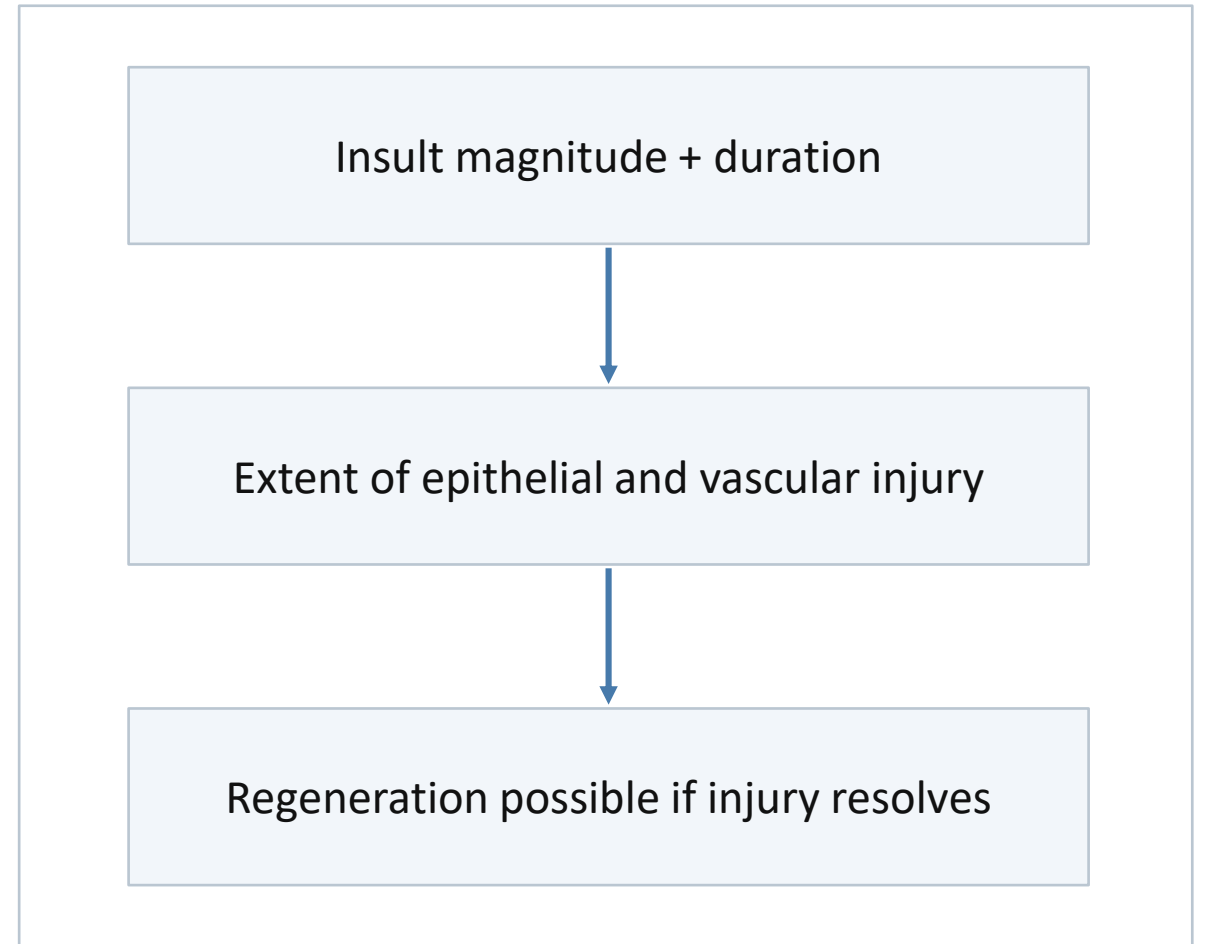
Three linked observations • schematic



What determines reversibility?

- Magnitude and duration of the insult influence outcome.
- Patchy epithelial damage often leaves surviving cells able to repair.
- Severe systemic illness may dominate prognosis despite renal repair potential.

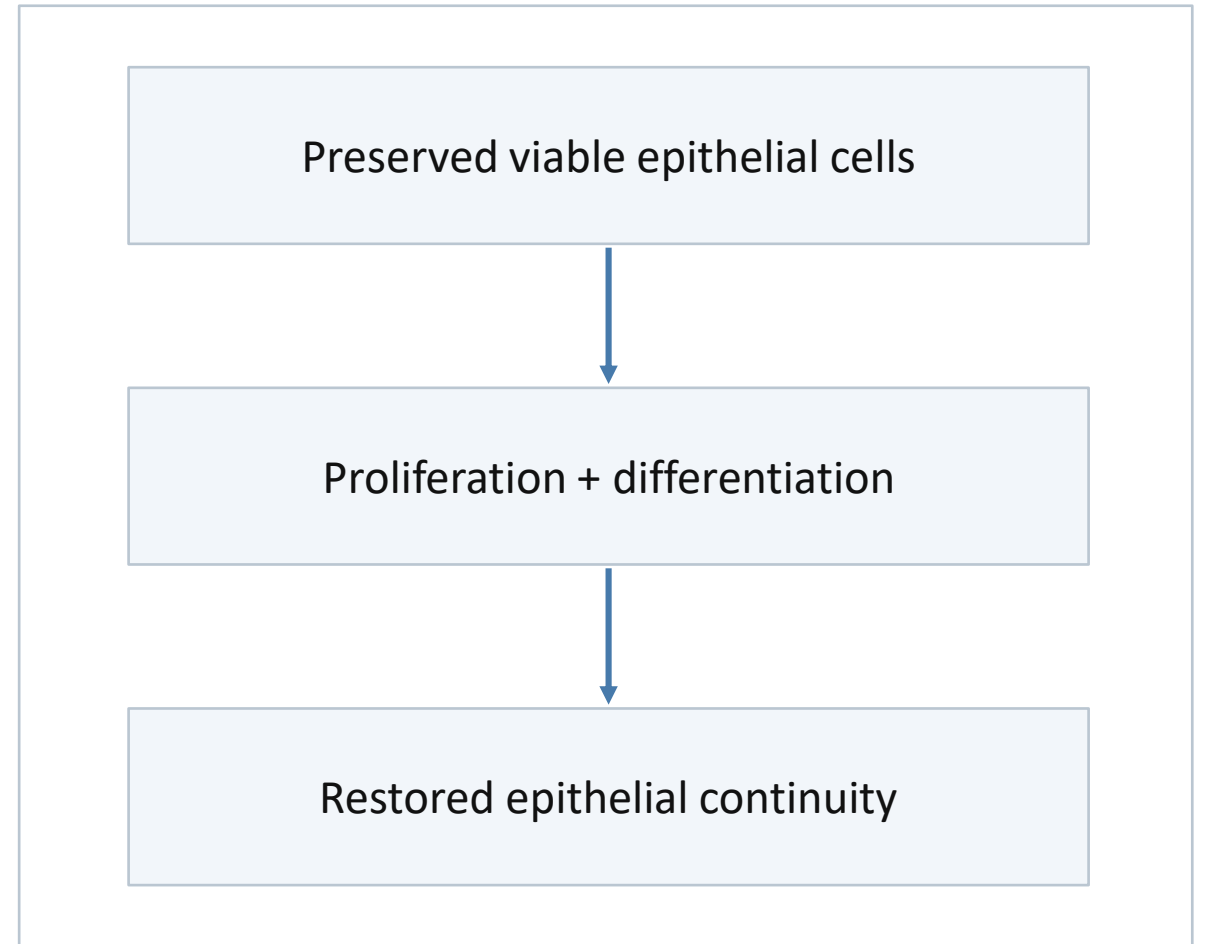
Mechanistic sequence · schematic



Tubular recovery requires living epithelial precursors

- Viable epithelial cells can proliferate after injury.
- New cells differentiate and re-epithelialize denuded segments.
- Locally produced growth factors and cytokines contribute to repair.

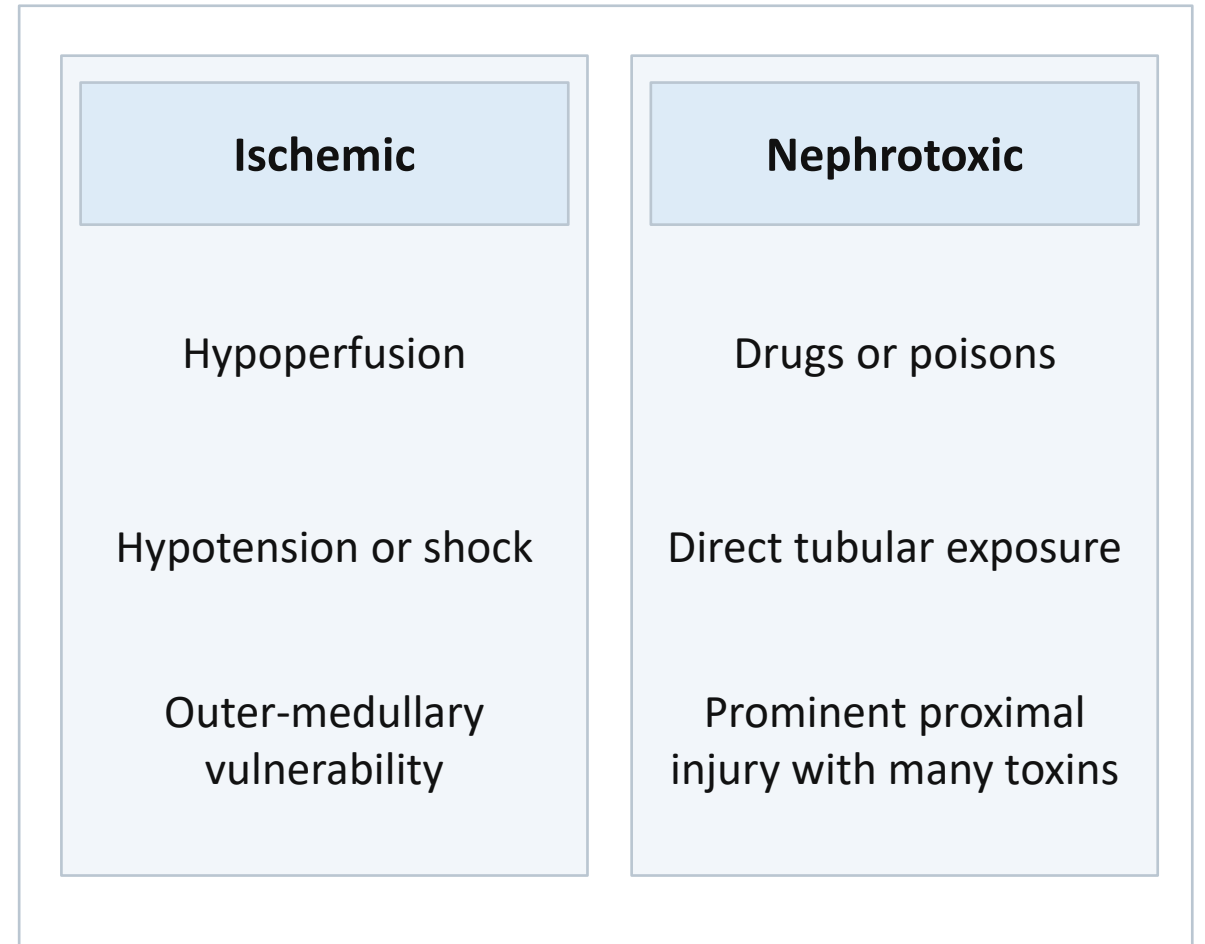
Mechanistic sequence • schematic



Two major etiologic patterns

- Ischemic ATI follows inadequate organ perfusion.
- Nephrotoxic ATI follows exposure to tubular toxins.
- A single patient can have both mechanisms.

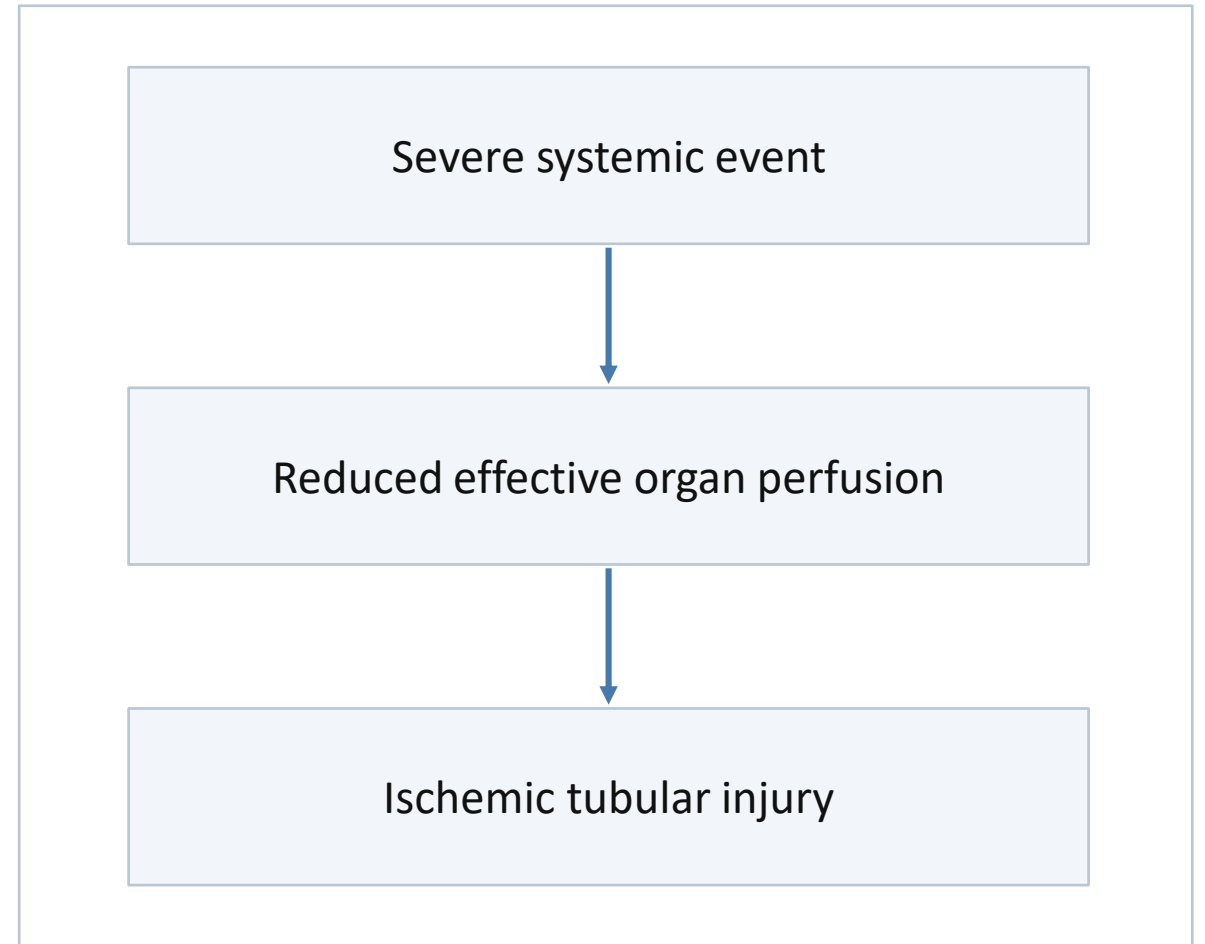
Comparison · conceptual



Clinical contexts of ischemic ATI

- Severe trauma and acute pancreatitis are examples.
- Marked hypotension or shock commonly accompanies the insult.
- The shared event is inadequate blood flow to peripheral organs.

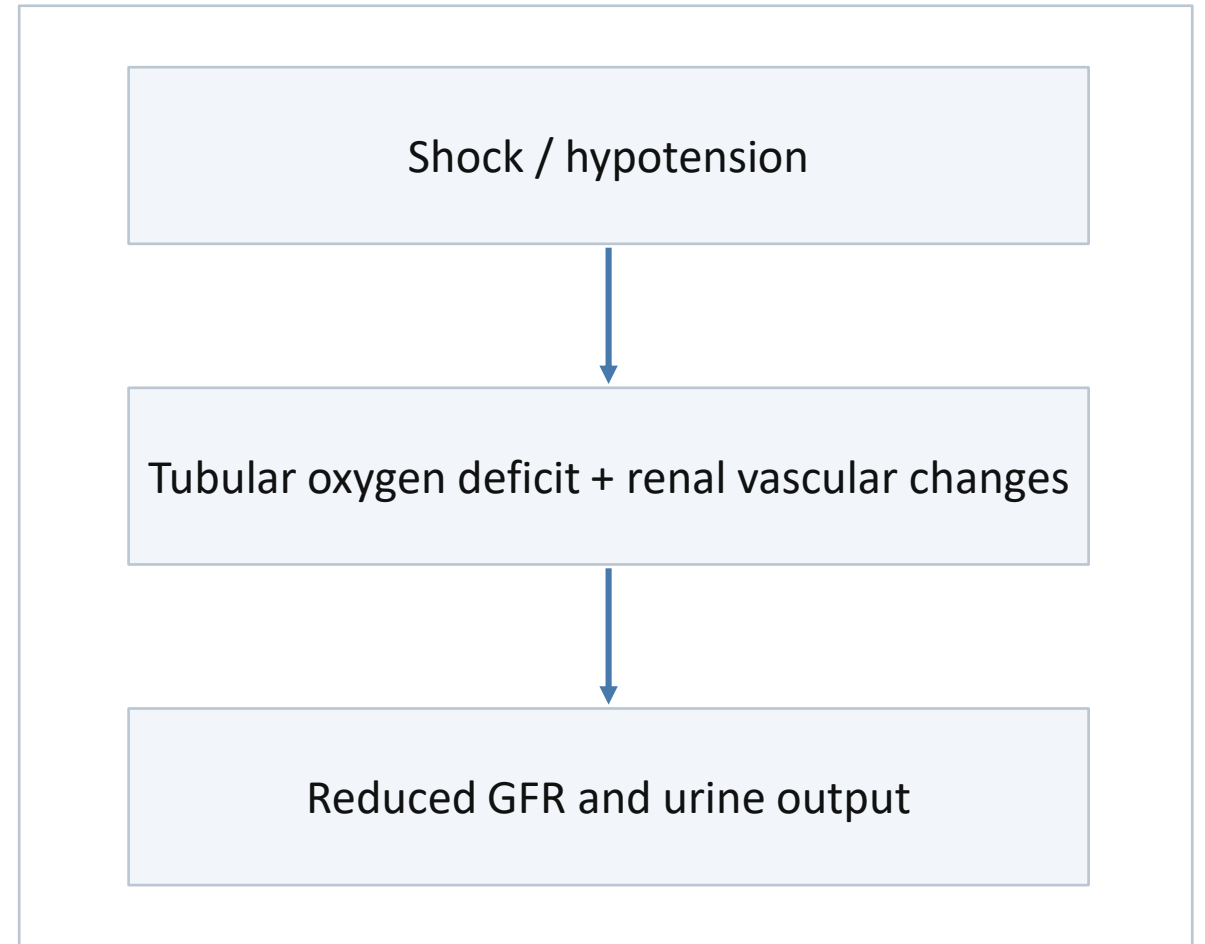
Mechanistic sequence • schematic



Shock links systemic hypoperfusion to AKI

- Renal oxygen delivery falls during circulatory compromise.
- Tubular transport persists as an energy-intensive process.
- Tubular injury and vasoconstriction together depress GFR.

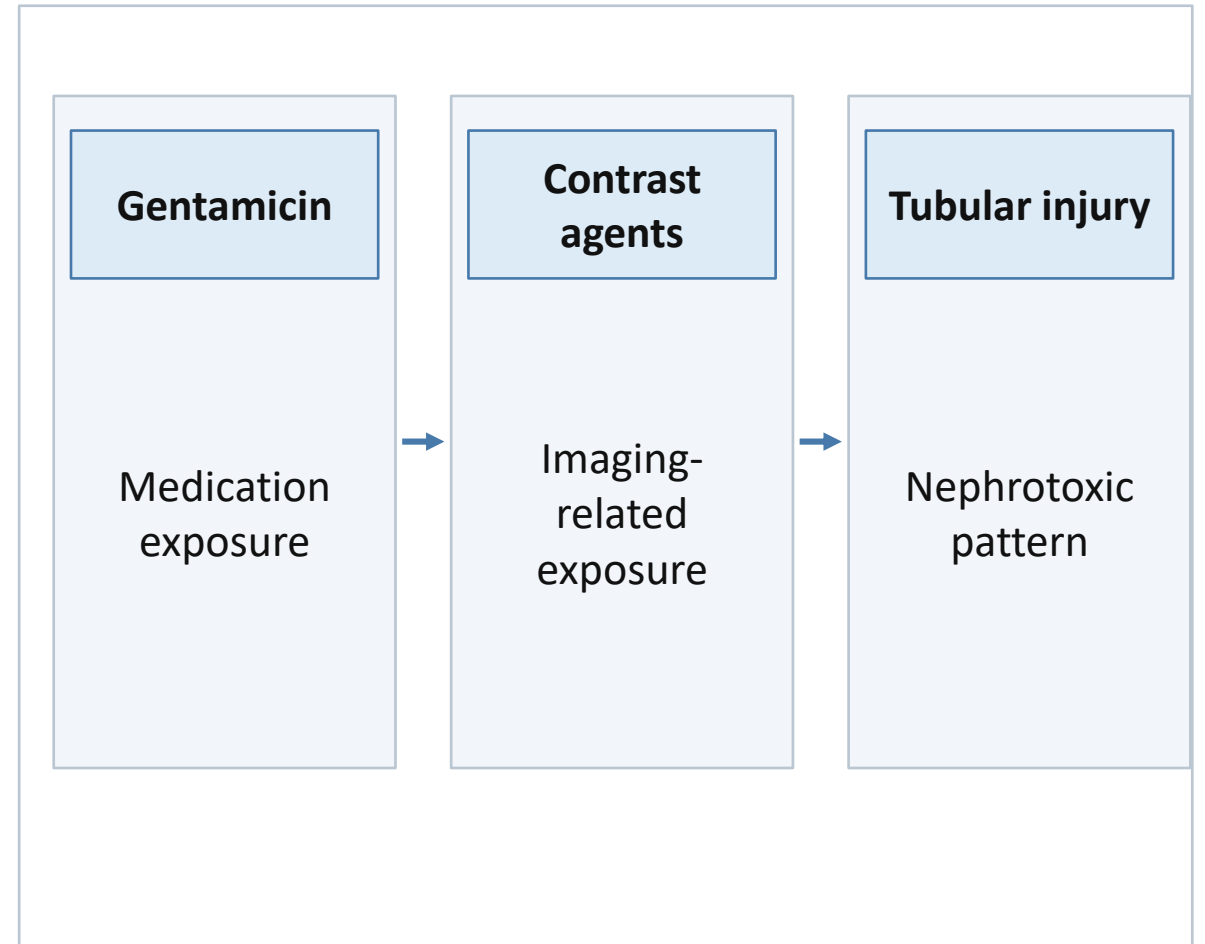
Mechanistic sequence • schematic



Nephrotoxic drugs: Examples

- Gentamicin is listed as a nephrotoxic agent.
- Radiographic contrast agents are also included.
- Toxin-related tubular damage may interact with hemodynamic injury.

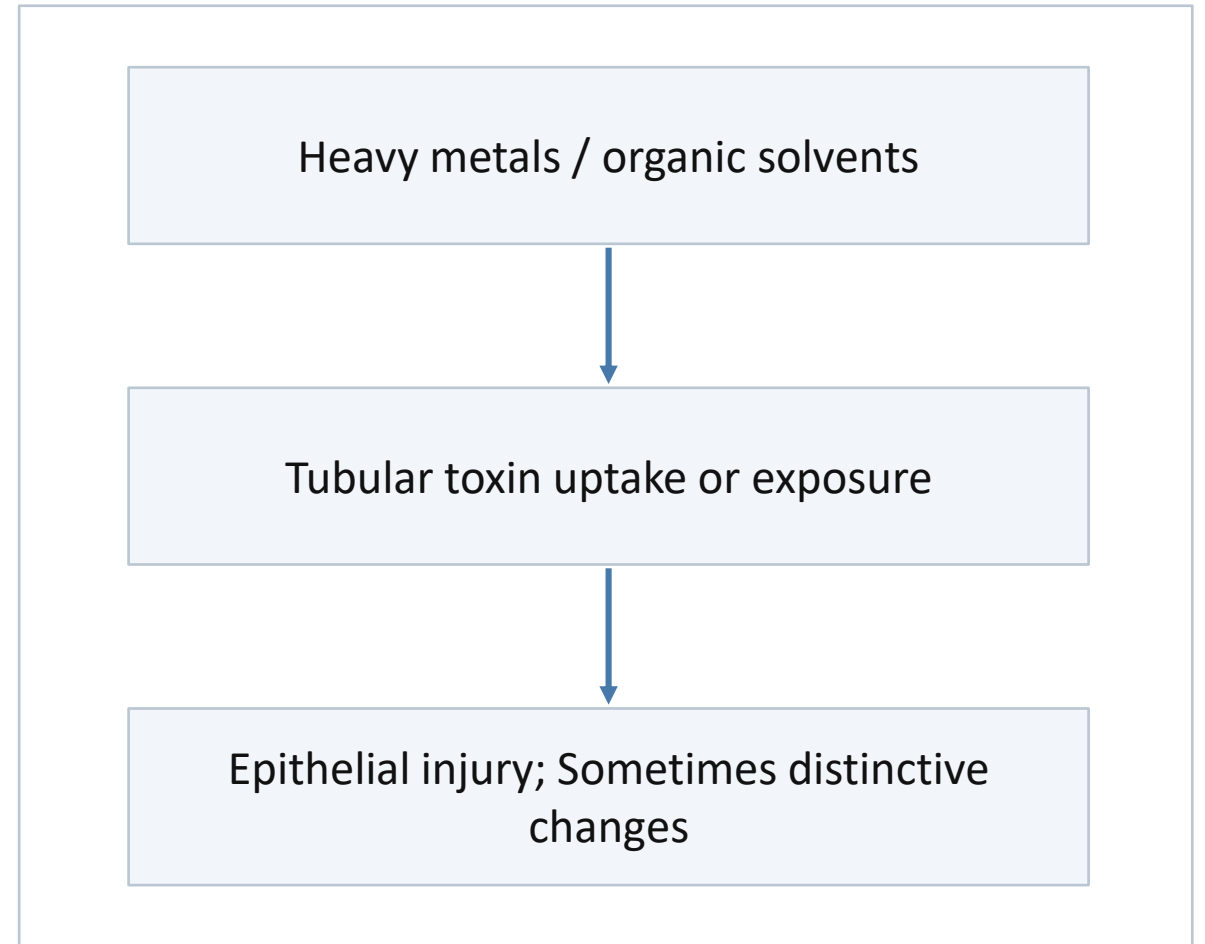
Three linked observations · schematic



Environmental and chemical nephrotoxins

- Mercury is an example of a heavy-metal toxin.
- Carbon tetrachloride is an example of an organic solvent.
- Specific agents can produce distinctive tubular morphologies.

