ACUTE KIDNEY INJURY

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Objectives

- List the causes of acute kidney injury.
- Describe the pathogenesis of acute tubular injury.
- Describe the macroscopy and microscopy of ATI.
- Describe the macroscopy and microscopy of papillary necrosis and cortical necrosis.

Acute Kidney injury

Acute kidney injury (AKI) has now replaced the term acute renal failure.

AKI is a characterized by:

- **Rapid decline in GFR**

  (falling within 24 hours to less than 400 mL /day**)**
- **Retention of nitrogenous wastes**

Acute Kidney Injury

Causes

Prerenal

- Hypotension
- Fluid loss
- Septicaemia
- Crush injury
- Burns
- Cardiac causes

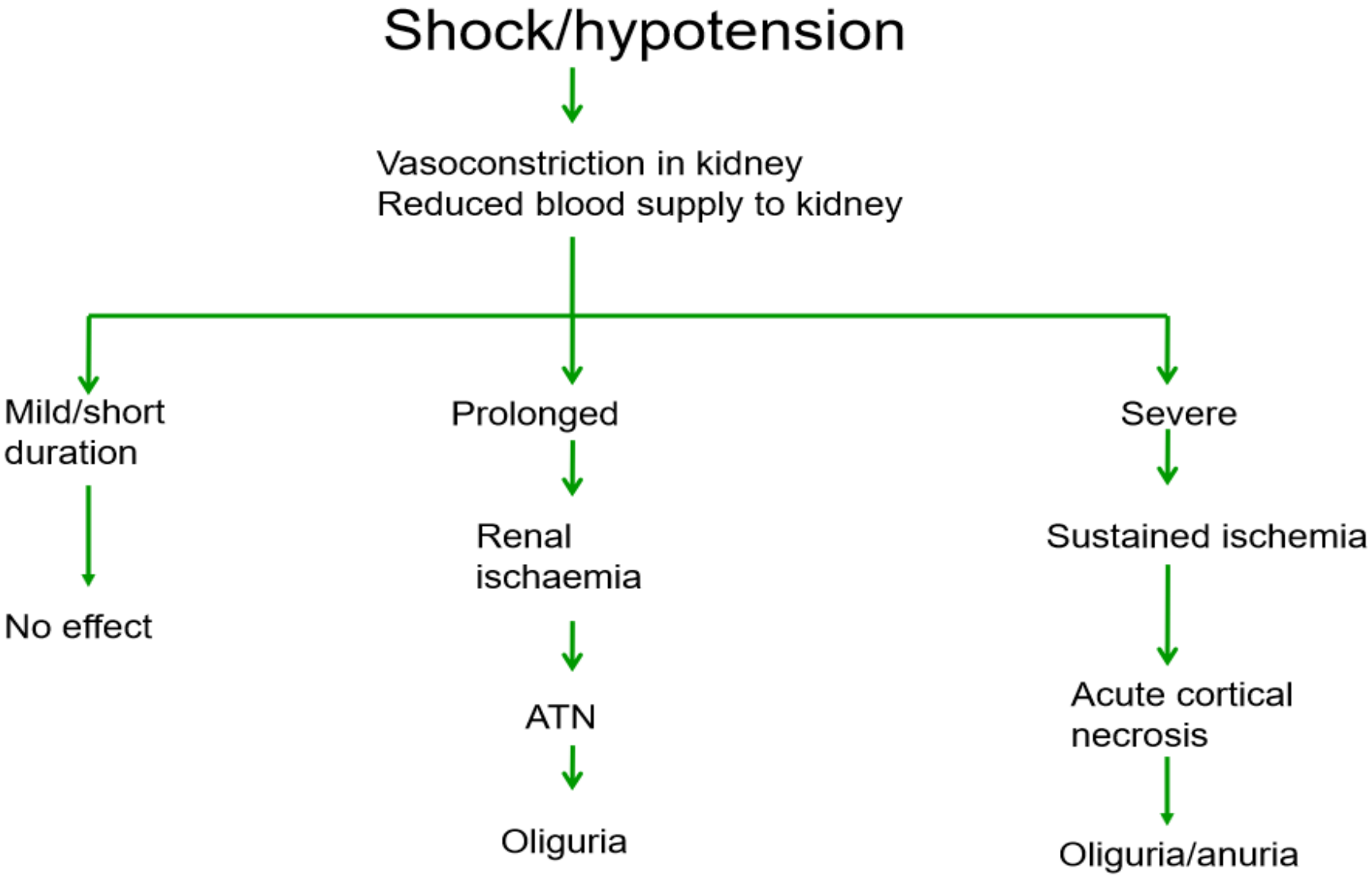
Postrenal

Obstruction

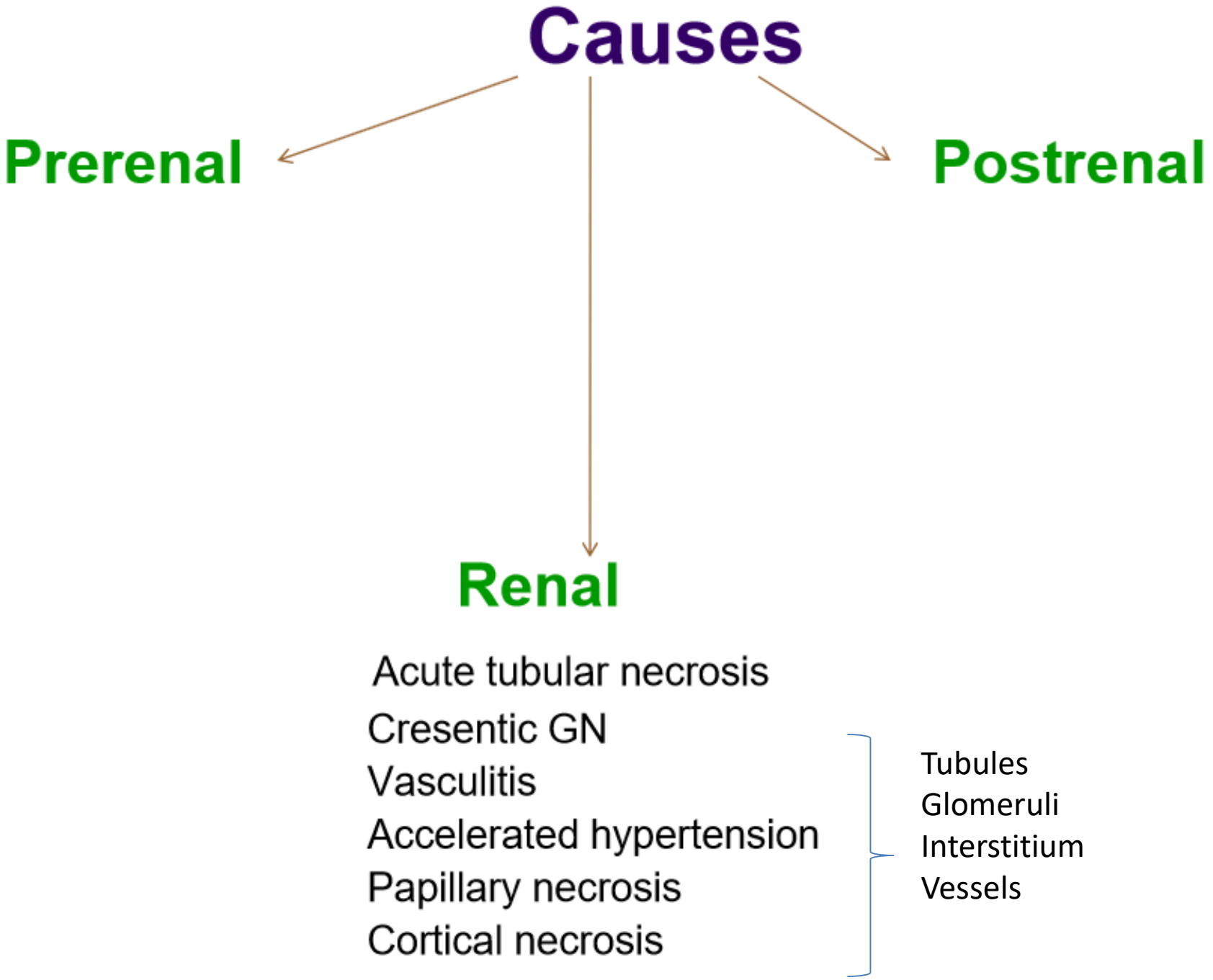
Renal

Acute tubular necrosis
Cresentic GN
Vasculitis
Accelerated hypertension
Papillary necrosis
Cortical necrosis