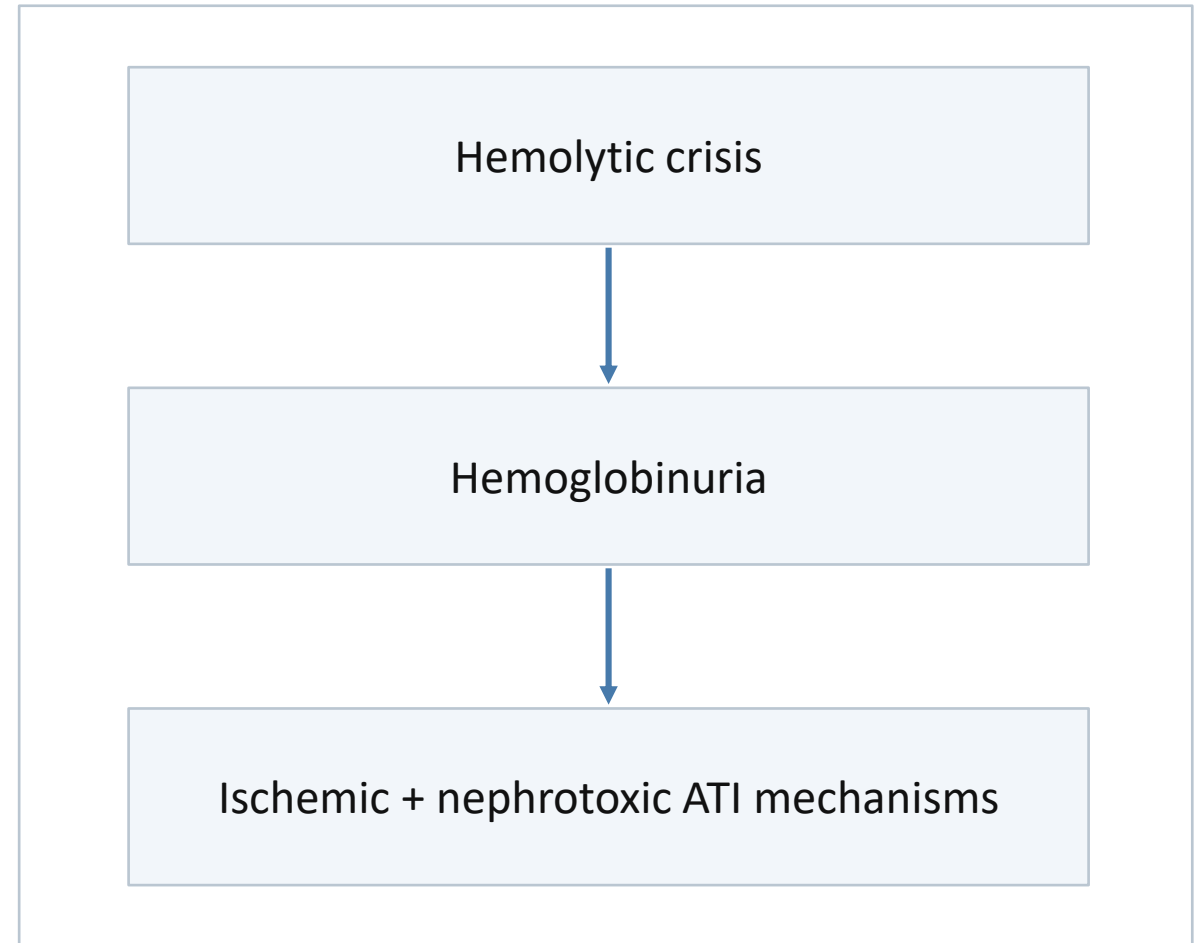
Mechanistic sequence • schematic



Hemoglobinuria can combine ischemia and toxicity

- Mismatched blood transfusions and hemolytic crises are examples.
- Released hemoglobin reaches the nephron in the source context.
- The text presents pigment-associated injury as potentially mixed.

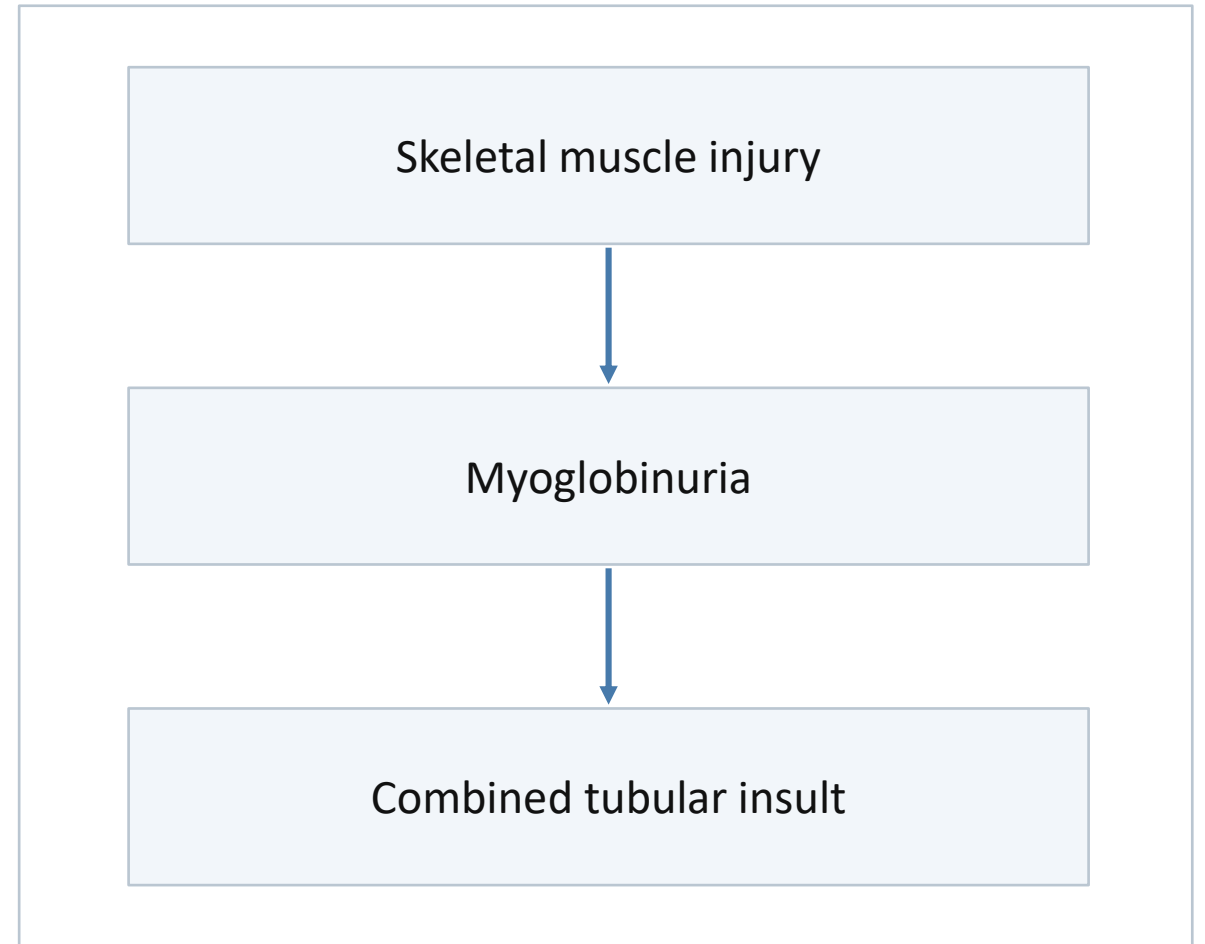
Mechanistic sequence · schematic



Myoglobinuria connects muscle injury to ATI

- Skeletal muscle injury can cause myoglobinuria.
- It is another example of mixed ischemic and nephrotoxic ATI.
- Consider the antecedent systemic injury when interpreting AKI.

Mechanistic sequence • schematic



Real-world insults may not respect two categories

- Pure ischemic and pure toxic forms are useful teaching patterns.
- Hemolysis and muscle injury can combine mechanisms.
- The histologic pattern should not be interpreted without exposures.

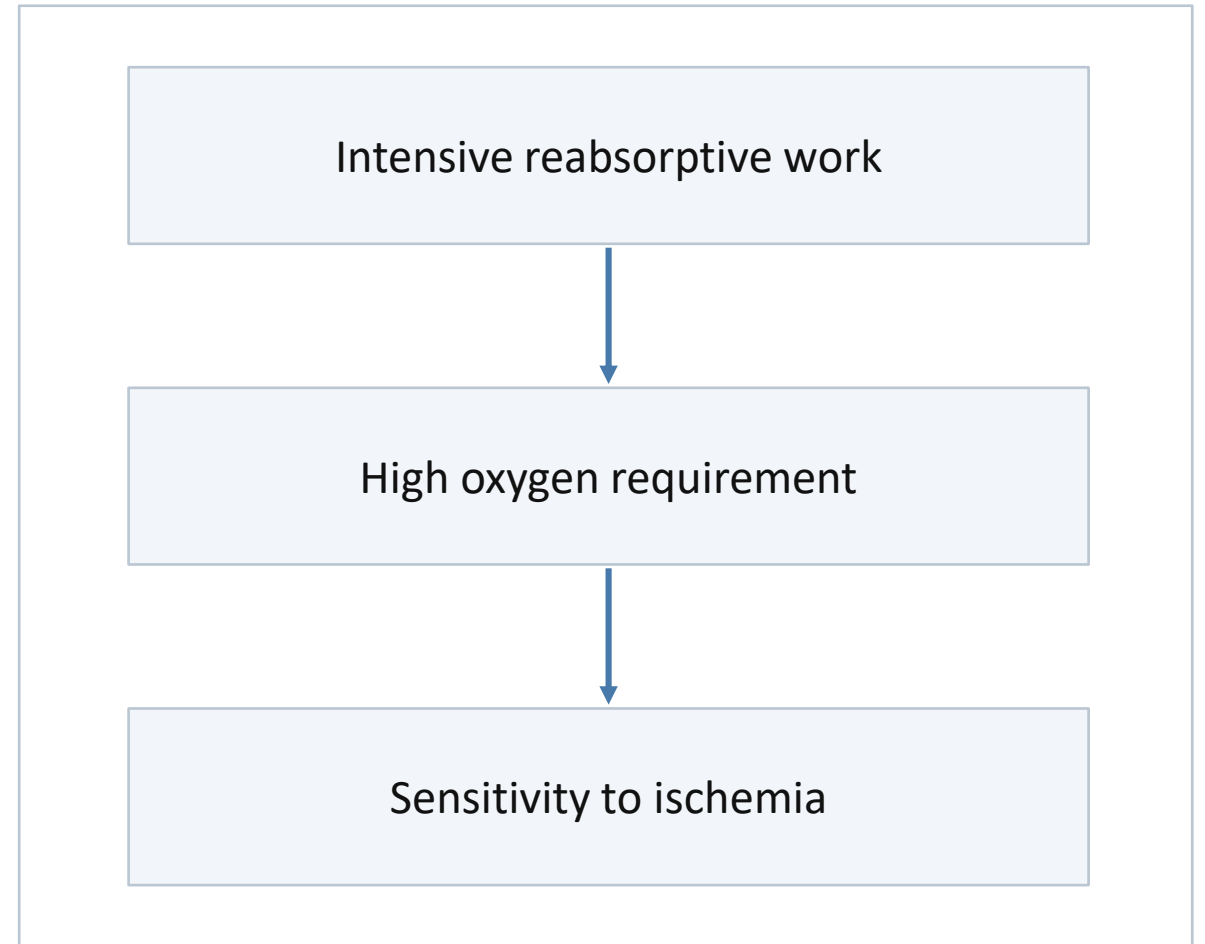
Comparison · conceptual

Teaching pattern	Clinical overlap
Ischemic	Shock + nephrotoxins
Nephrotoxic	Pigment-associated crises
Canonical segment preference	Variable mixed morphology

High transport demand predisposes tubules to ischemia

- Proximal cells have substantial metabolic and oxygen demands.
- Active solute reabsorption depends on intact epithelial transport.
- Oxygen deprivation rapidly impairs tubular function.

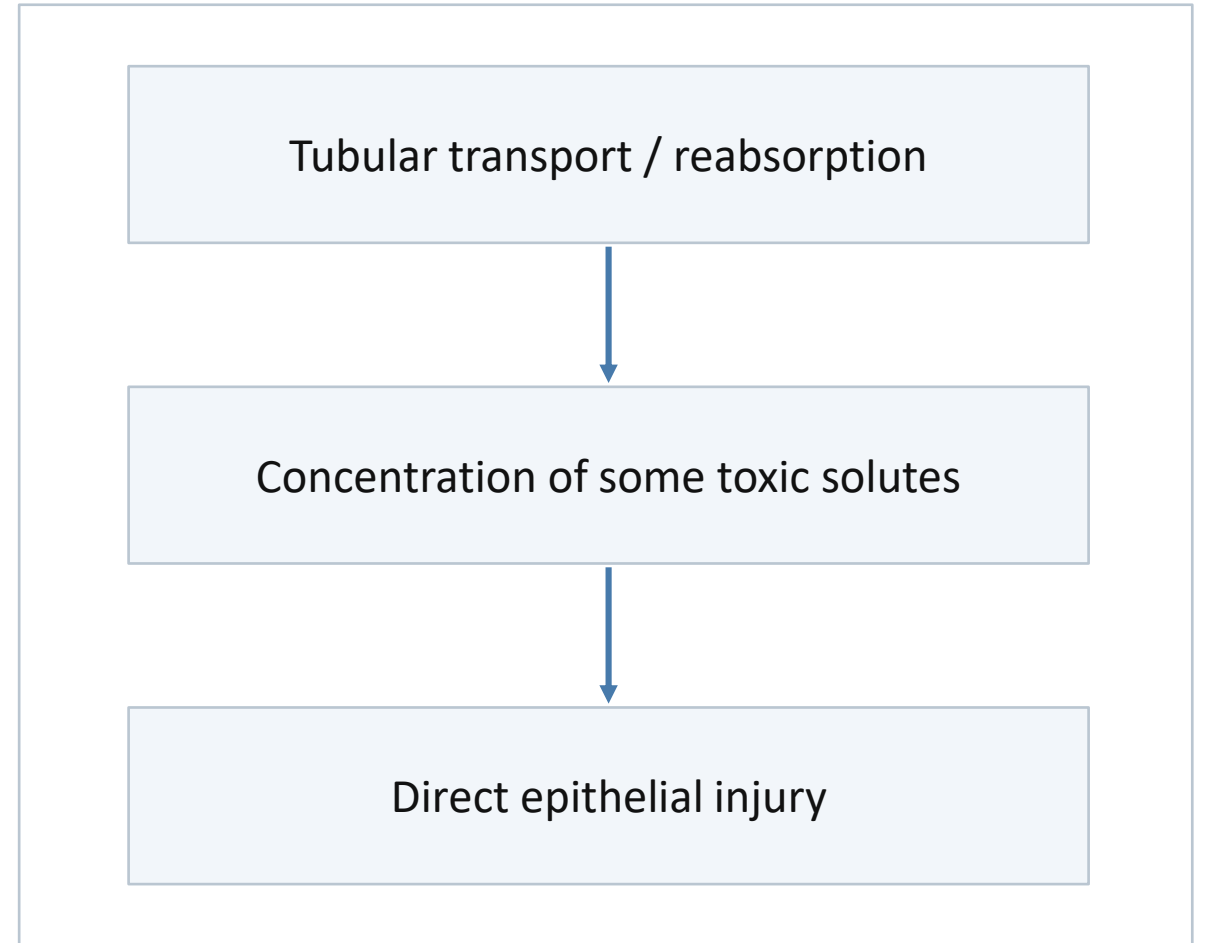
Mechanistic sequence • schematic



Proximal cells can concentrate injurious substances

- Tubular epithelial surfaces contact filtrate extensively.
- Active ion and organic-acid transport facilitates exposure.
- Reabsorptive processes may concentrate toxins within cells.

Mechanistic sequence • schematic



Why the outer medulla is a critical target

- The proximal straight tubule is vulnerable.
- The thick ascending limb also requires considerable energy.
- Injurious perfusion changes can impair oxygen delivery to both.

Segmental involvement · original schematic, not an anatomical scale

Proximal convoluted tubule

Proximal straight tubule

INJURY

Thick ascending limb

INJURY

Distal convoluted tubule

Collecting duct

Segment-specific susceptibility predicts morphology

- Ischemia preferentially affects proximal straight and ascending limbs.
- Many toxins chiefly damage proximal convoluted tubules.
- Distal segments may contain cellular debris and casts.

Segmental involvement · original schematic, not an anatomical scale

Proximal convoluted tubule

INJURY

Proximal straight tubule

Thick ascending limb

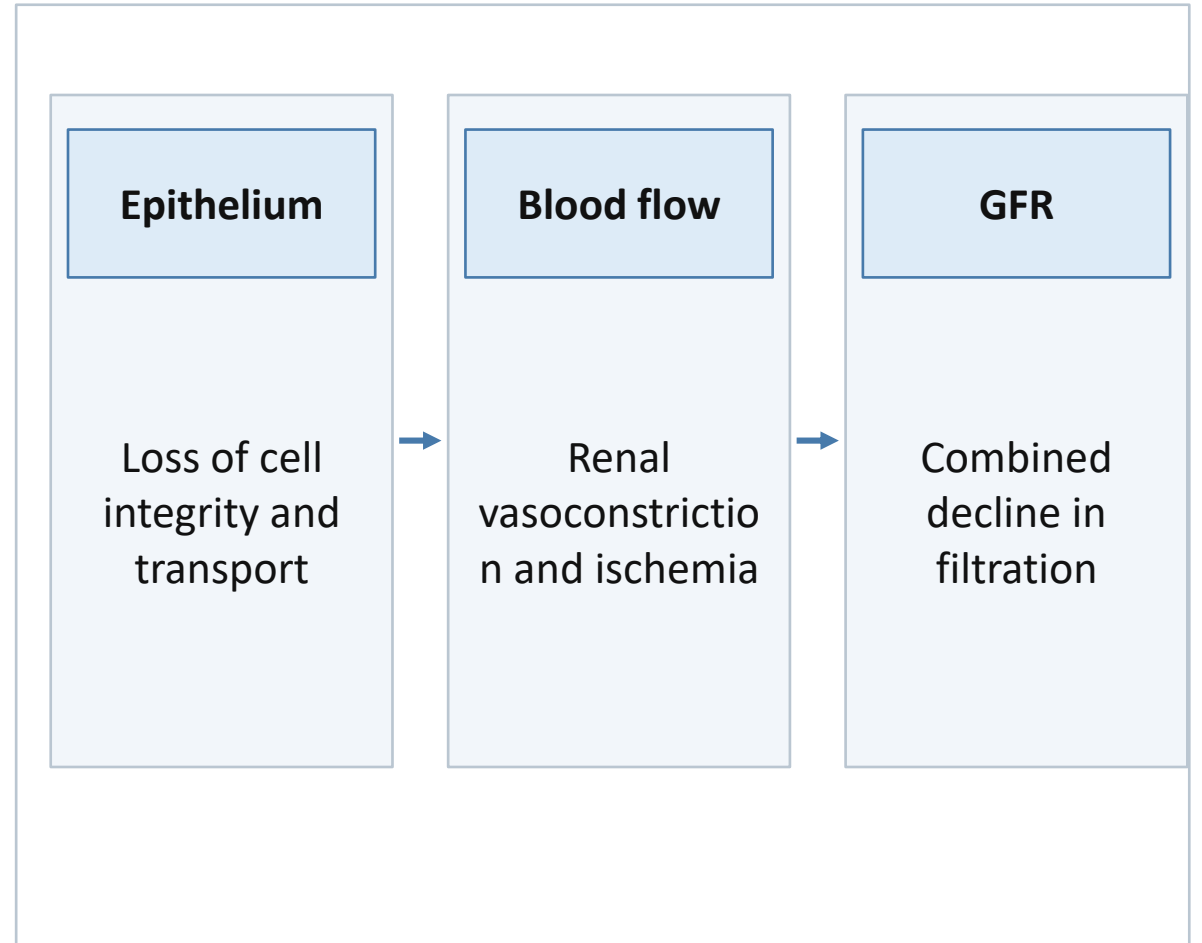
Distal convoluted tubule

Collecting duct

Two linked processes drive ATI

- Tubular epithelial cell injury impairs filtration indirectly.
- Persistent disturbance of intrarenal blood flow lowers filtration.
- The two processes amplify each other.

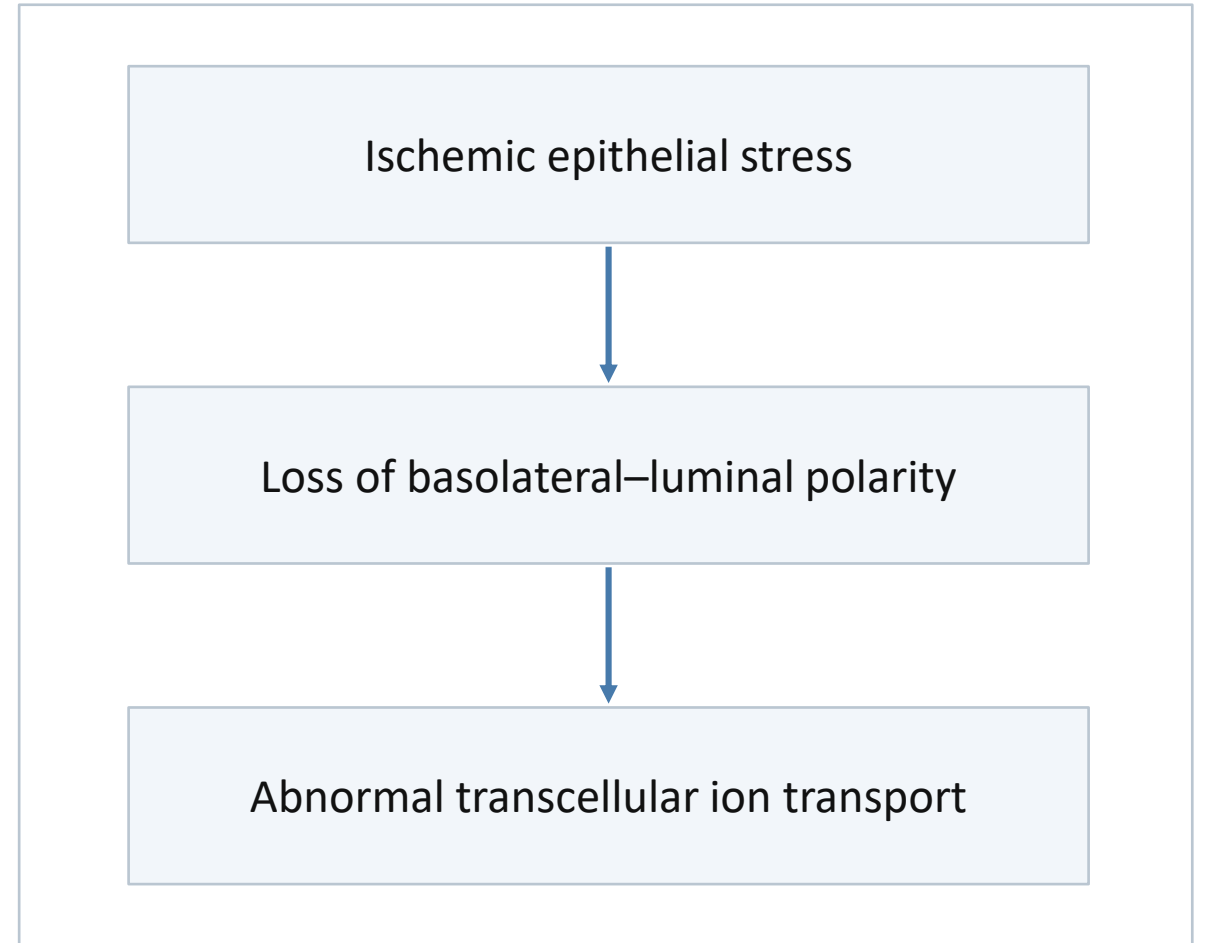
Three linked observations • schematic



Loss of tubular cell polarity is an early response

- Normal epithelial transport proteins have polarized localization.
- Ischemia redistributes these proteins to inappropriate membranes.
- The resulting transport defect may precede epithelial necrosis.

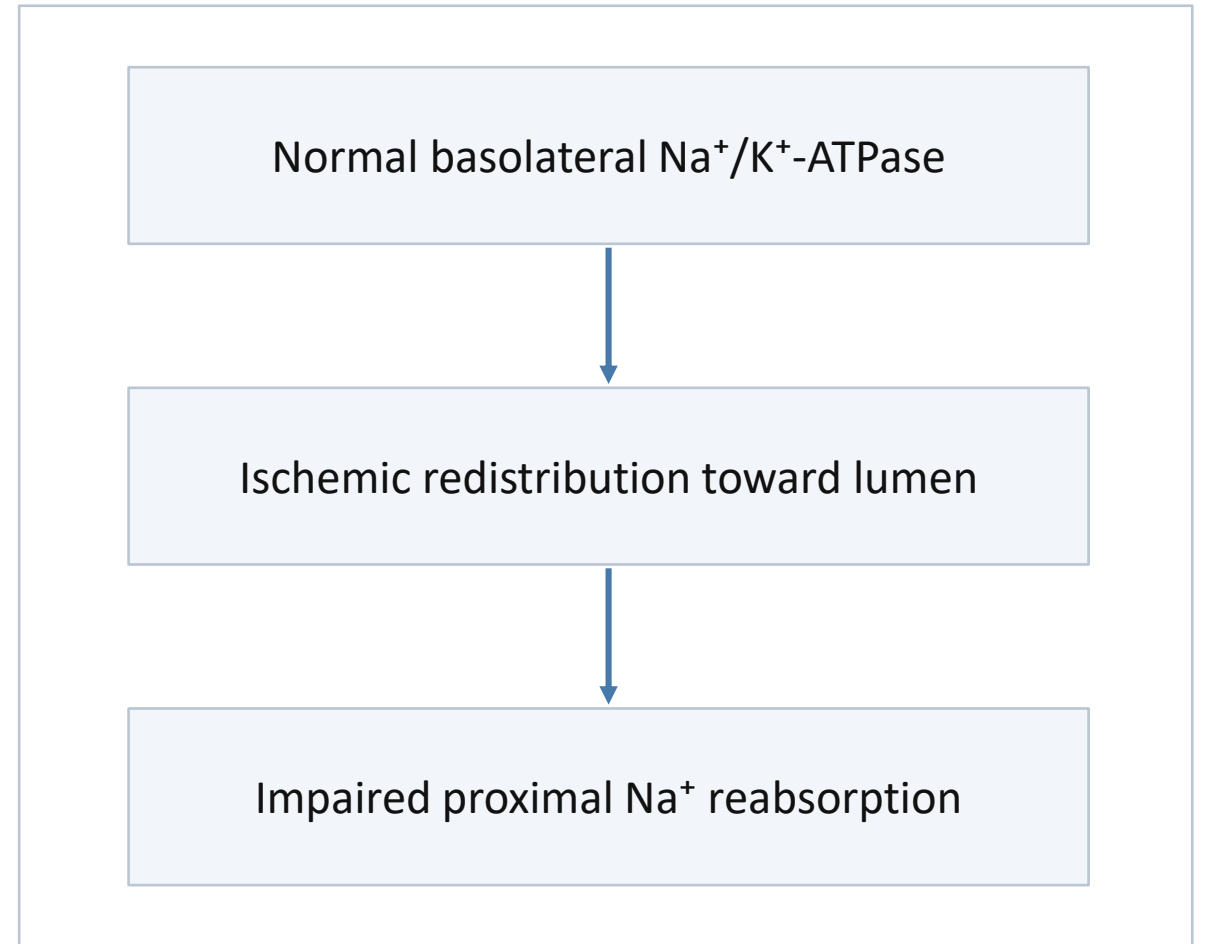
Mechanistic sequence • schematic



Na^+/K^+ -ATPase mislocalization impairs sodium handling

- The textbook specifically identifies Na^+/K^+ -ATPase.
- Ischemia moves it from the basolateral toward the luminal surface.
- Abnormal ion transport increases sodium delivery downstream.

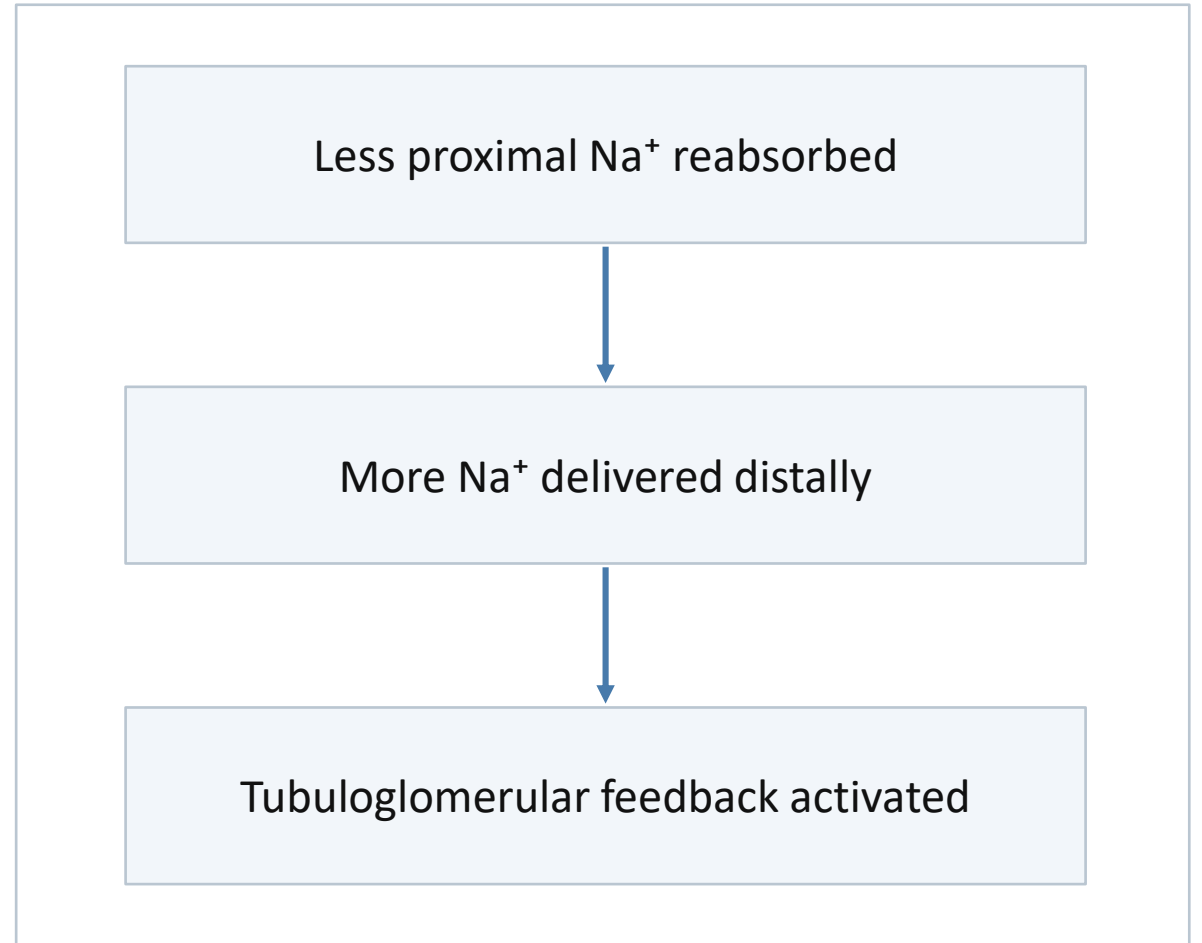
Mechanistic sequence · schematic



Distal sodium delivery becomes a feedback signal

- Reduced proximal sodium reabsorption raises distal sodium delivery.
- Distal sodium sensing engages tubuloglomerular feedback.
- This feedback influences the afferent arteriole and filtration.

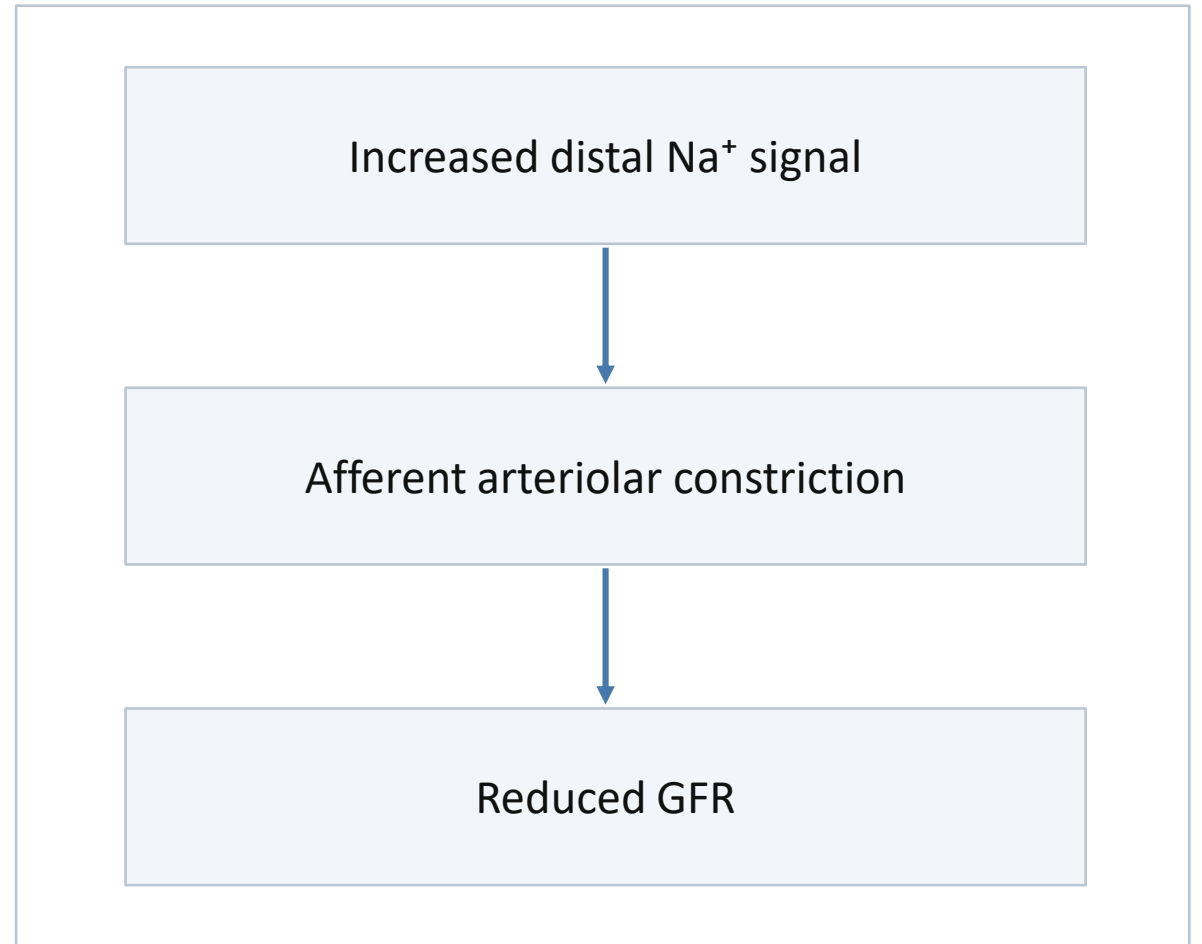
Mechanistic sequence • schematic



Tubuloglomerular feedback can lower GFR

- The source describes afferent arteriolar vasoconstriction.
- The resulting fall in glomerular blood flow decreases GFR.
- A transport defect therefore produces a hemodynamic consequence.

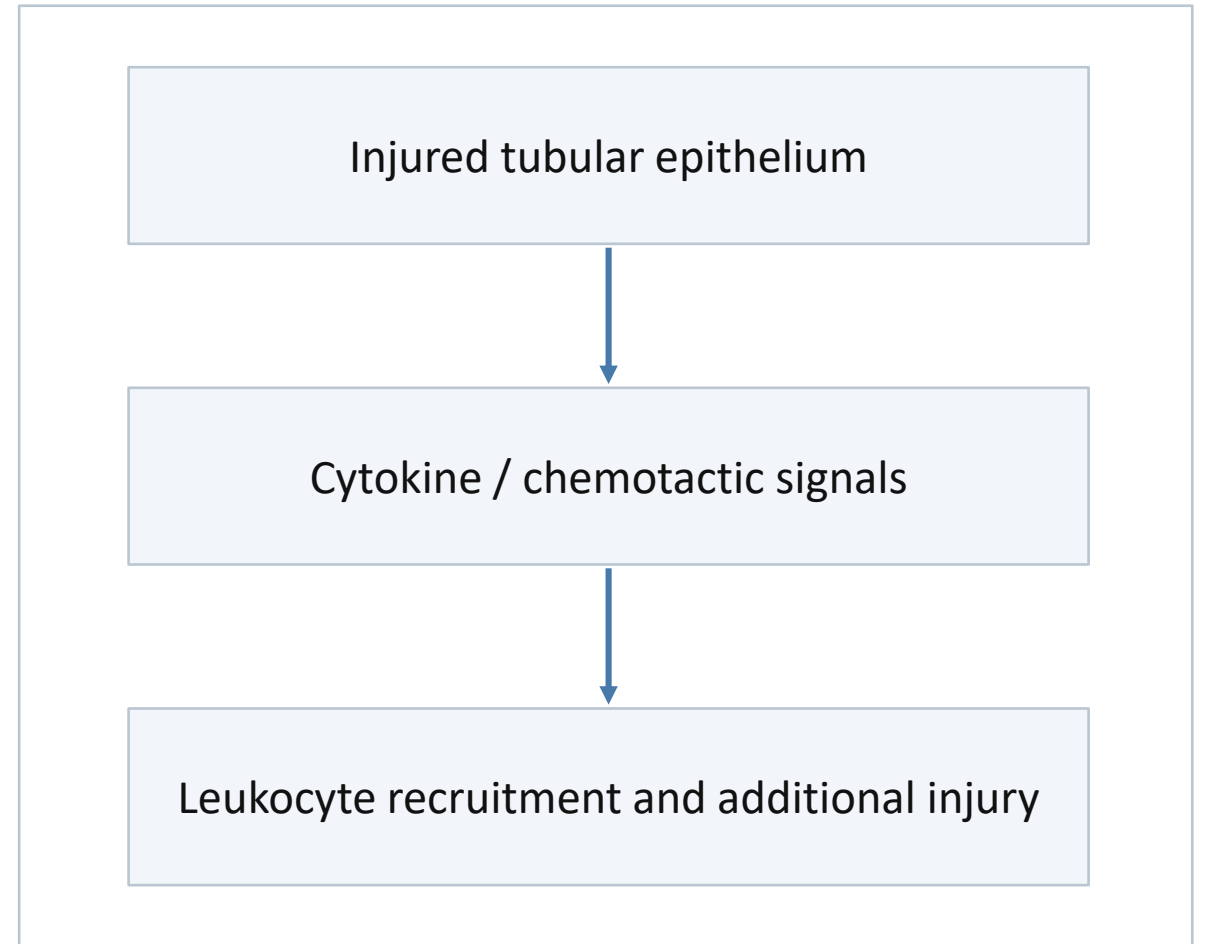
Mechanistic sequence • schematic



Injured tubular cells recruit inflammatory cells

- Ischemic tubules express cytokines and chemotactic molecules.
- Leukocytes are recruited to the injured region.
- Inflammatory cells may contribute to subsequent tubular damage.

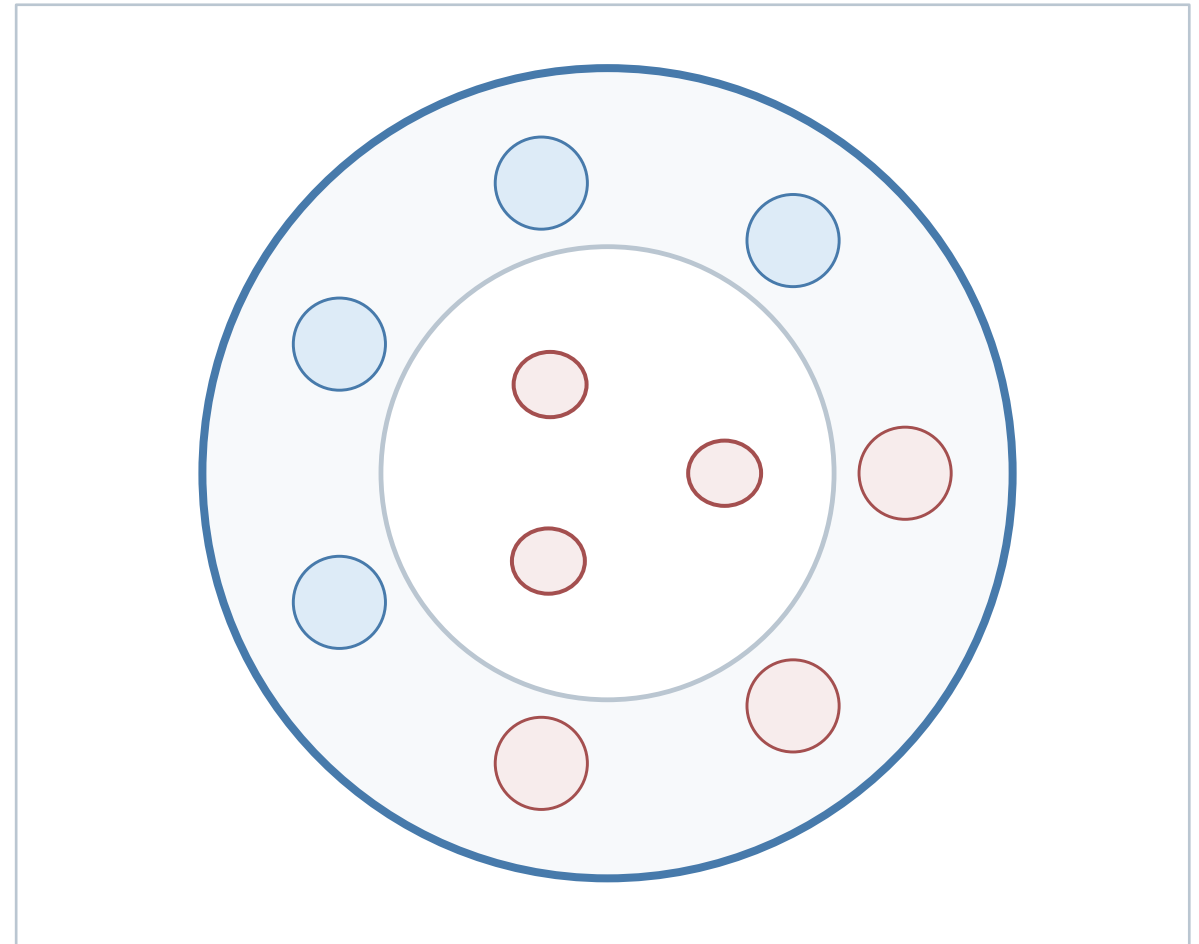
Mechanistic sequence • schematic



Tubular epithelial detachment creates a second lesion

- Damaged cells lose attachment to basement membranes.
- Cells enter and accumulate within tubular lumens.
- This creates the substrate for luminal obstruction.

Tubule cross-section • schematic only; Not a micrograph

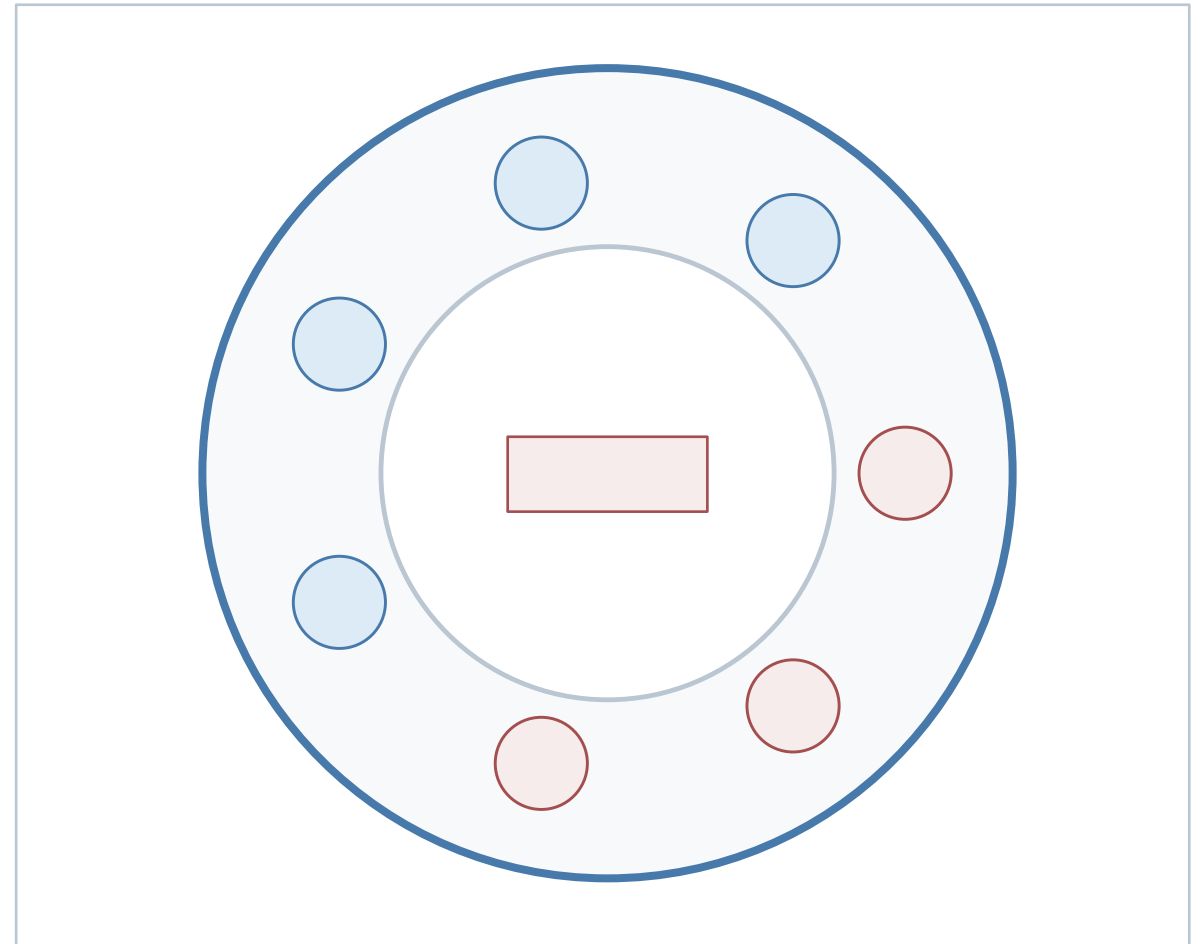


Detached epithelial cells

Cellular debris contributes to cast formation

- Sloughed epithelial cells remain within the tubular lumen.
- Debris and casts occupy distal nephron segments.
- Cast-related obstruction contributes to reduced urine flow.

Tubule cross-section • schematic only; Not a micrograph

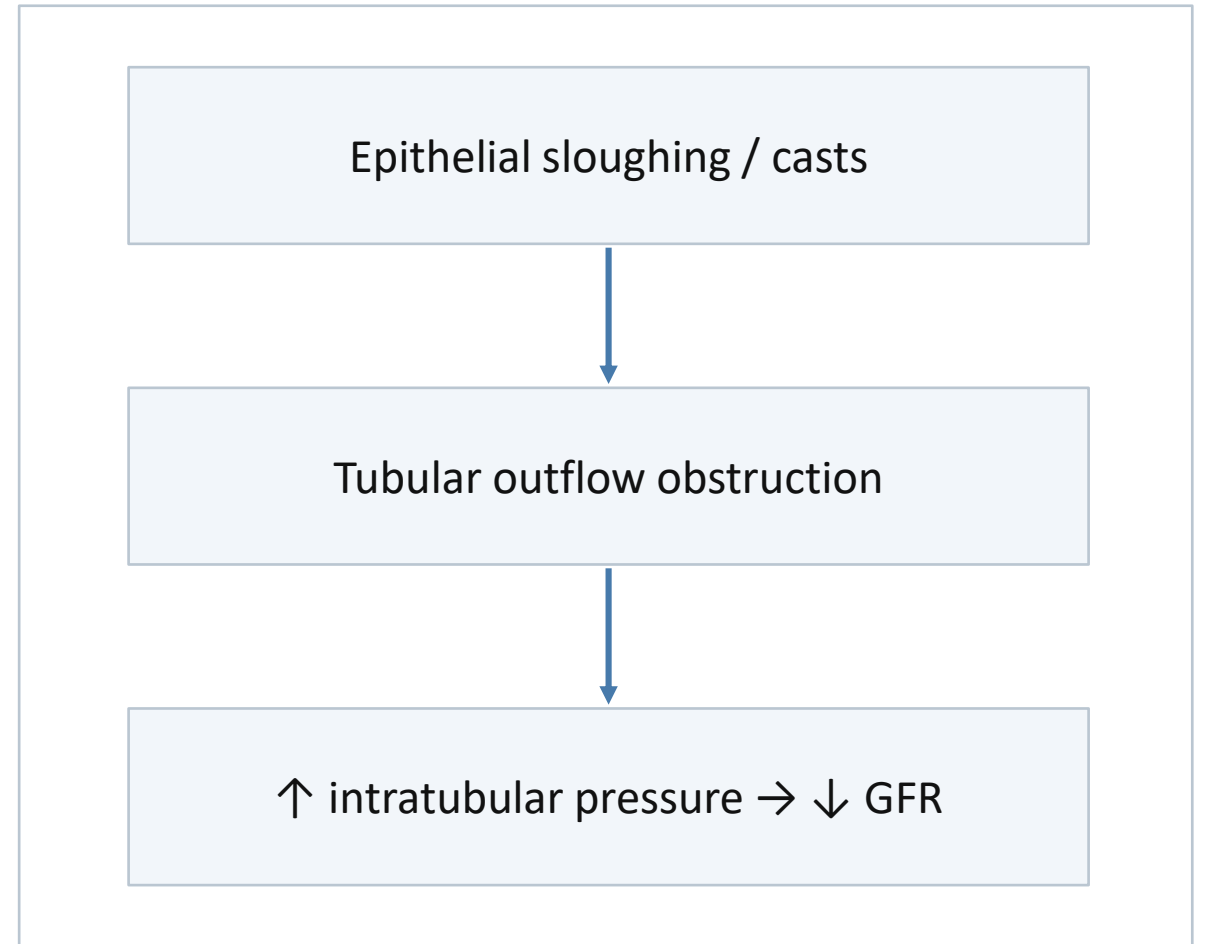


Luminal debris/cast

Obstruction increases intratubular pressure

- Sloughed cells and casts impede tubular flow.
- Increased pressure opposes normal filtration downstream.
- The functional consequence is an additional decrease in GFR.

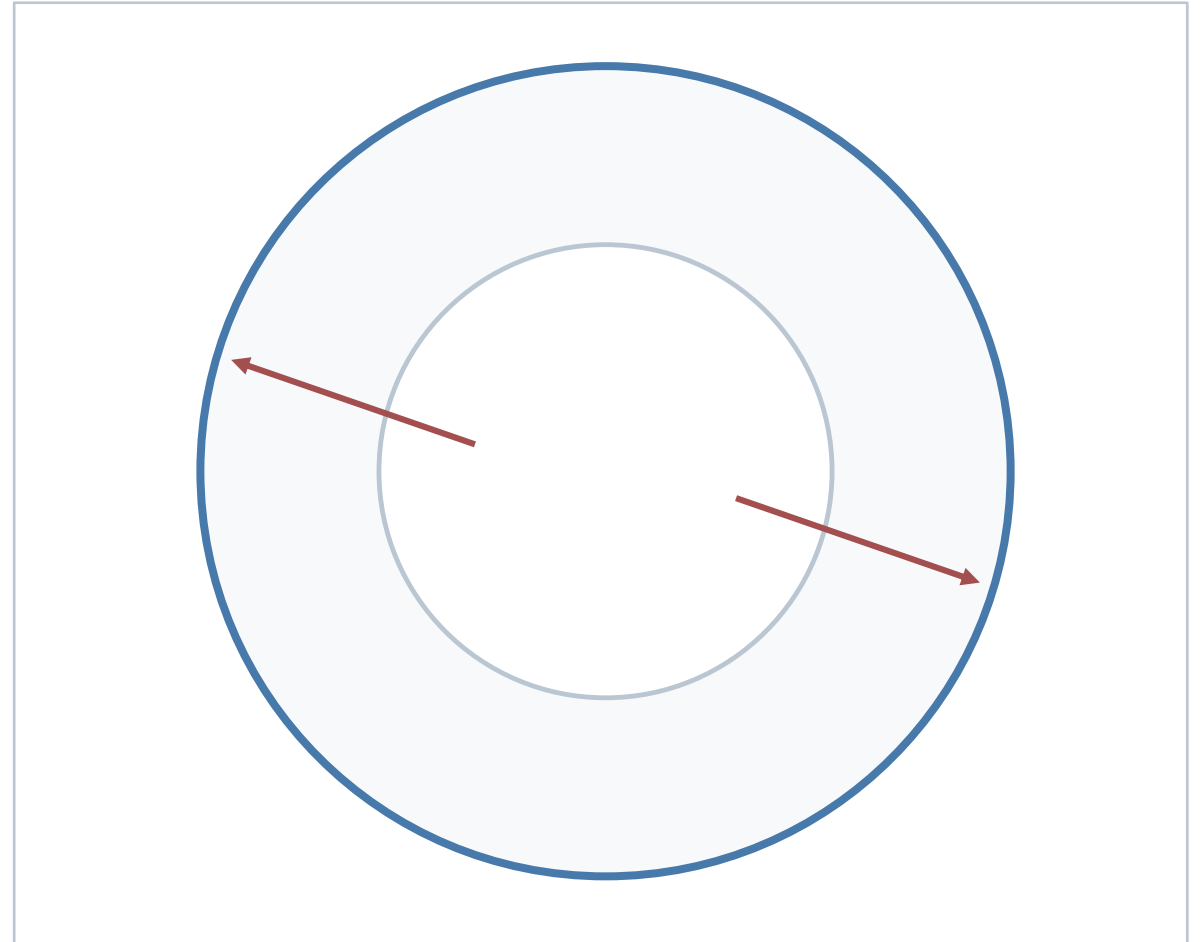
Mechanistic sequence • schematic



Damaged epithelium allows filtrate backleak

- Filtrate may escape from the damaged tubular lumen.
- Leaked fluid enters the interstitial compartment.
- Backleak limits effective urine formation.

Tubule cross-section · schematic only; Not a micrograph

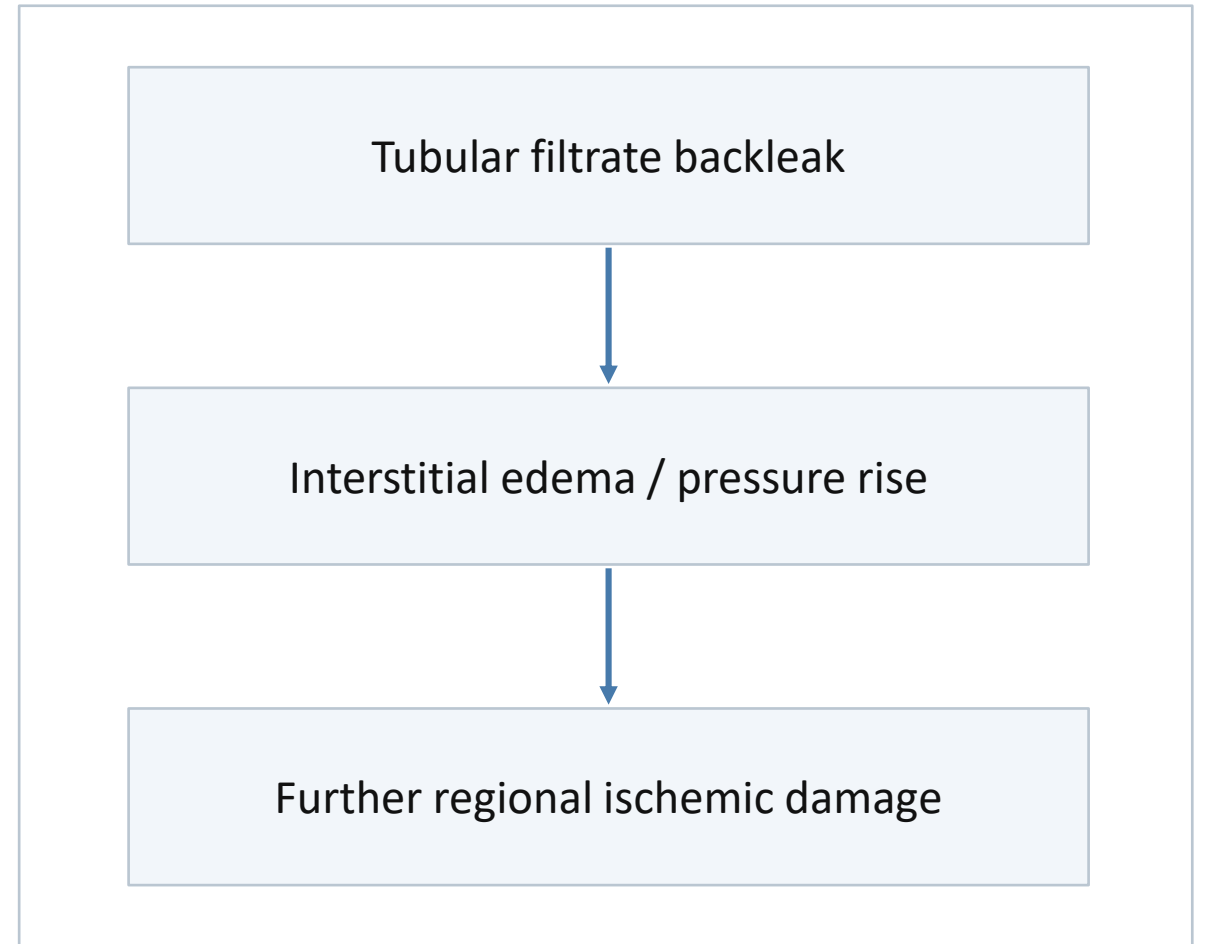


Filtrate leak across damaged epithelium

Interstitial fluid accumulation perpetuates injury

- Backleak causes interstitial edema.
- Raised interstitial pressure impairs regional microperfusion.
- Additional tubular ischemia can result.

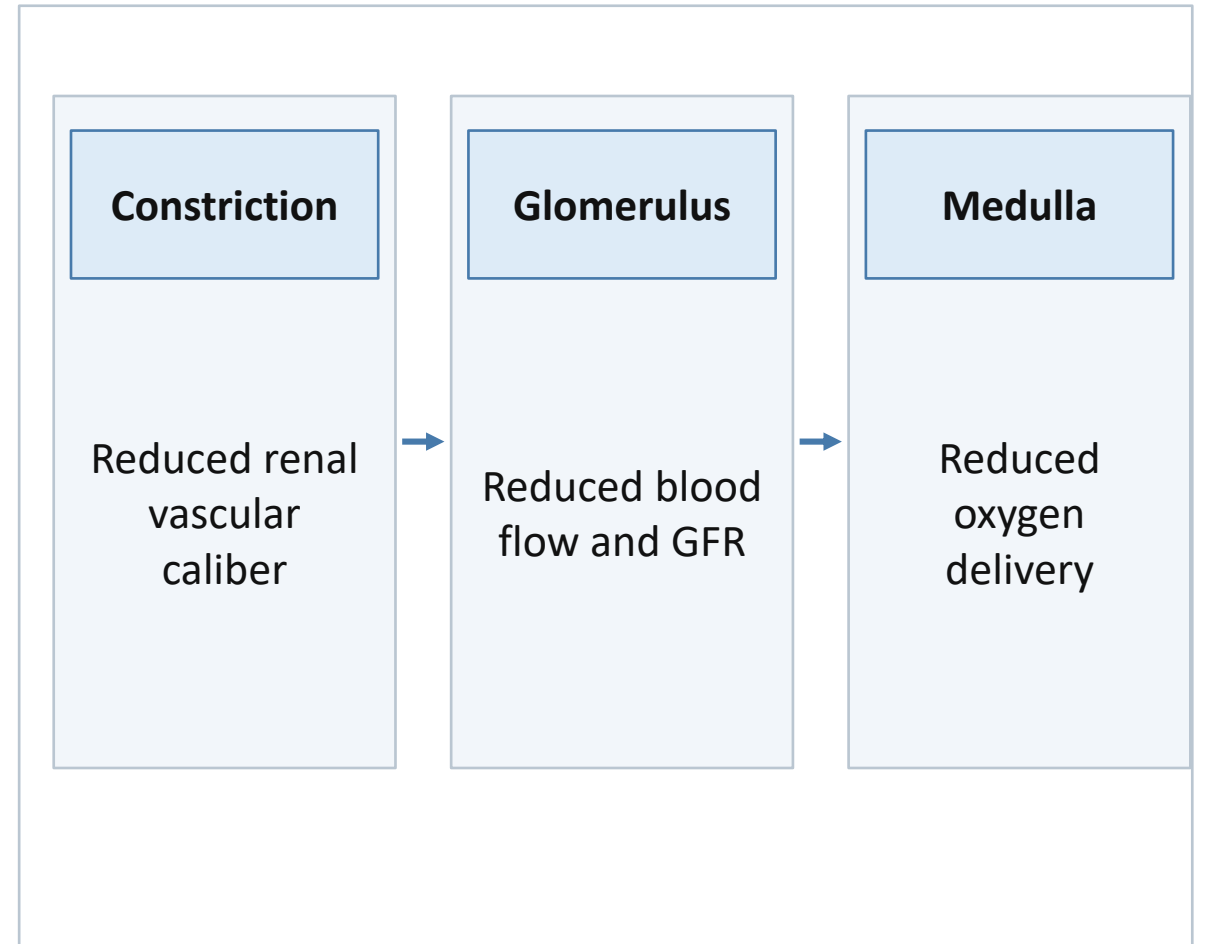
Mechanistic sequence • schematic



Intrarenal vasoconstriction directly lowers filtration

- Reduced renal microvascular flow is central to ischemic ATI.
- Glomerular blood flow declines as intrarenal vessels constrict.
- Oxygen delivery to vulnerable tubules falls further.

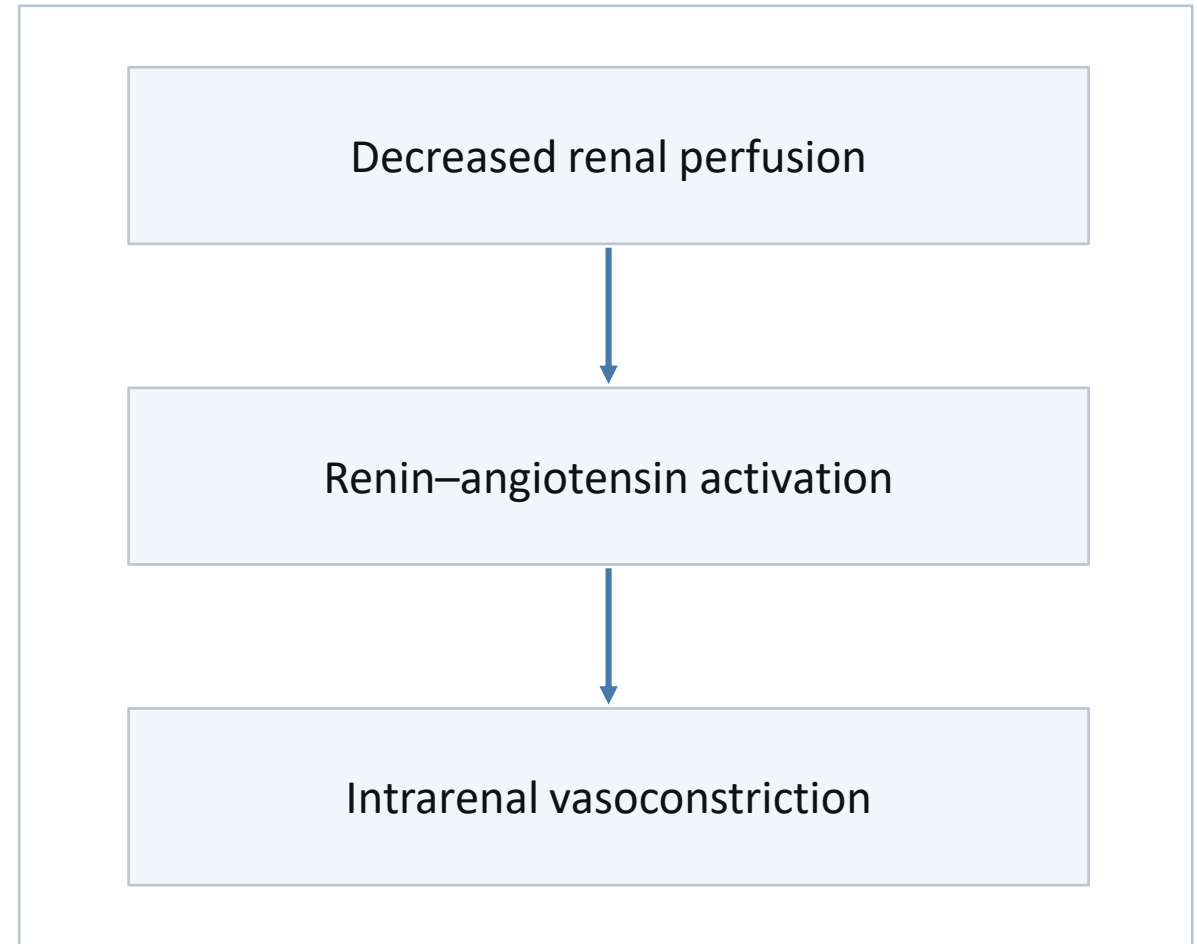
Three linked observations • schematic



The renin–angiotensin system participates in vasoconstriction

- The textbook implicates the renin–angiotensin system.
- Renal hypoperfusion engages vasoconstrictor pathways.
- This contributes to persistent reductions in perfusion.

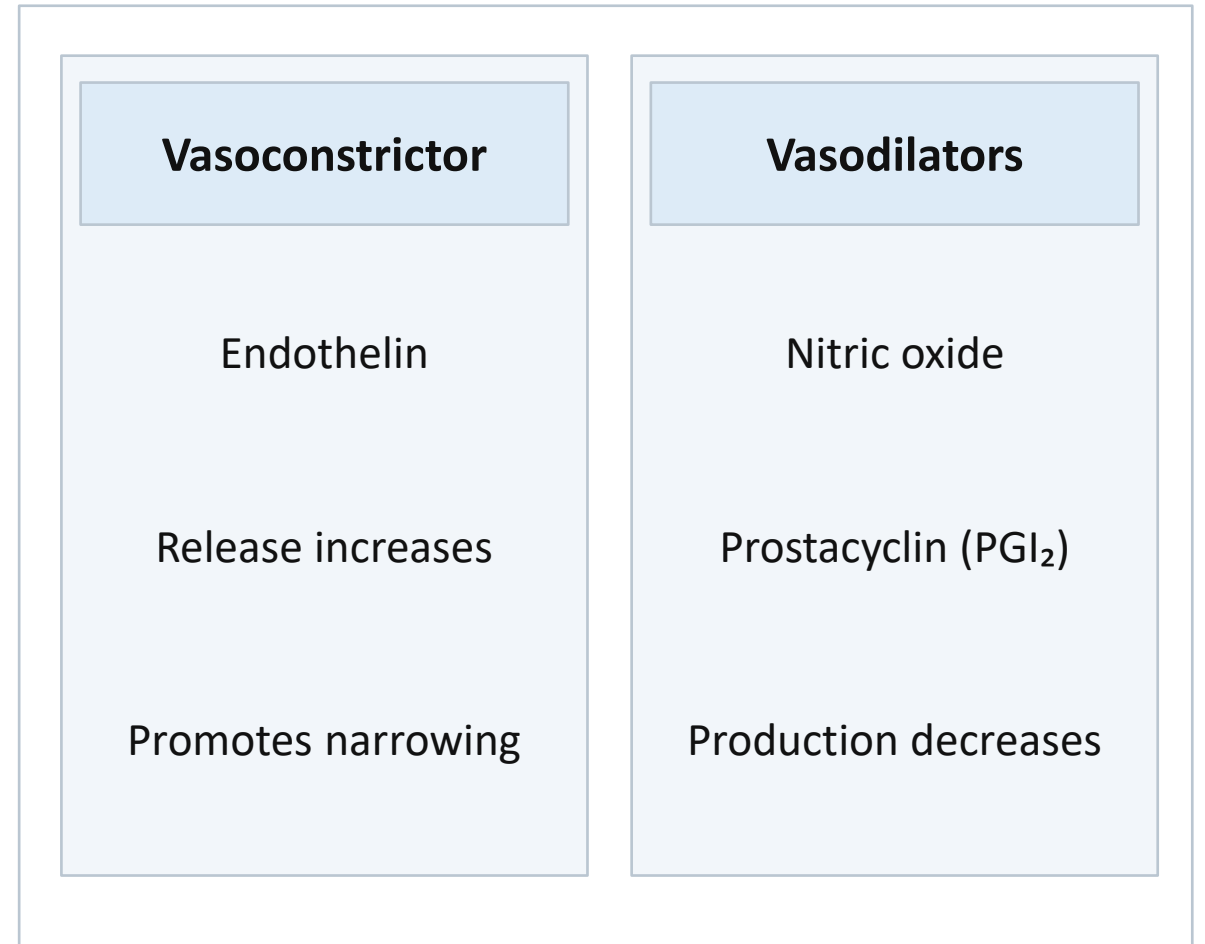
Mechanistic sequence • schematic



Endothelial dysfunction alters vasoactive balance

- Sublethal endothelial injury increases endothelin release.
- The source describes reduced nitric oxide and prostacyclin.
- The altered balance favors intrarenal vasoconstriction.

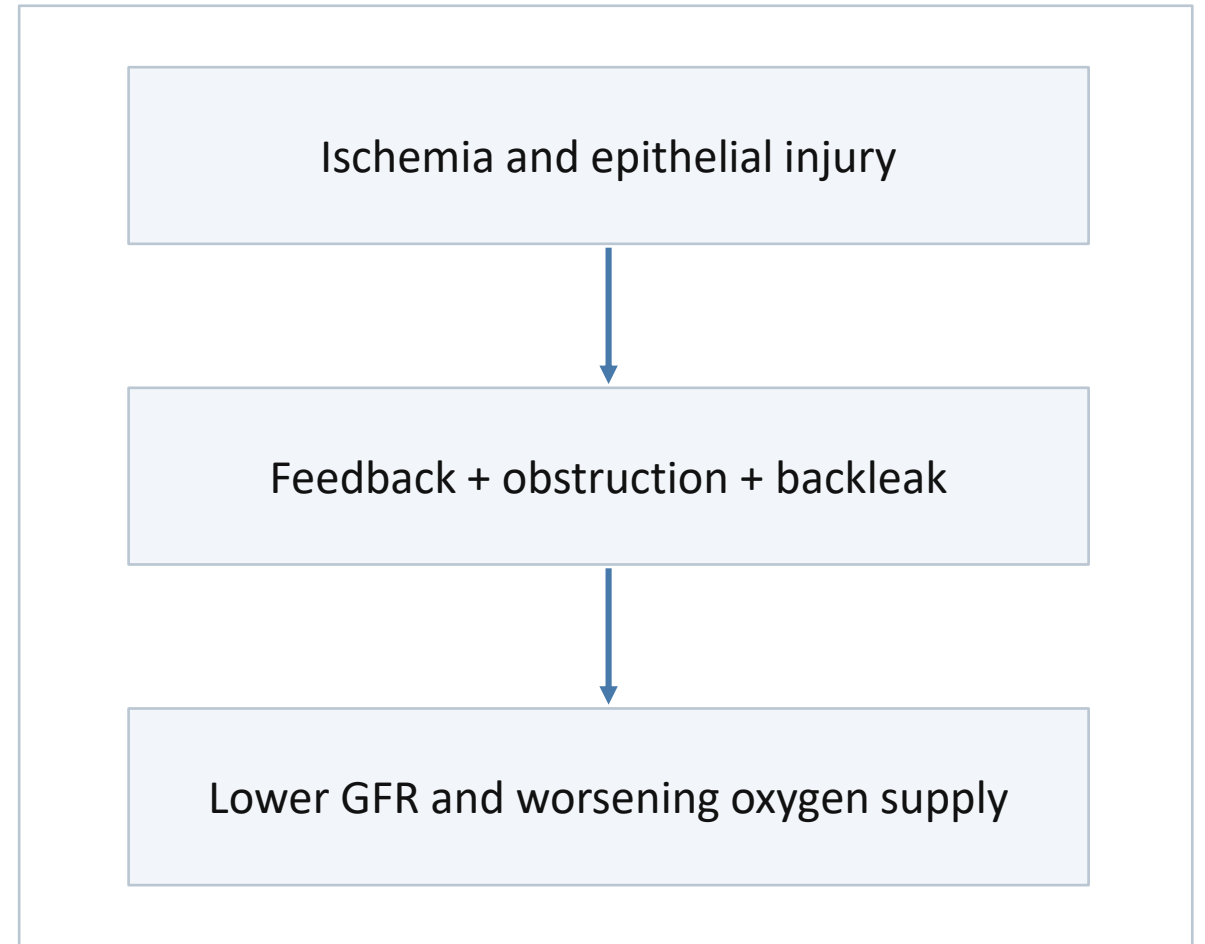
Comparison · conceptual



Hemodynamic and epithelial injury amplify one another

- Reduced microvascular flow worsens tubular ischemia.
- Injured epithelia send feedback signals and obstruct flow.
- The combined effects sustain a decline in GFR.

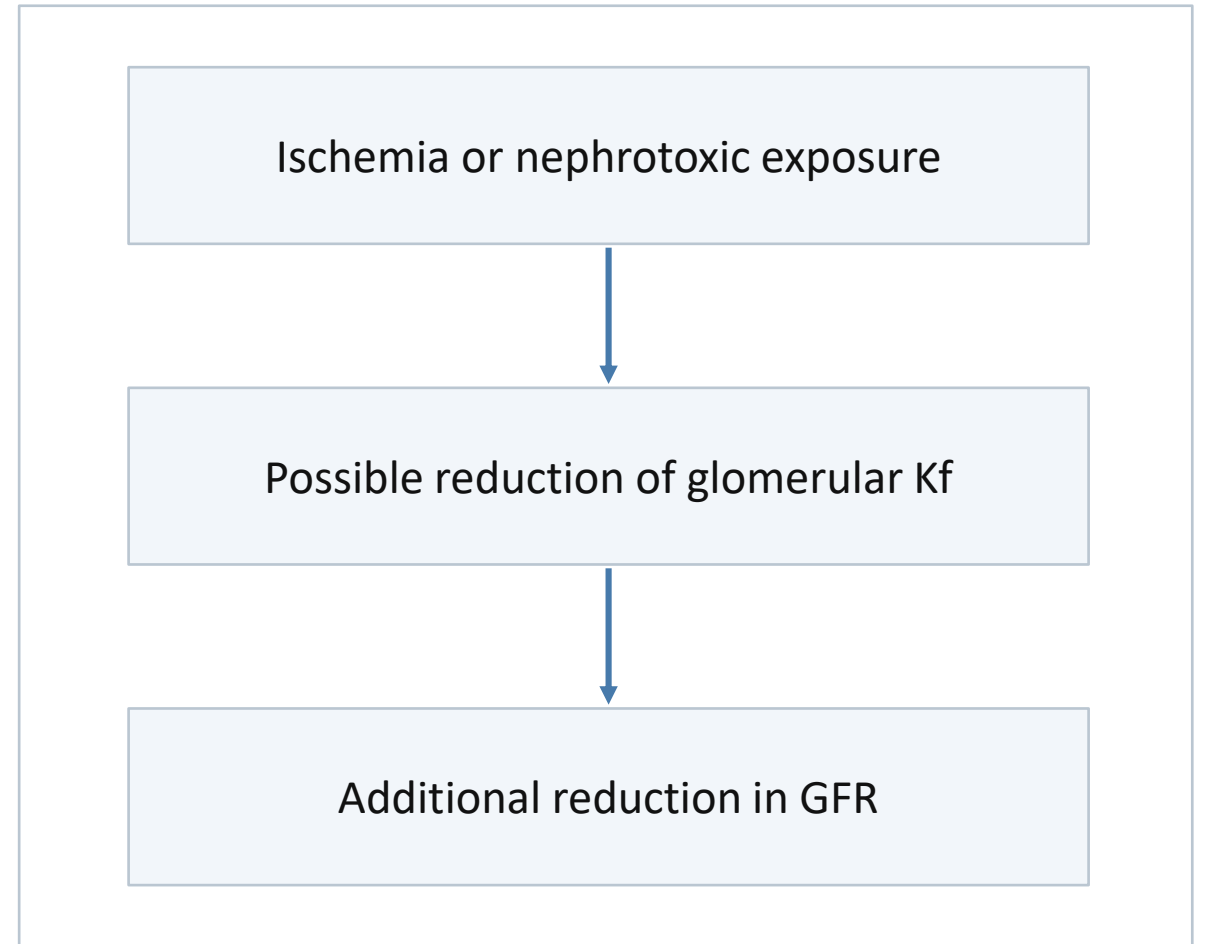
Mechanistic sequence • schematic



A glomerular component is possible but less established

- The source notes some evidence for a direct glomerular effect.
- Ischemia or toxins may decrease the ultrafiltration coefficient.
- This is presented as a possibility, not the principal mechanism.

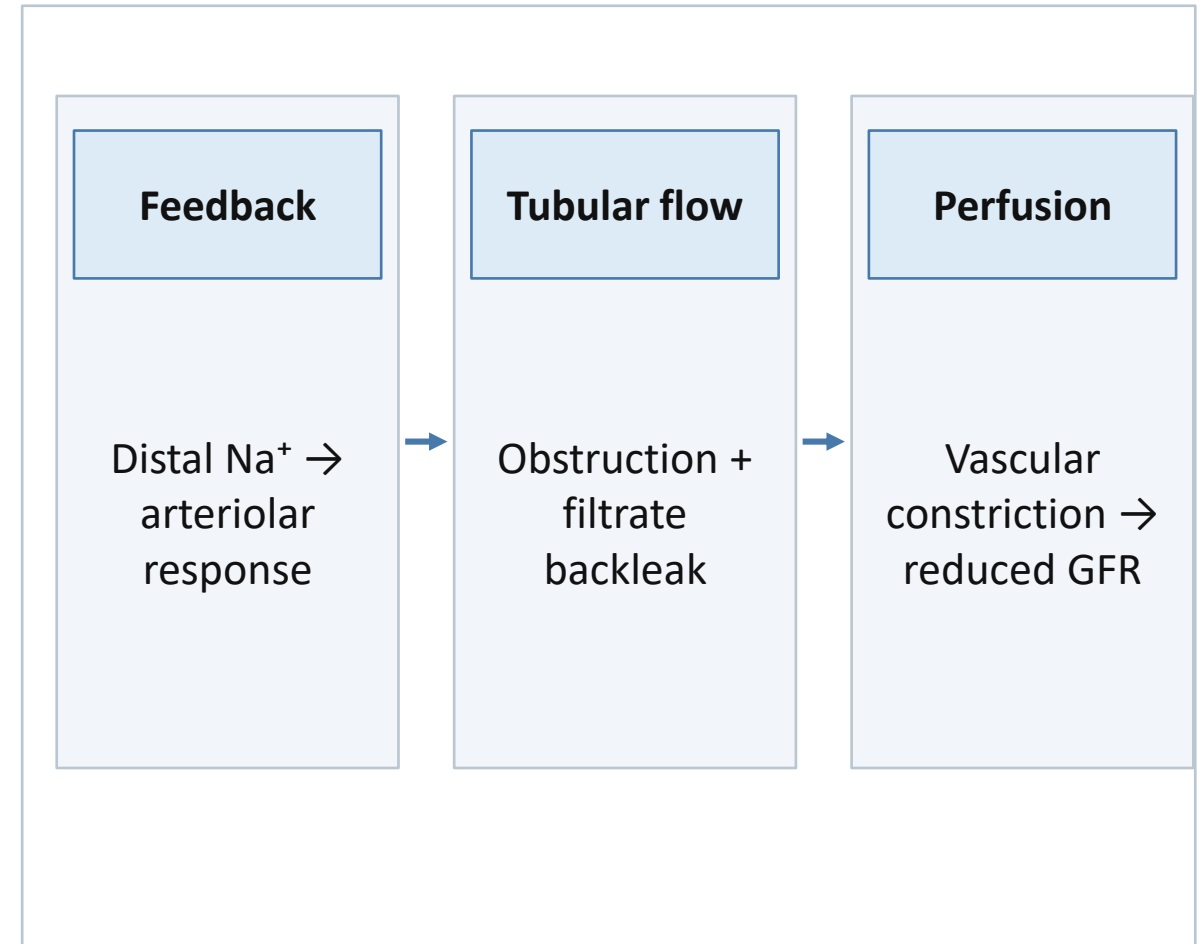
Mechanistic sequence • schematic



The GFR decline has several simultaneous causes

- Tubuloglomerular feedback narrows afferent arterioles.
- Obstruction and backleak compromise tubular flow.
- Microvascular vasoconstriction limits renal blood supply.

Three linked observations • schematic



Ischemic necrosis is characteristically patchy

- Short damaged stretches alternate with preserved tubules.
- The nephron may contain substantial intervening intact segments.
- This helps explain the capacity for repair.

Segmental involvement · original schematic, not an anatomical scale

Proximal convoluted tubule

Proximal straight tubule

INJURY

Thick ascending limb

INJURY

Distal convoluted tubule

Collecting duct

The ischemic pattern favors two nephron segments

- Proximal straight tubules are especially vulnerable.
- Ascending limbs of the loop of Henle are also affected.
- Necrosis is typically discontinuous rather than confluent.

Segmental involvement · original schematic, not an anatomical scale

Proximal convoluted tubule

Proximal straight tubule

INJURY

Thick ascending limb

INJURY

Distal convoluted tubule

Collecting duct

Toxic injury often centers on proximal convoluted tubules

- Many toxins produce extensive proximal convoluted tubular necrosis.
- Some toxic injuries also affect distal tubules and ascending limbs.
- The specific distribution varies by agent.

Segmental involvement · original schematic, not an anatomical scale

Proximal convoluted tubule

INJURY

Proximal straight tubule

Thick ascending limb

Distal convoluted tubule

Collecting duct

Ischemic and toxic patterns are not identical

- Distribution, not merely presence of necrosis, is informative.
- Ischemic injury tends to be discontinuous in specific segments.
- Some nephrotoxins cause more extensive proximal injury.

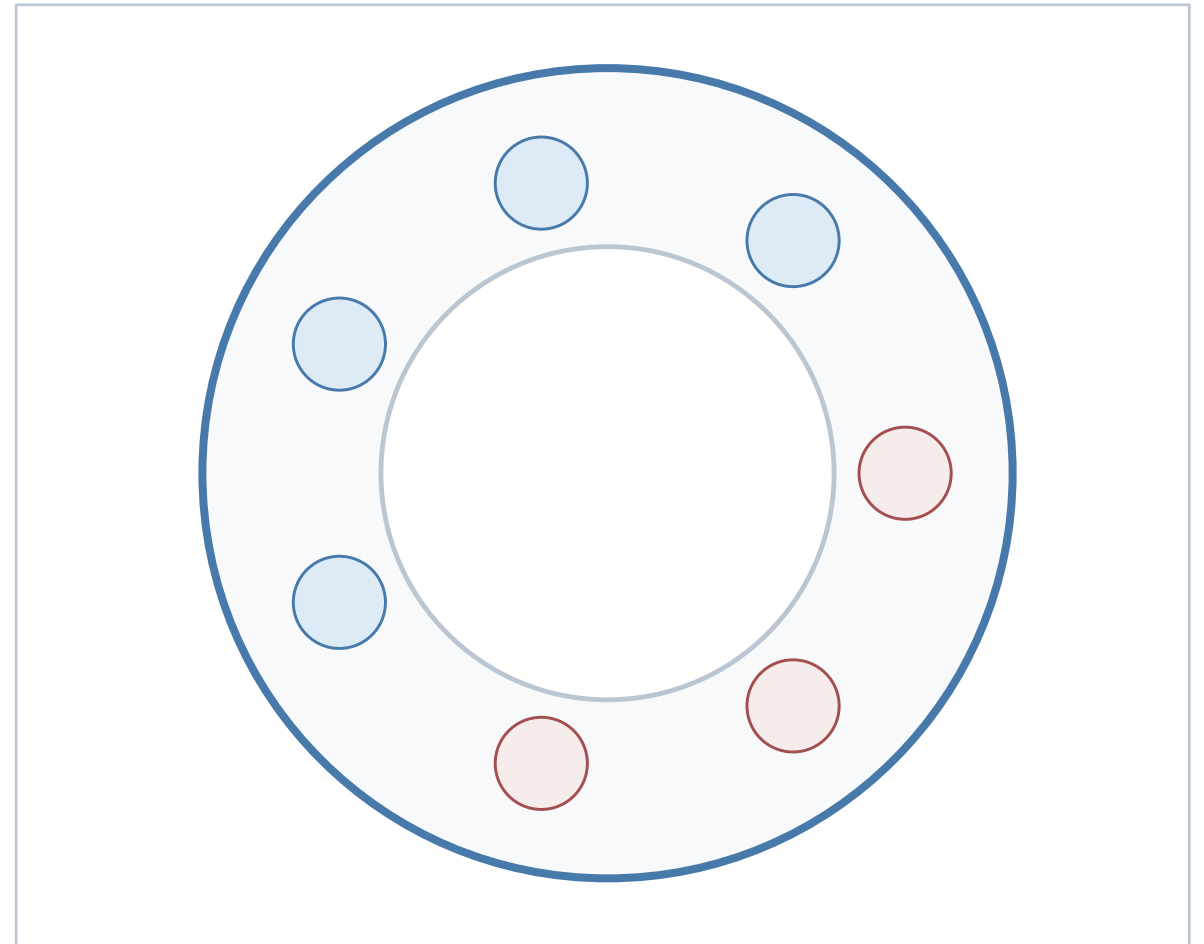
Comparison · conceptual

Ischemic ATI	Toxic ATI
Patchy lesions	Often prominent PCT necrosis
Proximal straight segment	Agent-dependent specificity
Ascending limb	May involve ascending limb

Necrosis is one manifestation of epithelial injury

- Tubular epithelial abnormalities vary in extent and severity.
- Severe injury may produce overt epithelial necrosis.
- Absence of dramatic necrosis does not exclude functional ATI.

Tubule cross-section • schematic only; Not a micrograph

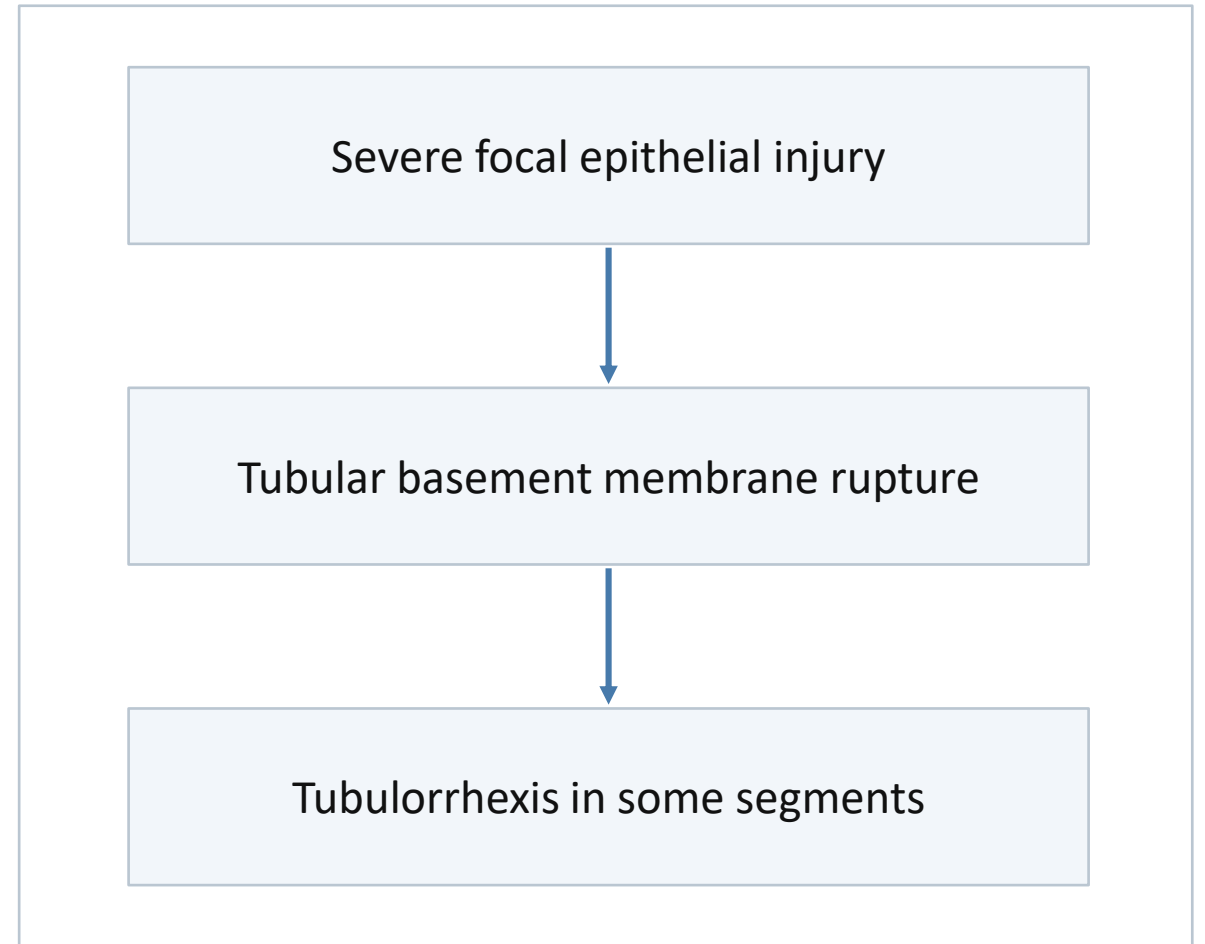


Basement membrane and tubular lumen

Tubulorrhexis denotes basement membrane rupture

- The morphology description includes focal tubular rupture.
- Injured segments may lose basement membrane integrity.
- Preserved segments provide a scaffold for subsequent repair.

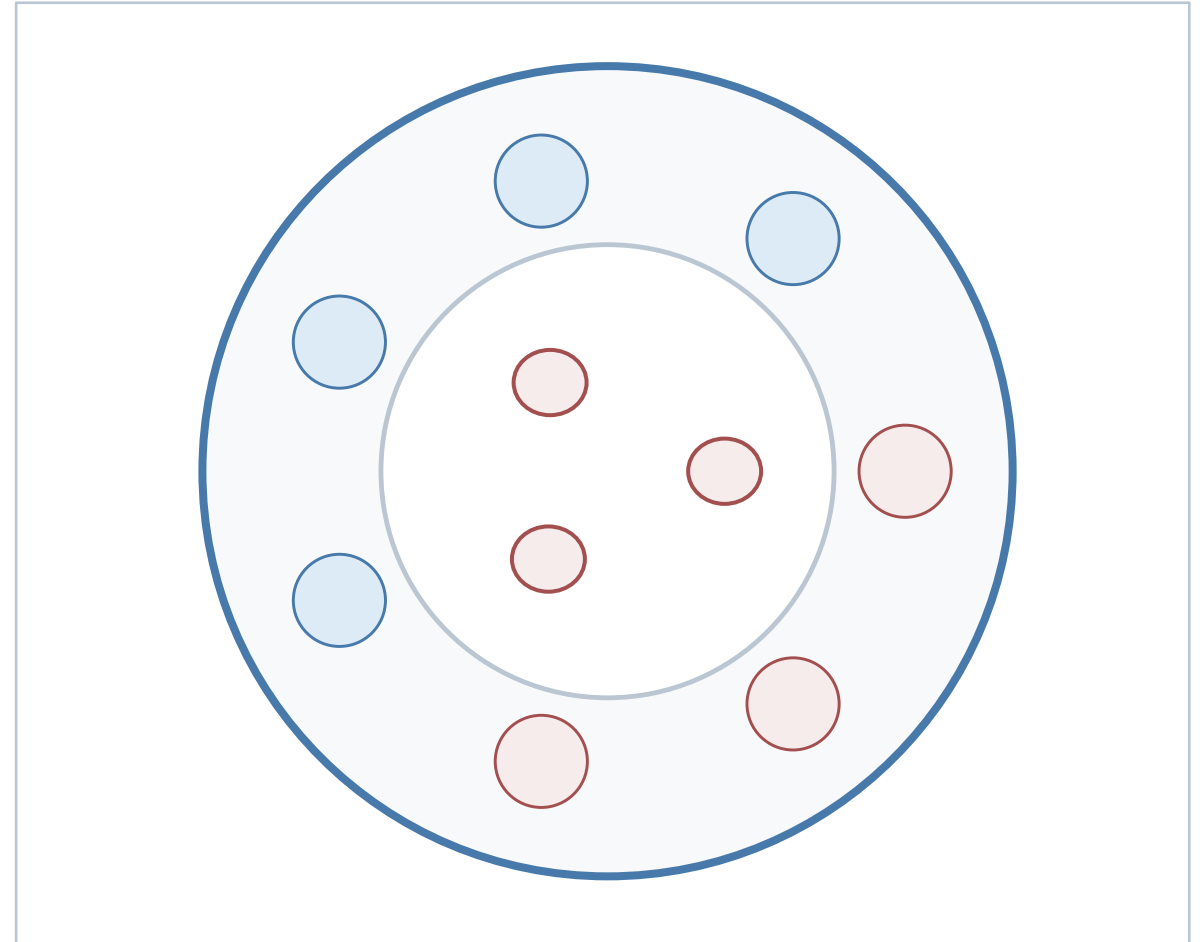
Mechanistic sequence • schematic



Sloughed epithelial cells appear within the lumen

- Necrotic cells detach from the basement membrane.
- Luminal cellular debris is a conspicuous lesion in examples.
- This structural injury also has an obstructive consequence.

Tubule cross-section • schematic only; Not a micrograph



Detached epithelial cells

Distal tubules and collecting ducts contain casts

- Luminal casts are described in both major ATI patterns.
- The distal convoluted tubule and collecting duct are common sites.
- Casts provide a morphological correlate of impaired tubular flow.

Segmental involvement · original schematic, not an anatomical scale

Proximal convoluted tubule

Proximal straight tubule

Thick ascending limb

Distal convoluted tubule

CASTS

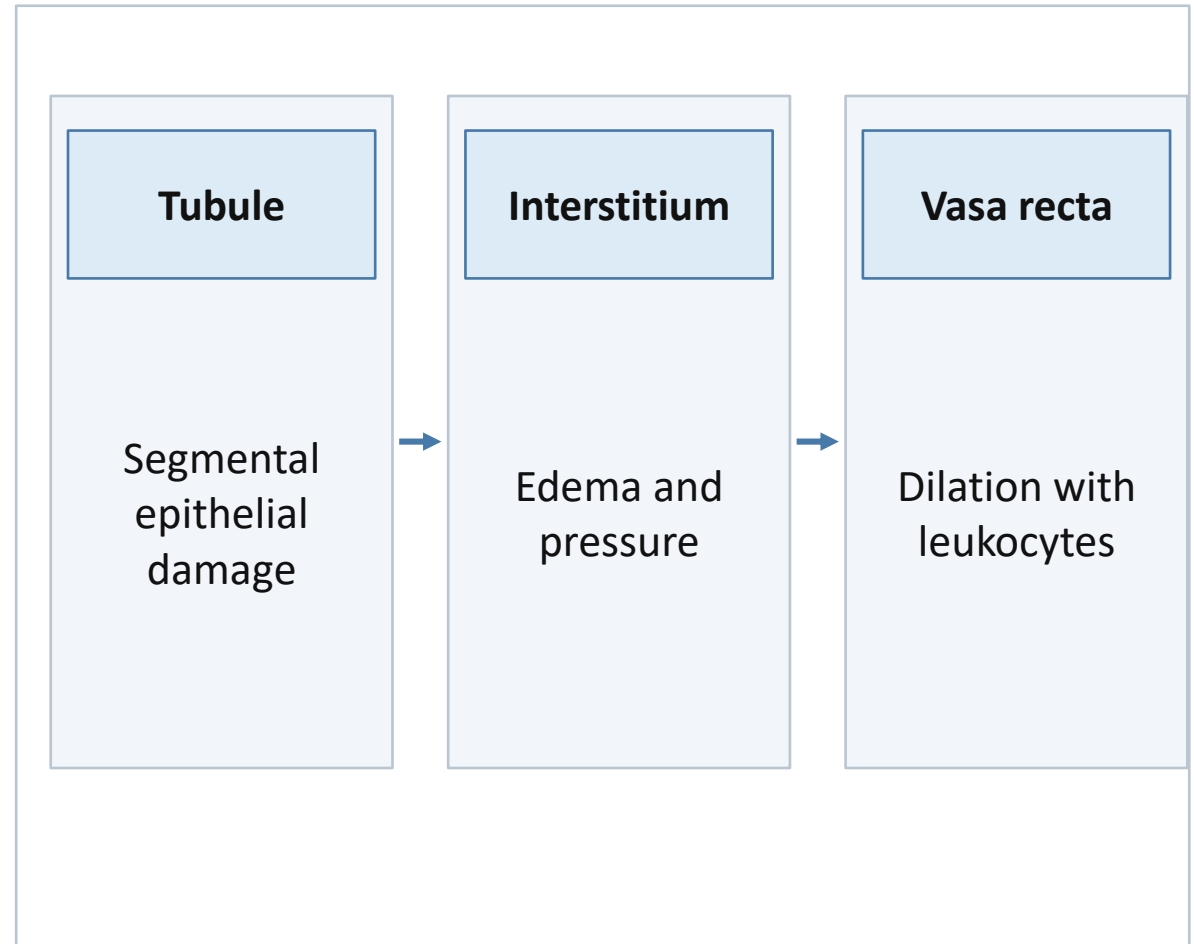
Collecting duct

CASTS

Ischemic ATI also affects the interstitium and vasa recta

- Interstitial edema is a common associated finding.
- Leukocytes may accumulate in dilated vasa recta.
- These abnormalities reflect injury beyond epithelial cells alone.

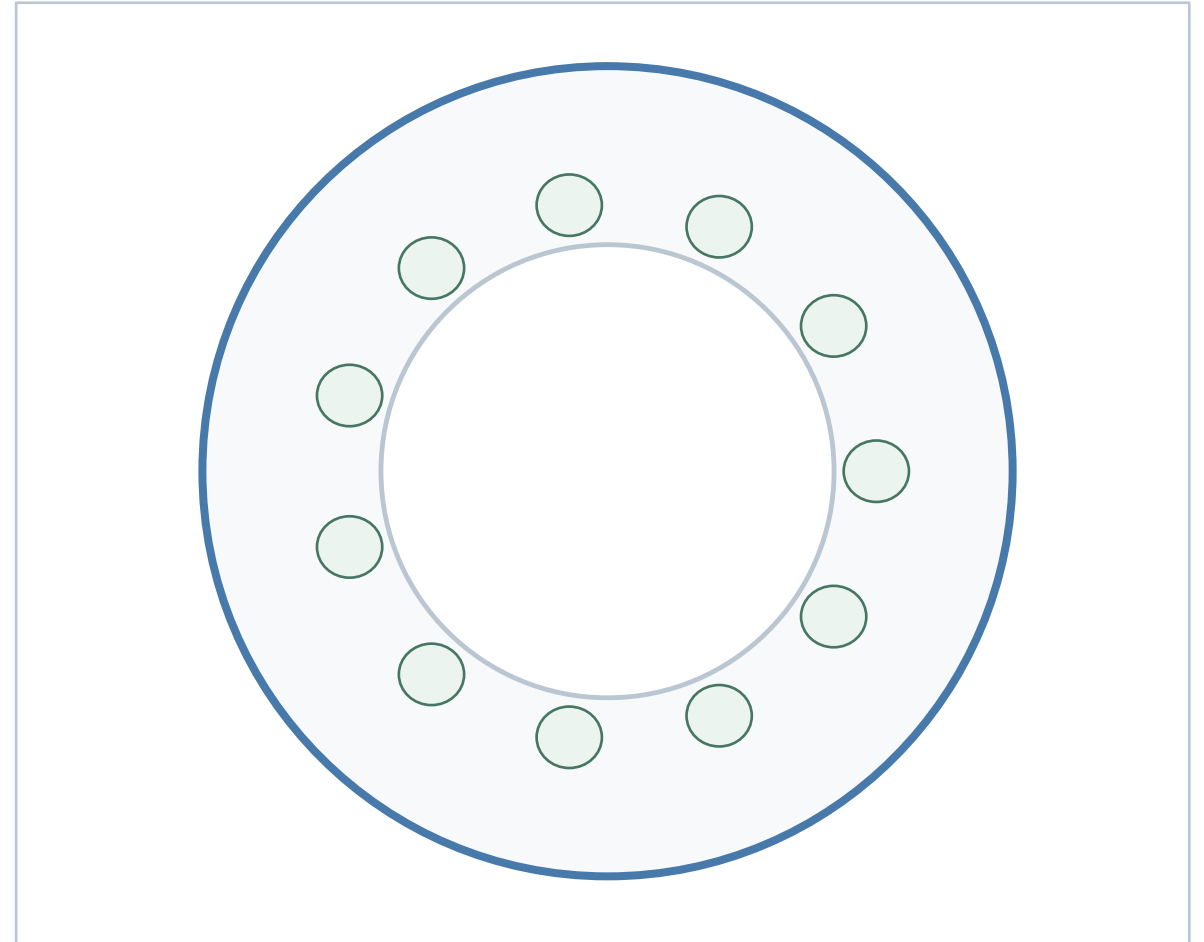
Three linked observations • schematic



Regeneration has identifiable morphologic features

- Reparative lining cells may be flattened.
- Hyperchromatic nuclei and mitotic figures can be present.
- With complete repair, recognizable damage may disappear.

Tubule cross-section • schematic only; Not a micrograph

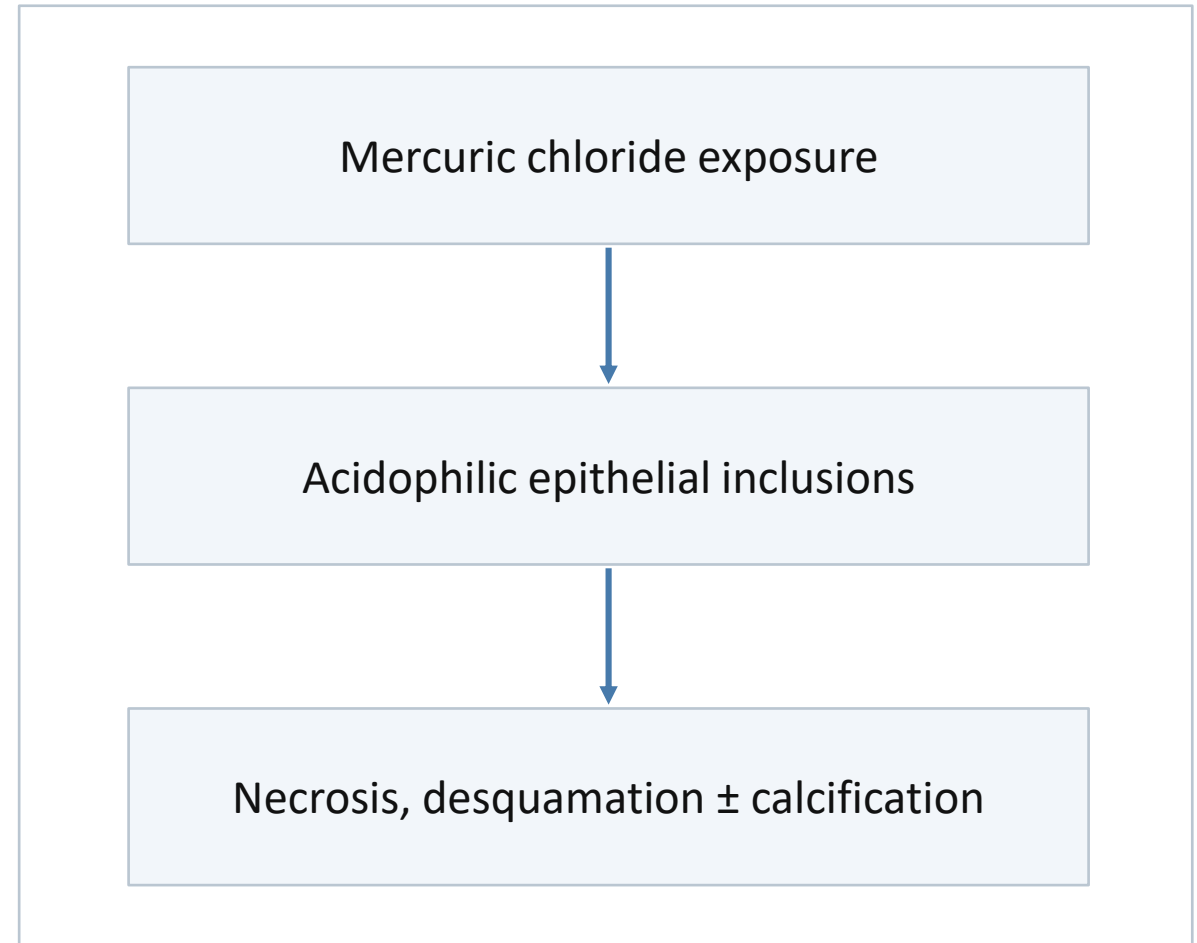


Re-epithelialization with surviving cells

Mercuric chloride can produce distinctive toxic changes

- Affected cells may contain large acidophilic inclusions.
- Severely injured cells become necrotic and desquamate.
- Some detached cells subsequently calcify.

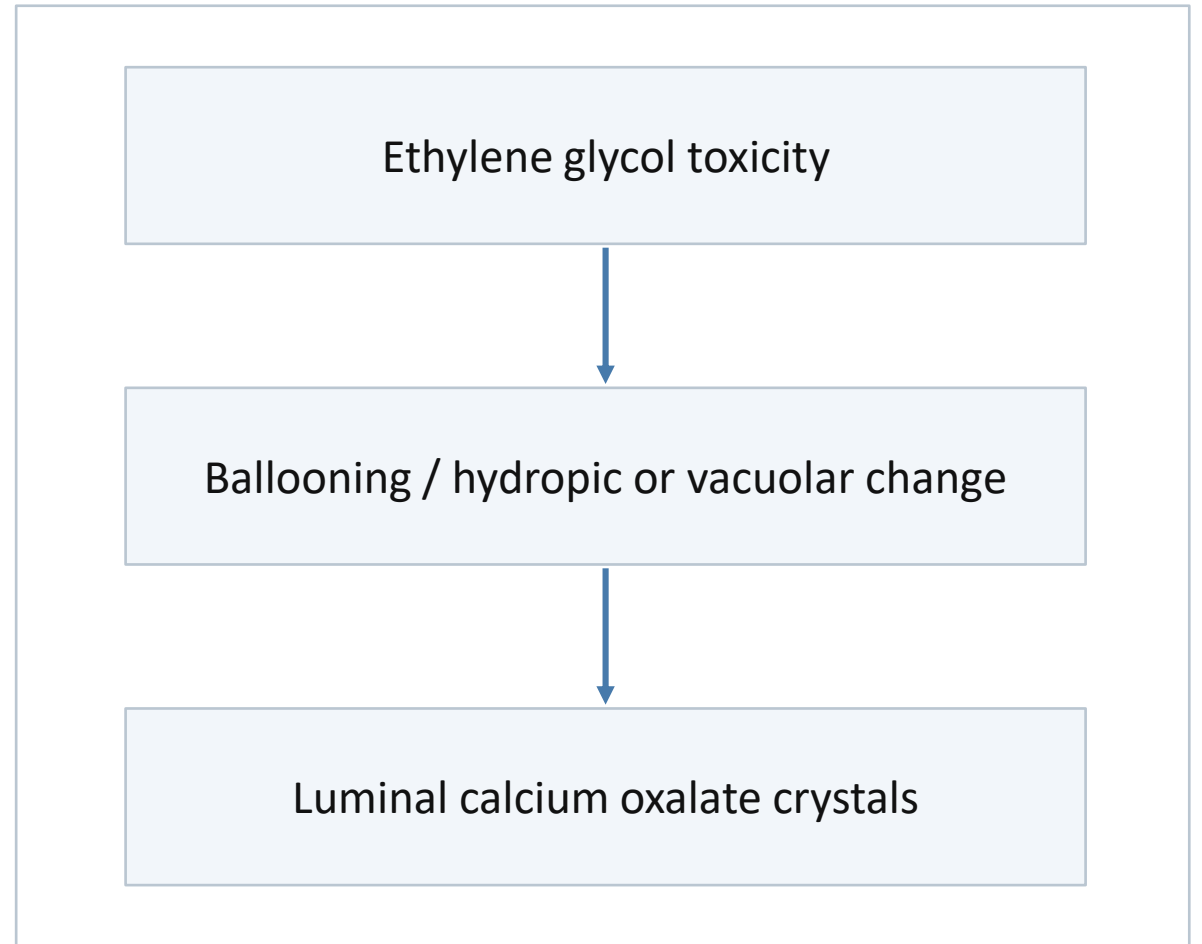
Mechanistic sequence • schematic



Ethylene glycol injury can show crystal-associated damage

- Proximal cells may become ballooned or vacuolated.
- Hydropic change is part of the described pattern.
- Calcium oxalate crystals can occur in tubular lumens.

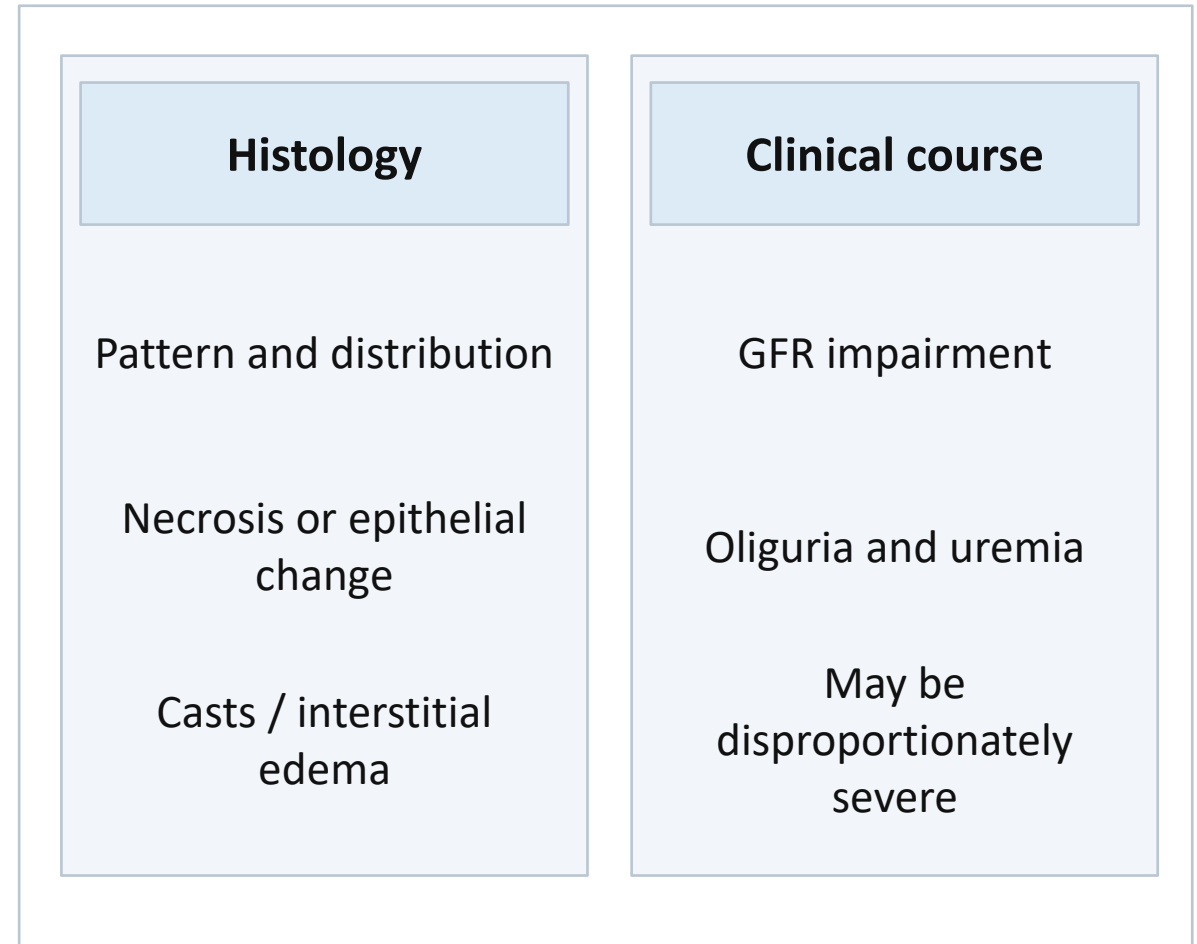
Mechanistic sequence • schematic



Histologic severity has imperfect clinical correlation

- The source explicitly cautions against morphologic–clinical equivalence.
- Marked renal dysfunction can occur with limited visible necrosis.
- Reported tissue changes must be integrated with renal function.

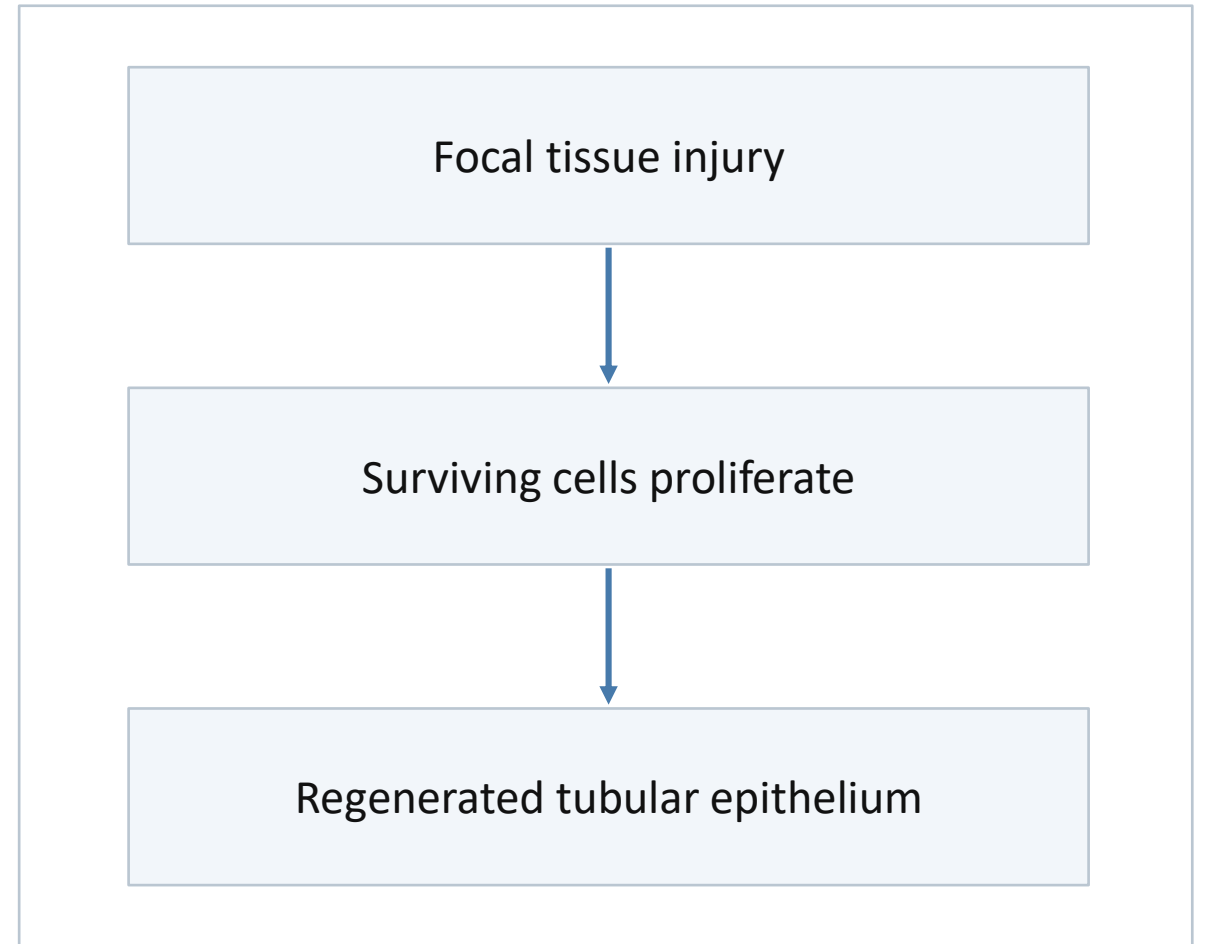
Comparison · conceptual



Successful repair can erase visible injury

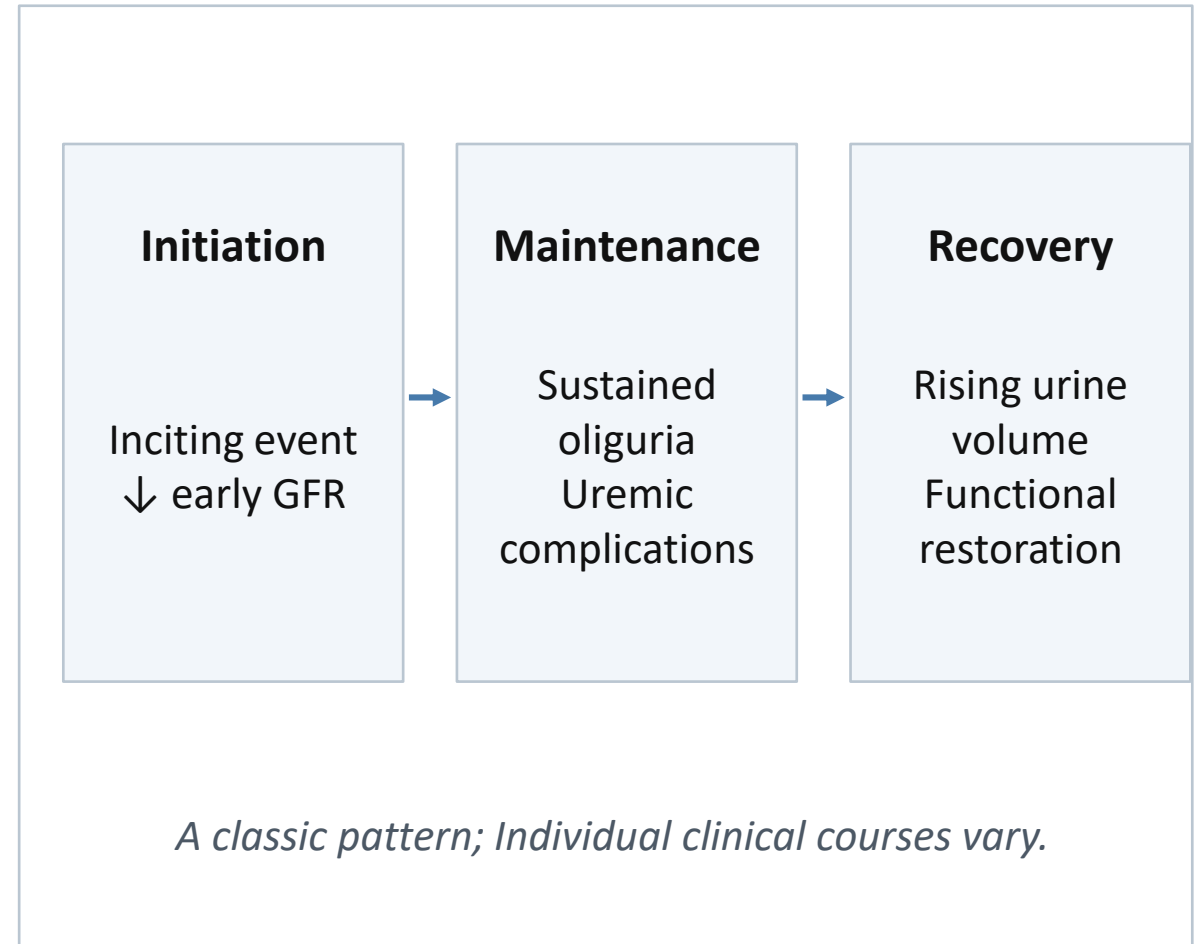
- In surviving tubules, epithelial proliferation repopulates surfaces.
- Tubular continuity and differentiation recover over time.
- Eventually, there may be no residual histologic damage.

Mechanistic sequence • schematic



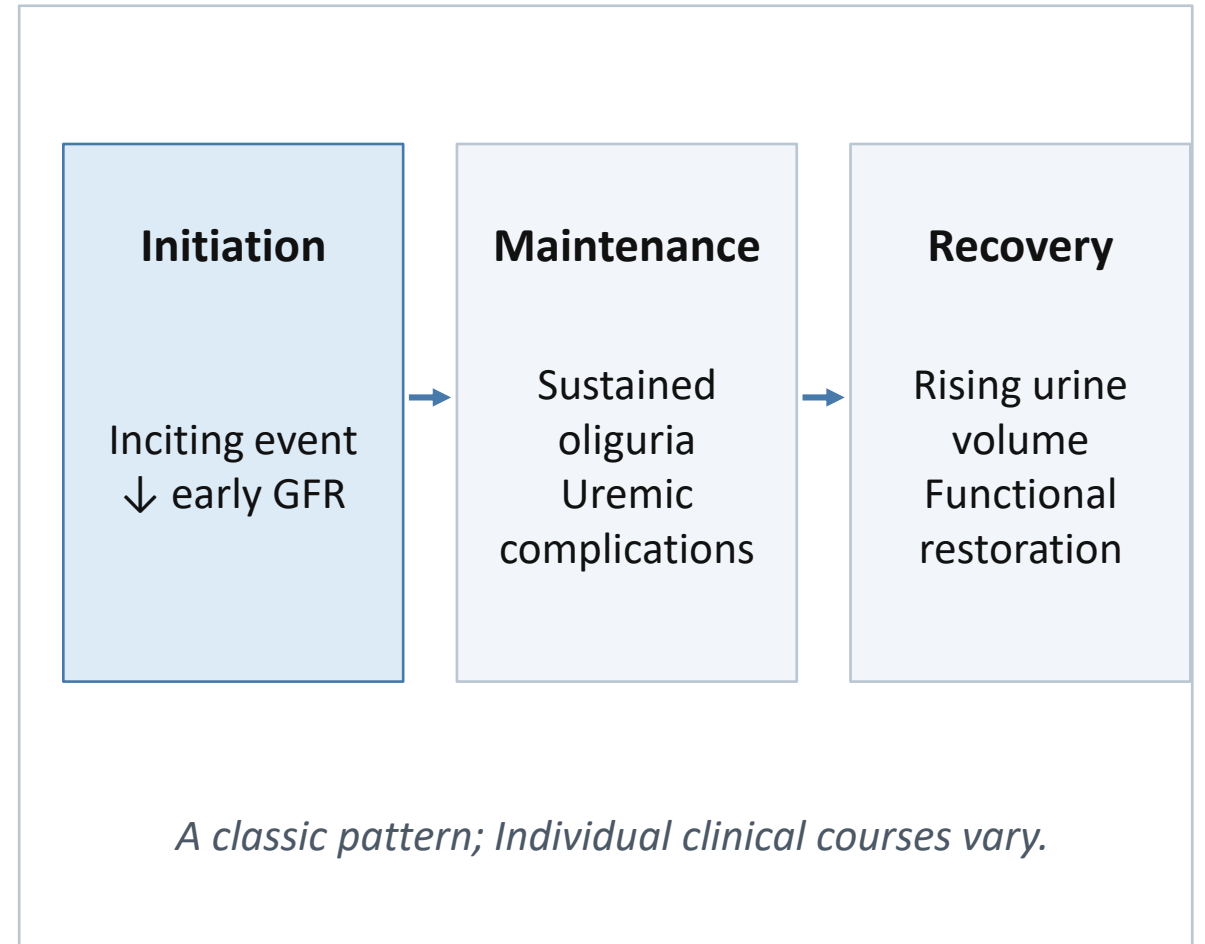
The classic clinical course has three phases

- The illustrative course into initiation, maintenance, and recovery.
- Clinical evolution is variable rather than universally stereotyped.
- Functional recovery may lag behind improving urine output.



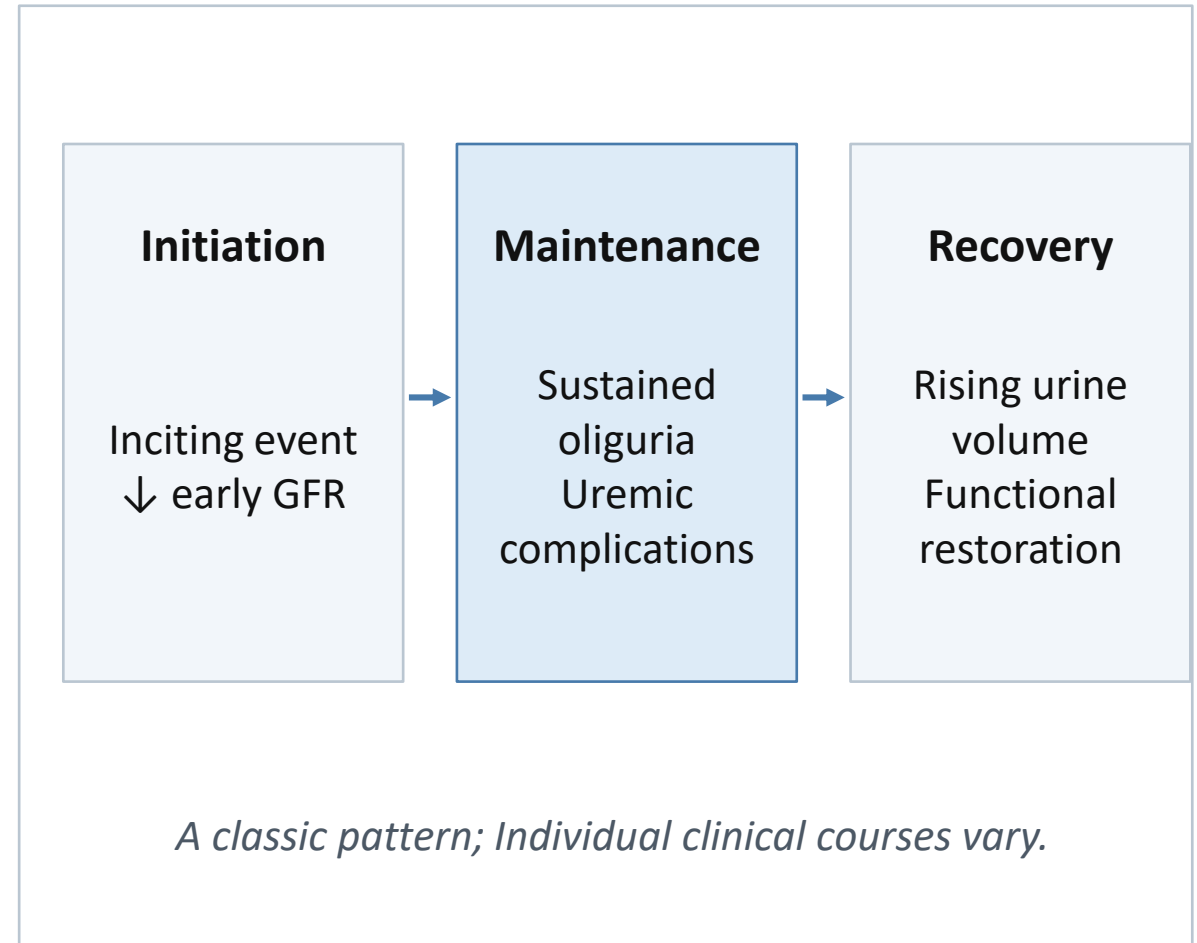
Initiation follows the precipitating event

- An initial period of about 36 hours.
- A modest fall in urine output and rise in BUN may be evident.
- Transient hypoperfusion and falling GFR can explain early oliguria.



Maintenance features persistent oliguria

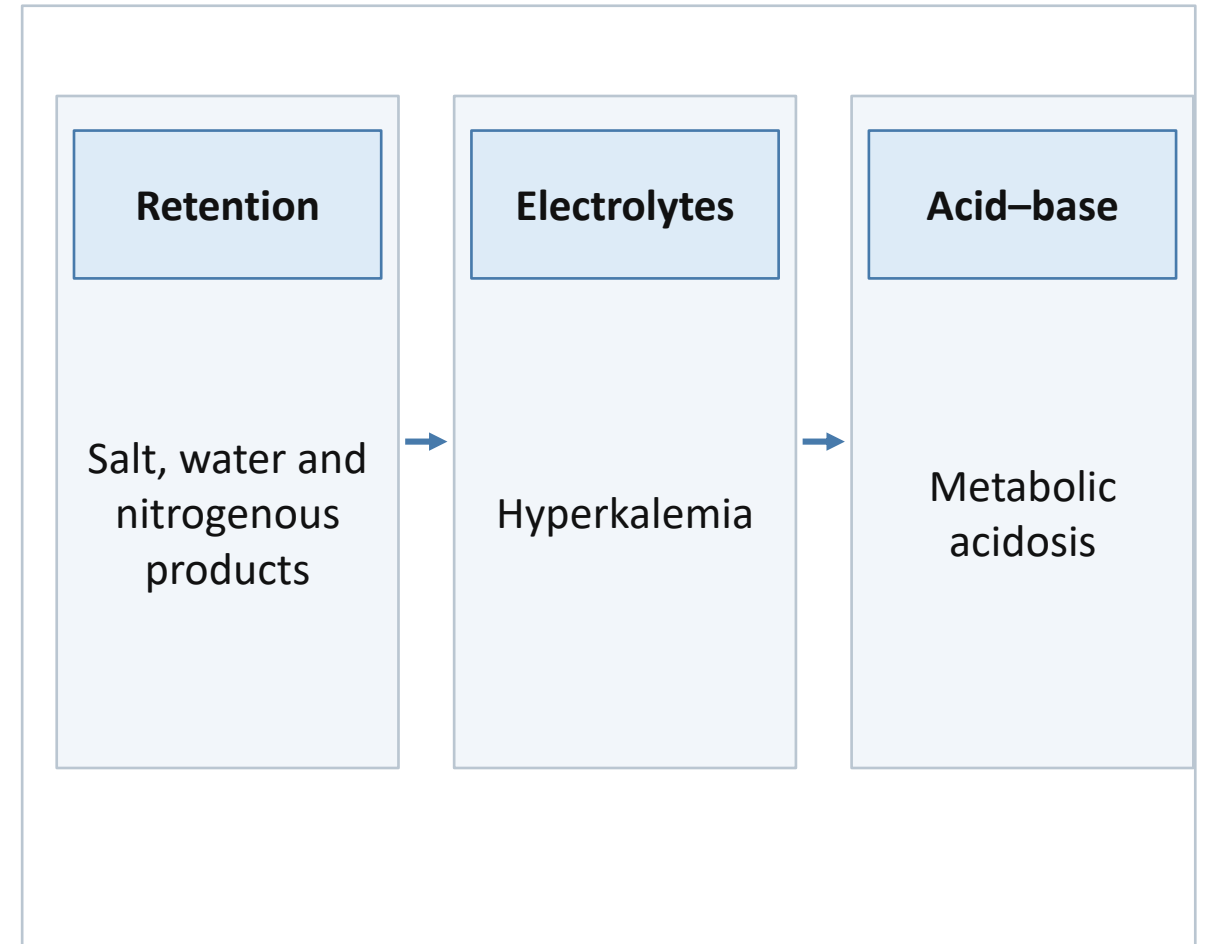
- The source gives an illustrative urine output of 40–400 mL/day.
- Urine flow remains markedly decreased during this period.
- Salt and water retention contribute to the clinical burden.



Maintenance produces systemic metabolic complications

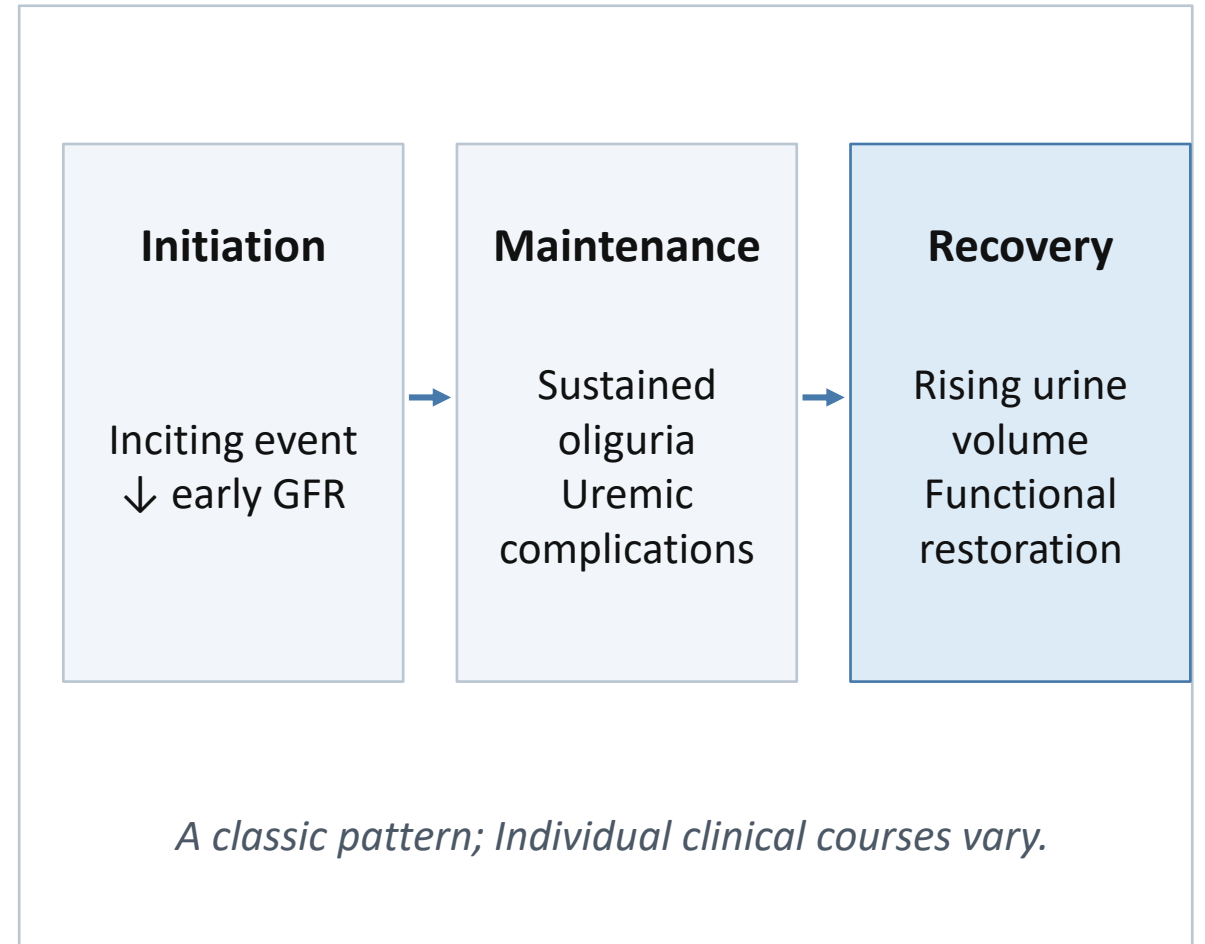
- Blood urea nitrogen continues to rise.
- Hyperkalemia and metabolic acidosis may develop.
- Uremic manifestations reflect sustained renal failure.

Three linked observations • schematic



Recovery begins with increasing urine volume

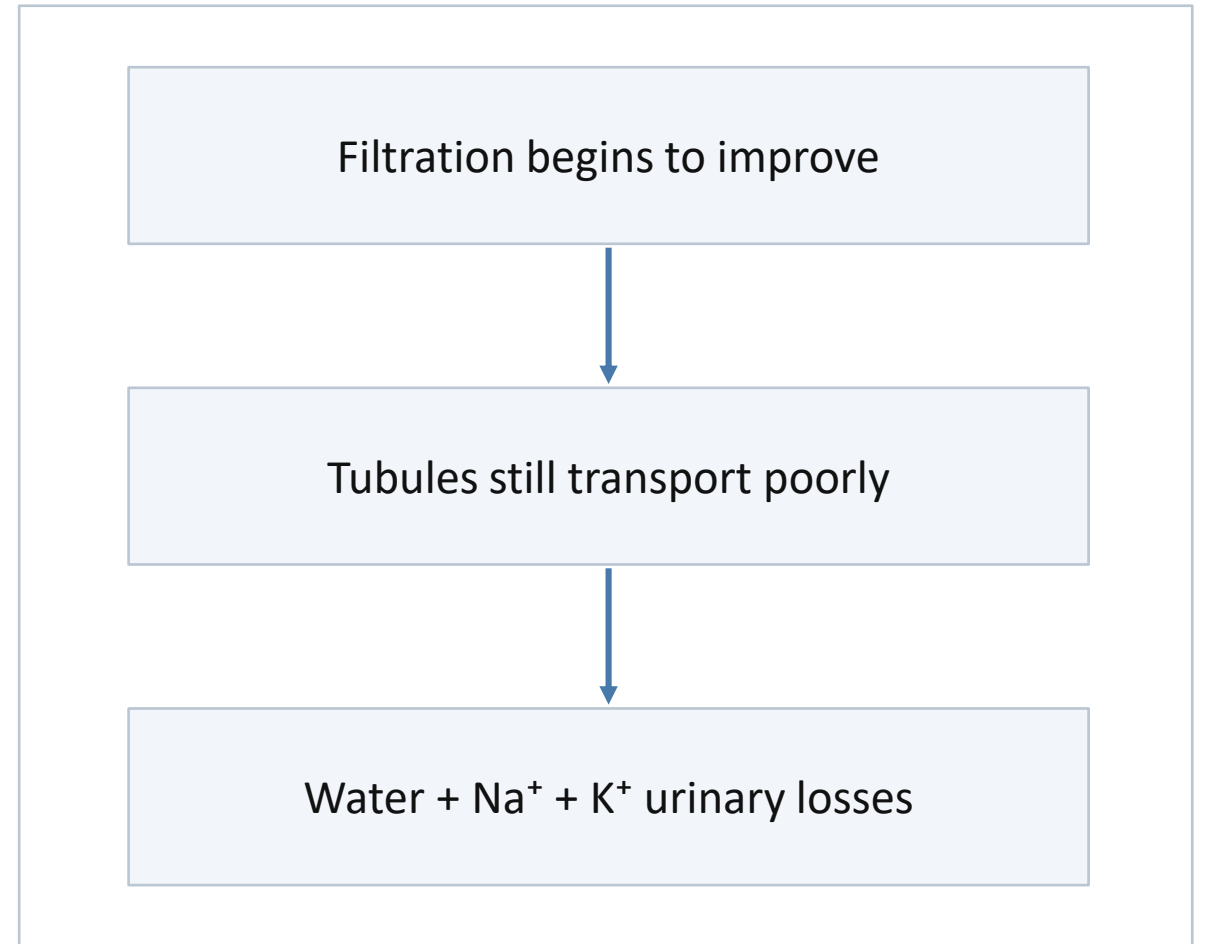
- The source describes progressive diuresis, sometimes to 3 L/day.
- Urine production may recover before full transport function.
- A rising urine output is therefore not synonymous with complete repair.



Early recovery may cause substantial solute loss

- Damaged tubules still reabsorb sodium and potassium inefficiently.
- Large volumes of water and solutes may be lost in urine.
- This explains why the diuretic phase requires attention to losses.

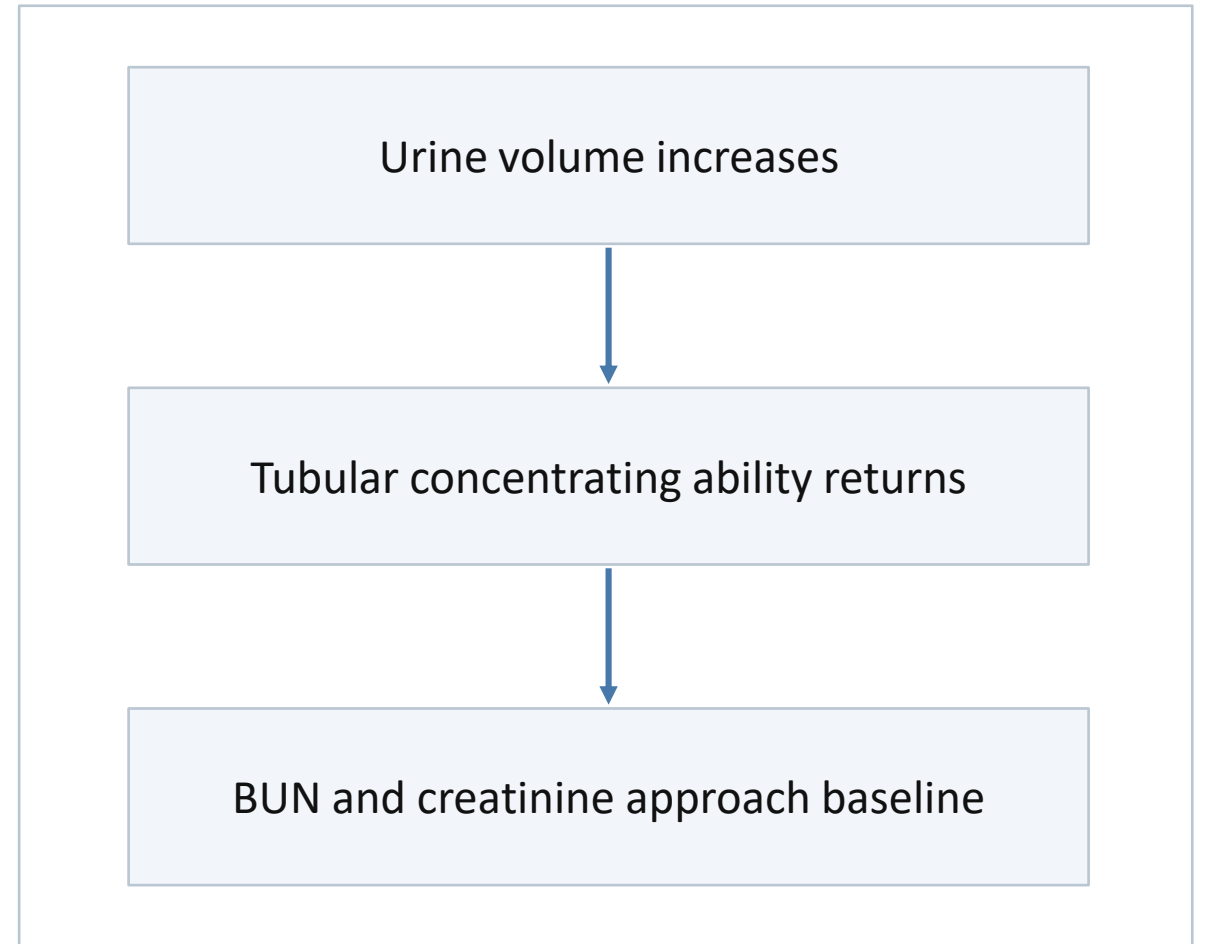
Mechanistic sequence • schematic



Biochemical recovery can lag behind diuresis

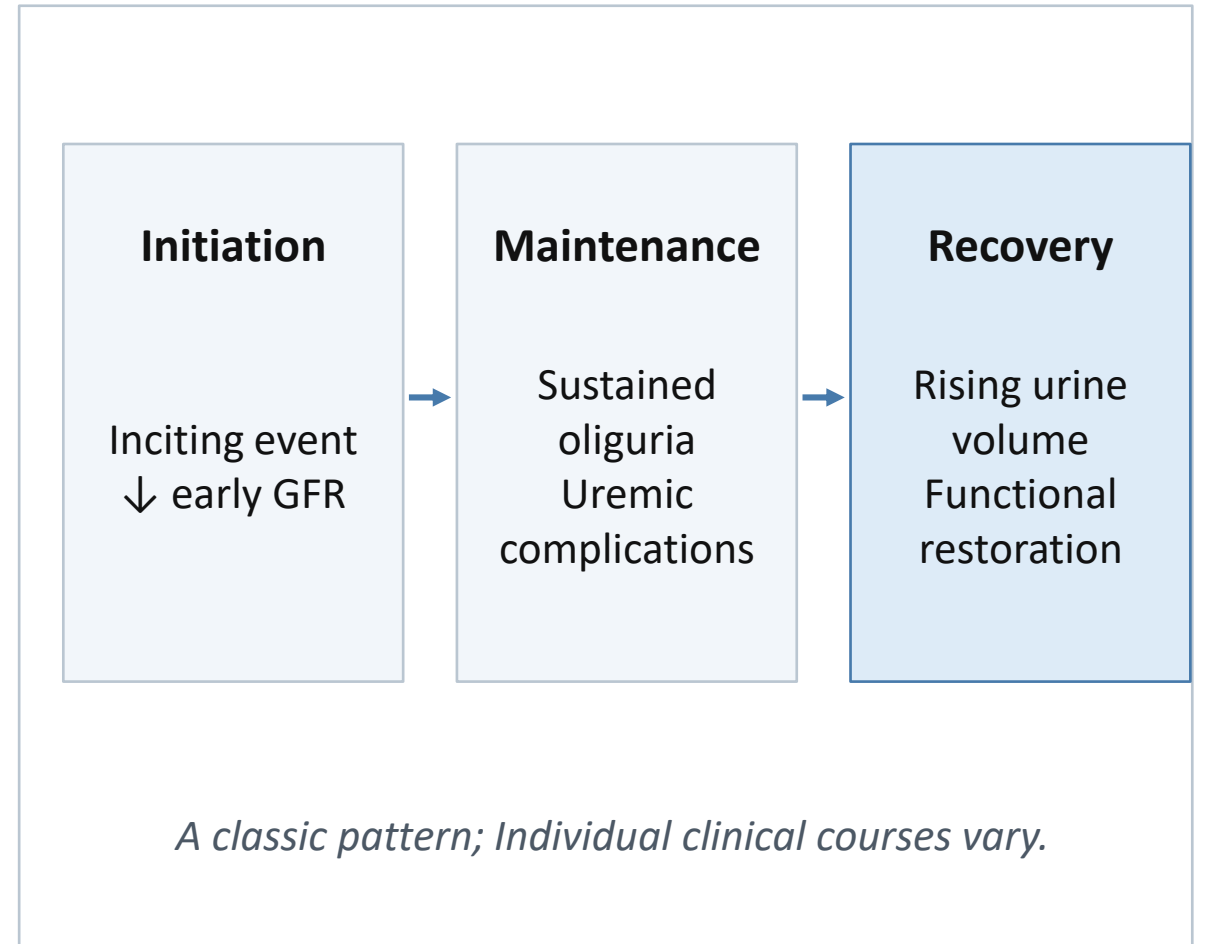
- Blood urea nitrogen and creatinine gradually normalize.
- Tubular concentrating capacity improves progressively.
- Different aspects of nephron function recover at different rates.

Mechanistic sequence • schematic



Residual functional defects may outlast acute injury

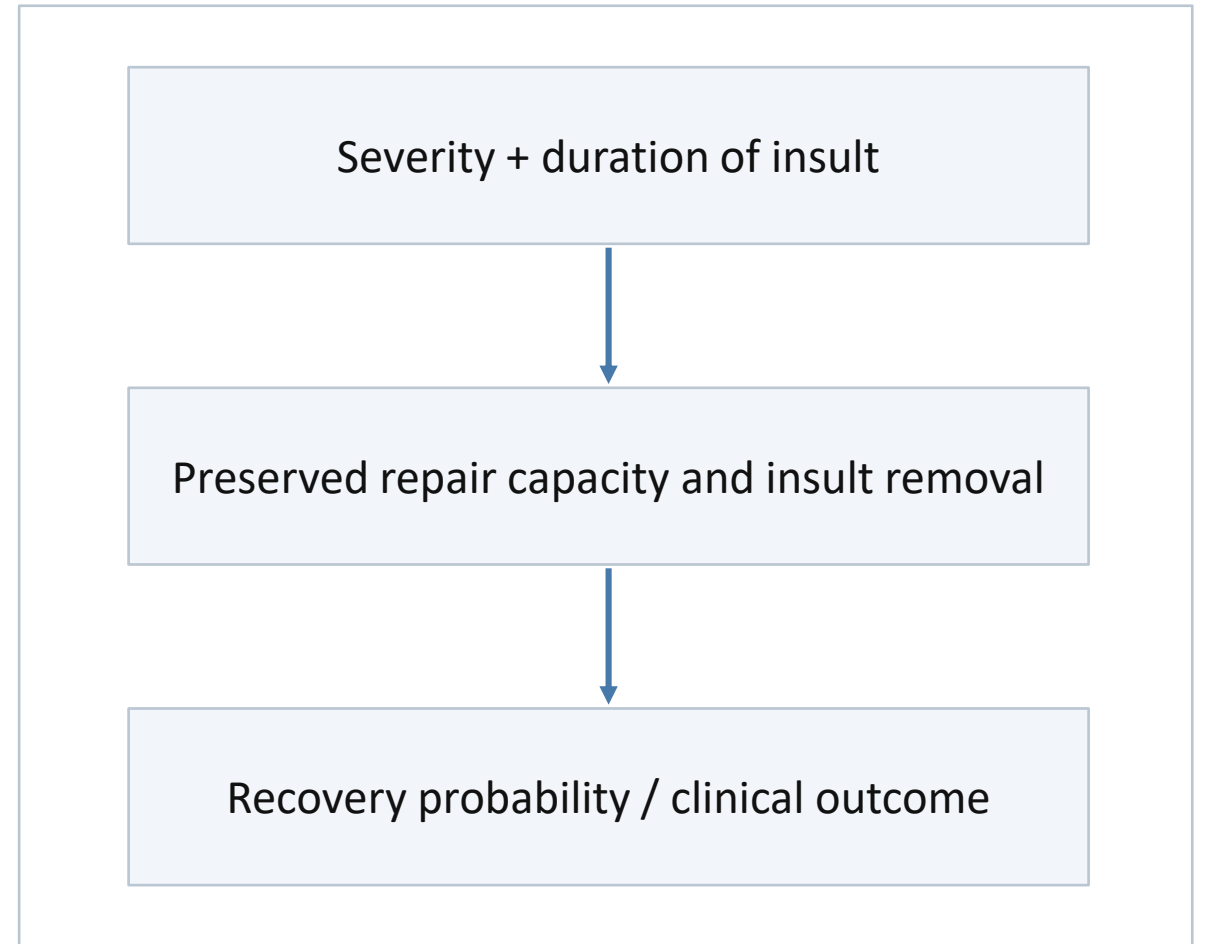
- Subtle tubular impairment may persist for months.
- The textbook also notes increased infection vulnerability during recovery.
- Most patients reaching recovery ultimately regain function.



Outcome depends on the initiating insult

- Magnitude and duration determine how much epithelium survives.
- Reversal of the cause supports regeneration.
- Concurrent organ injury changes the prognosis substantially.

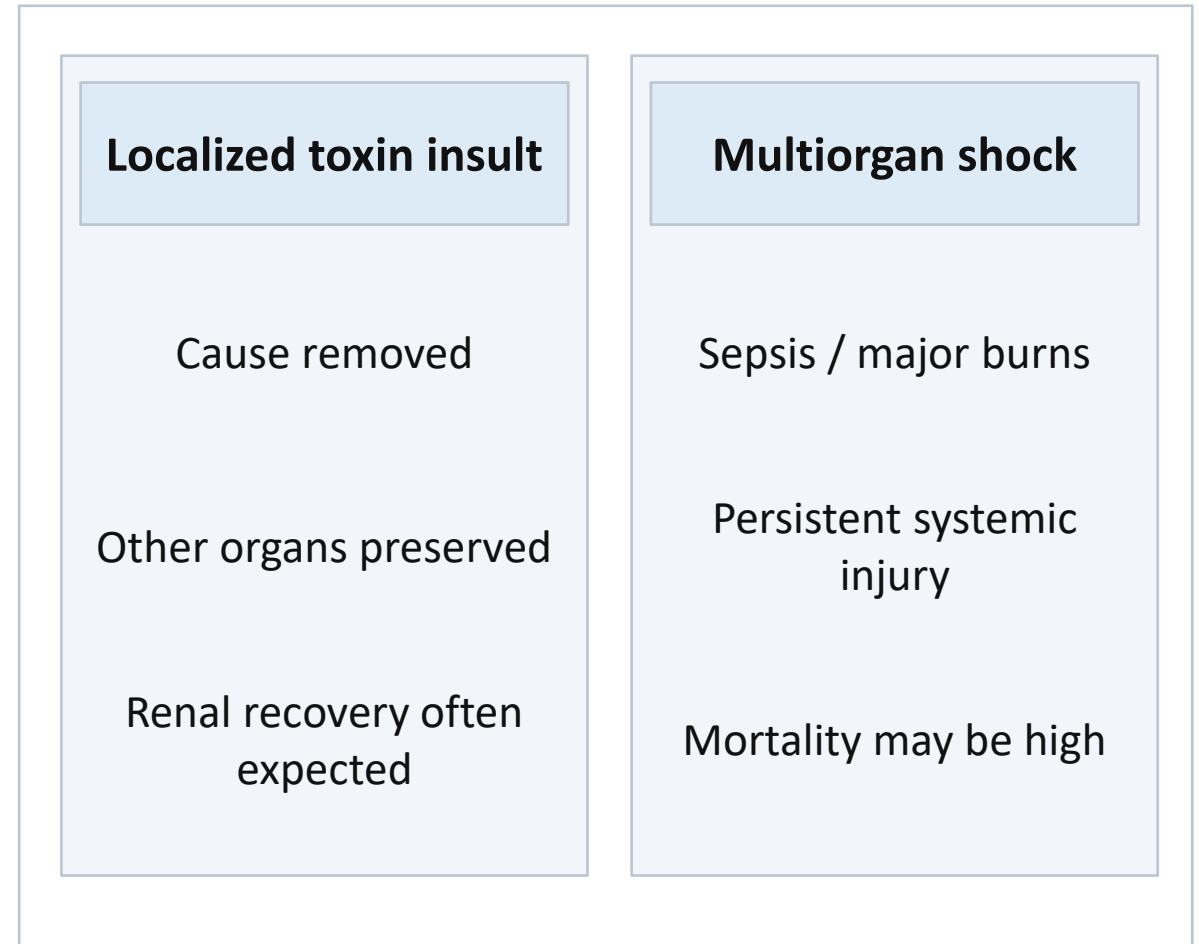
Mechanistic sequence • schematic



Renal repair and patient survival are distinct outcomes

- Nephrotoxic ATI may resolve if other organs are not severely damaged.
- High renal recovery among survivors of the precipitating event.
- Sepsis, extensive burns, and multiorgan failure greatly worsen survival.

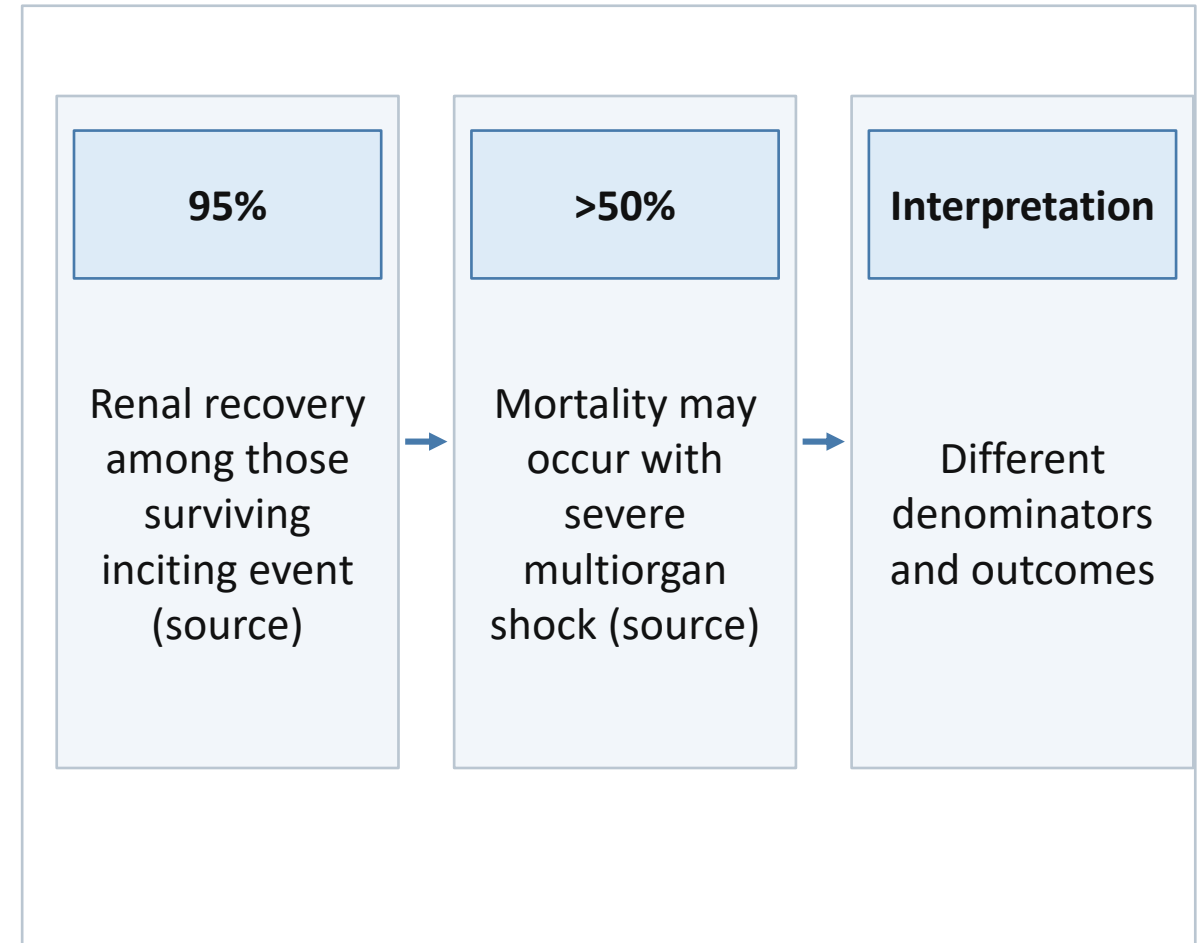
Comparison · conceptual



Interpret prognosis figures in their clinical context

- The source states 95% recovery with supportive care among patients who survive the precipitating event.
- It also reports mortality exceeding 50% in some severe shock or multiorgan failure settings.
- These figures describe different groups and endpoints; Do not compare them directly.

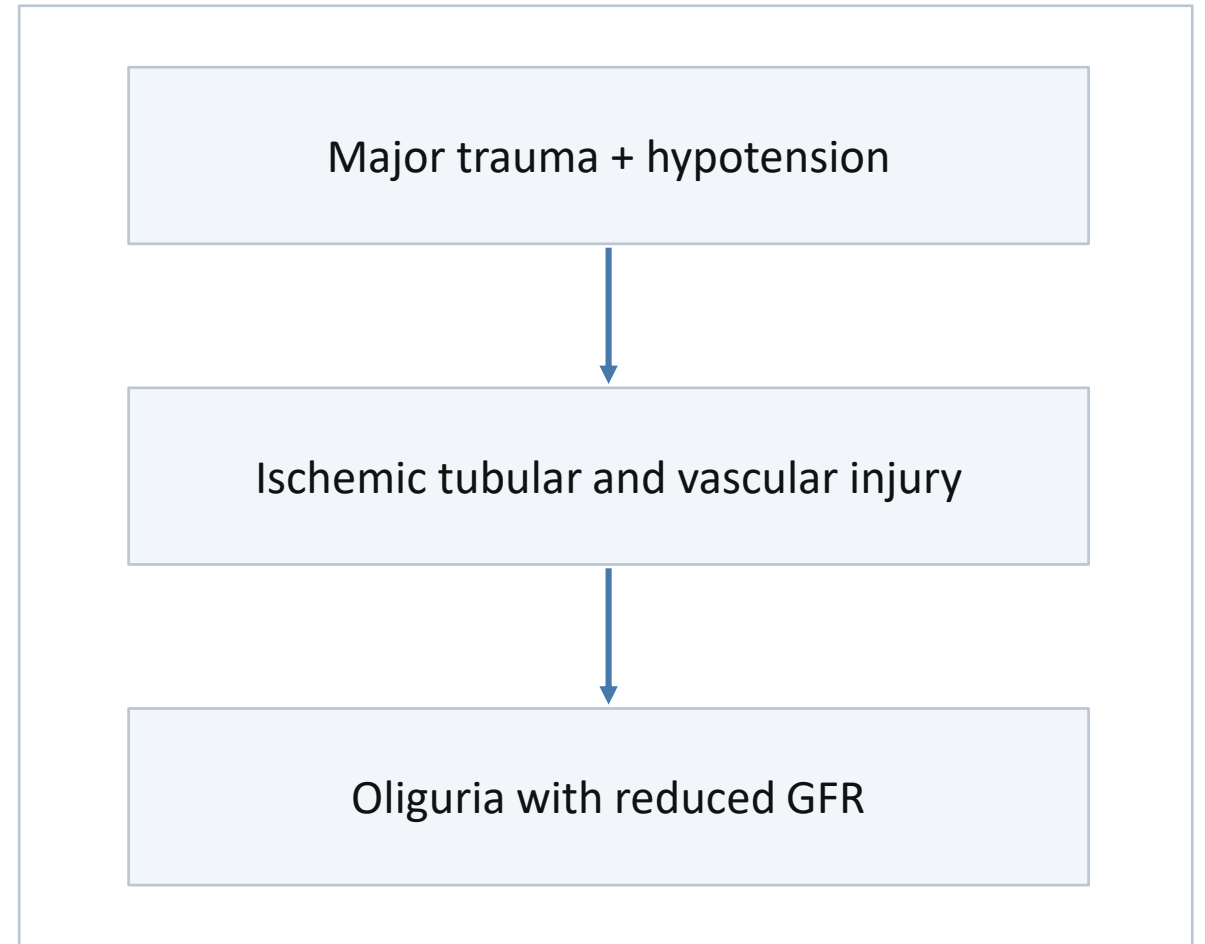
Three linked observations • schematic



Application: Hypotension with new oliguria

- A patient becomes hypotensive after major trauma.
- Urine output subsequently falls and renal indices worsen.
- Ischemic ATI is a plausible mechanism in this source-based scenario.

Mechanistic sequence • schematic



Application: Interpreting a toxic exposure

- A patient develops AKI after exposure to a tubular toxin.
- Predominant proximal convoluted tubular injury would fit many toxic patterns.
- The exact morphologic picture depends on the offending agent.

Segmental involvement · original schematic, not an anatomical scale

Proximal convoluted tubule

INJURY

Proximal straight tubule

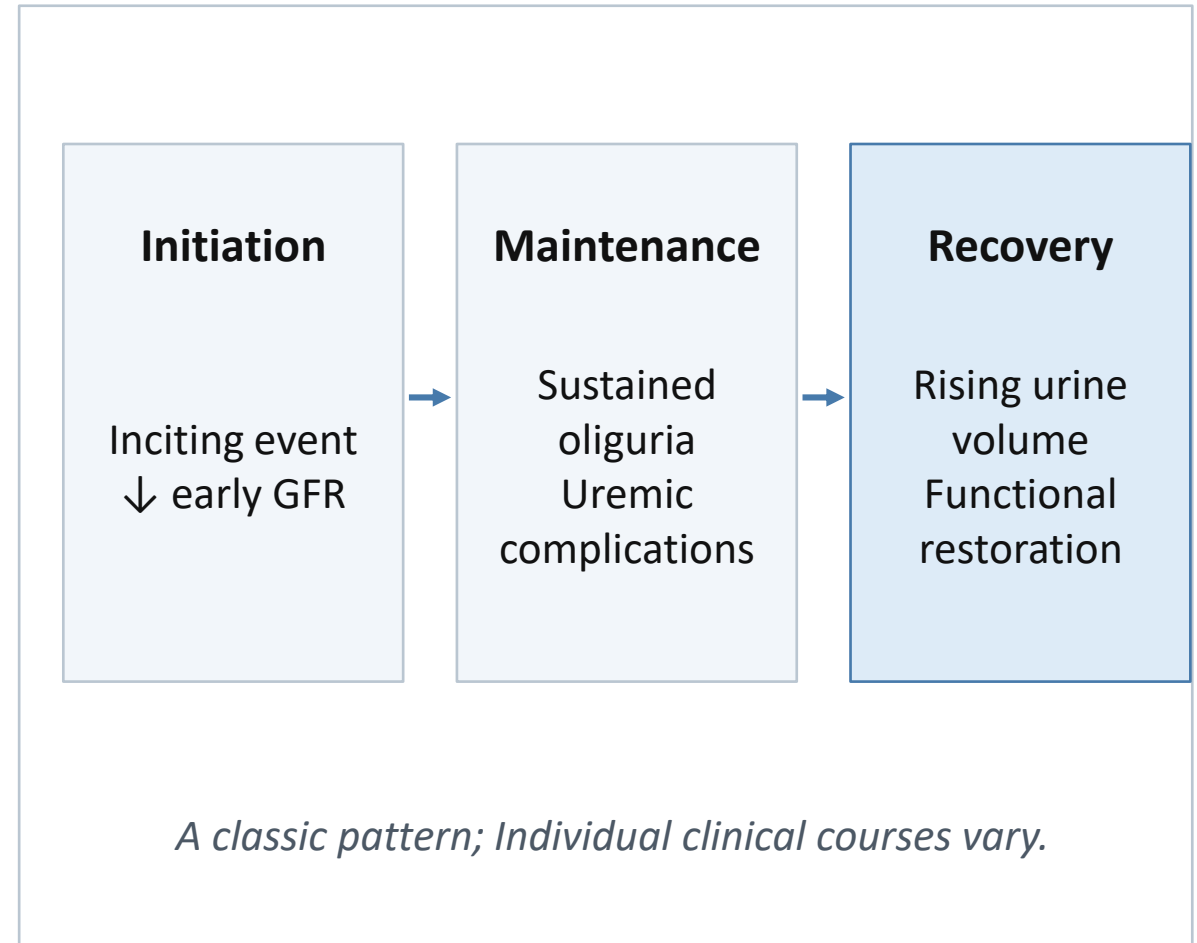
Thick ascending limb

Distal convoluted tubule

Collecting duct

Application: Increasing urine output after ATI

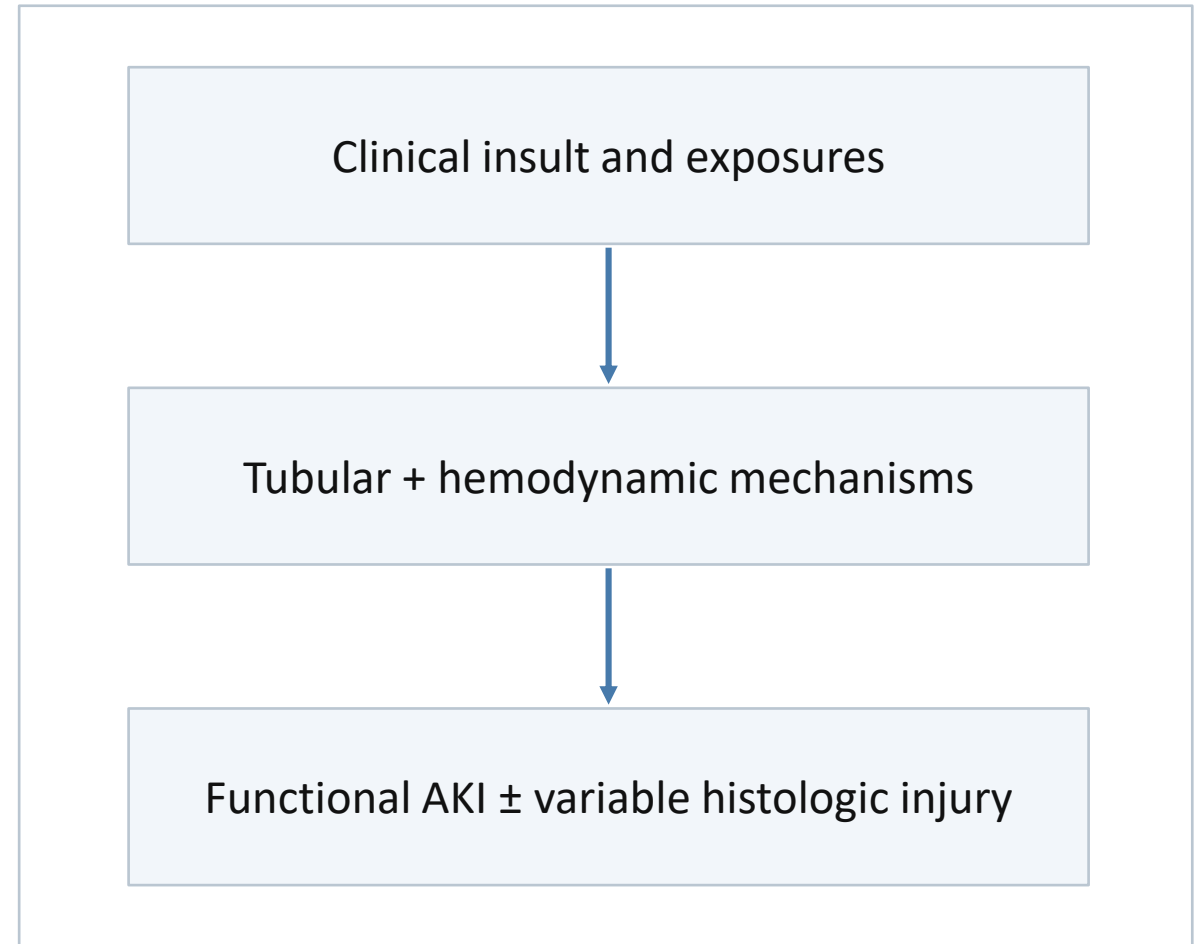
- A recovering patient begins to produce large urine volumes.
- Persistent tubular transport defects may cause water and electrolyte losses.
- Diuresis must be interpreted as a phase of recovery, not instant normalization.



Synthesize the mechanism before reading the biopsy

- The initiating context suggests ischemic, toxic, or mixed ATI.
- Tubular transport changes and hemodynamics explain reduced GFR.
- Morphology may support ATI without closely predicting severity.

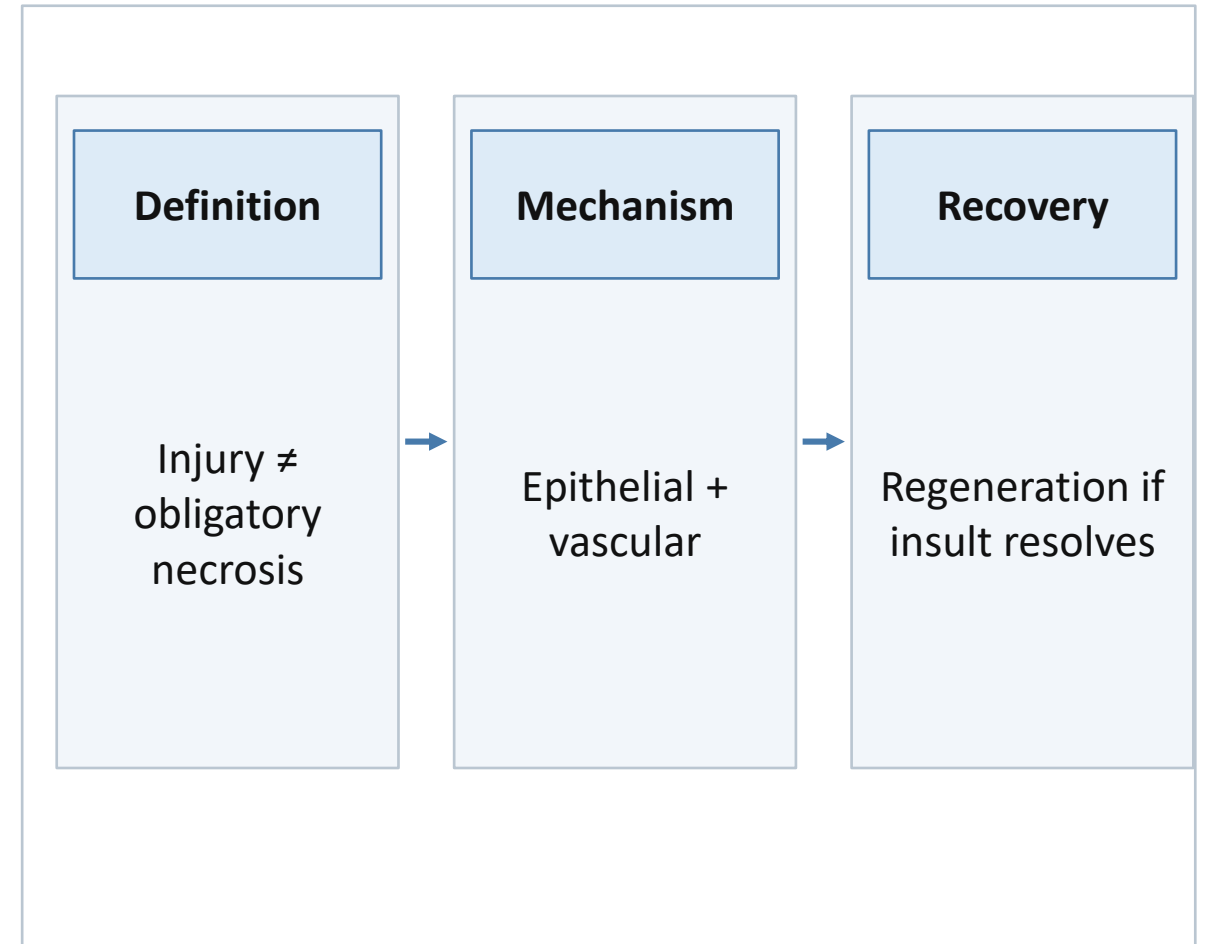
Mechanistic sequence • schematic



Three central pathology conclusions

- ATI need not contain widespread tubular necrosis.
- Sodium transport disruption, obstruction, backleak, and vasoconstriction reduce GFR.
- Renal recovery relies on survival and regeneration of tubular epithelium.

Three linked observations • schematic



Primary reference and source limitations

Robbins, Cotran & Kumar

Pathologic Basis of Disease, 11th edition (2026)

Chapter 20 — The Kidney

Lecture coverage: acute tubular injury/necrosis and closely adjacent mechanism text.

Original source chapter PDF and authentic figure assets were not provided. All illustrated pathology is explicitly schematic.