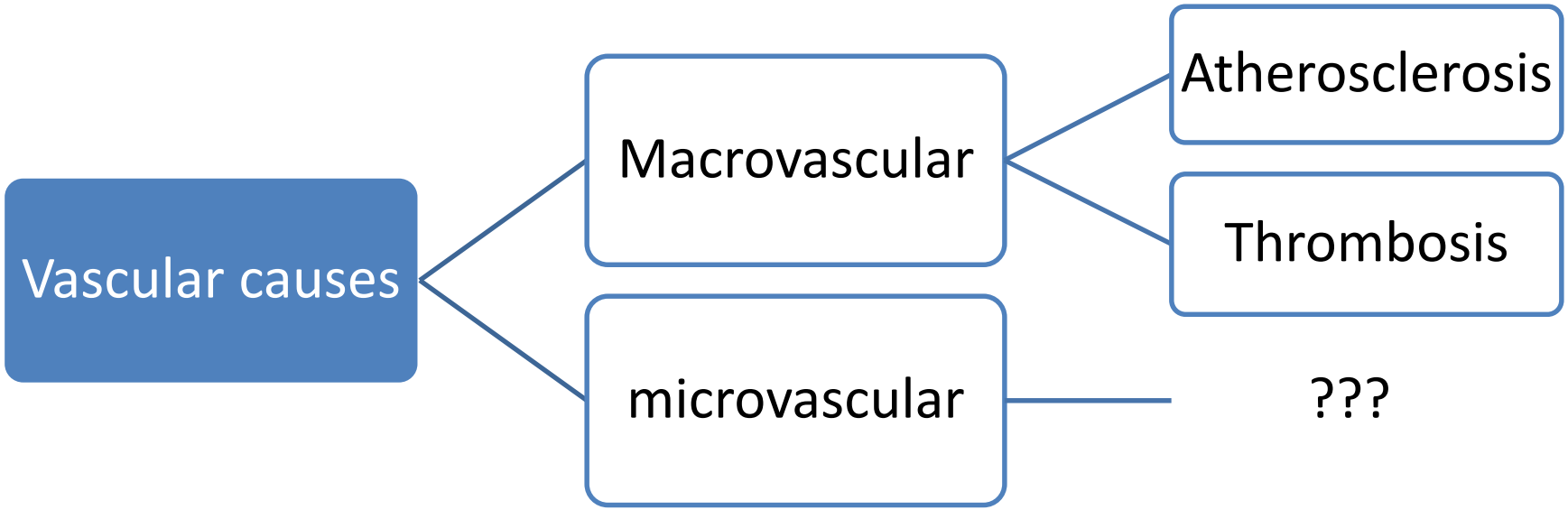
A) Pre renal AKI



B) Renal causes-AKI


Causes
Prerenal
Postrenal
Renal
Acute tubular necrosis
Cresentic GN
Vasculitis
Accelerated hypertension
Papillary necrosis
Cortical necrosis
Tubules
Glomeruli
Interstitium
Vessels

i)Vascular causes of AKI



ii)Glomeruli related causes of AKI

Usually associated with RPGN

…….

iii)Interstitial causes -AKI

Drugs - Penicillins, cephalosporins, NSAIDs, proton-pump inhibitors, allopurinol, rifampin, sulfonamides

Infections - Pyelonephritis, viral nephritides

Systemic disease - Sjögren syndrome, sarcoid, lupus, lymphoma, leukemia

iv)Tubular causes-AKI

Acute tubular injury

- ATI is the most common cause of AKI

  (50% of all cases)

- Clinical significance

  Reversible injury

  Early and proper management

  ↓

  Complete recovery

ATI can be caused by a variety of conditions

2 types

- **Ischaemic ATI** - caused by renal hypoxia
- **Nephrotoxic ATI** - by agents that directly damage the tubules

In both types the changes are due to

-Tubular damage

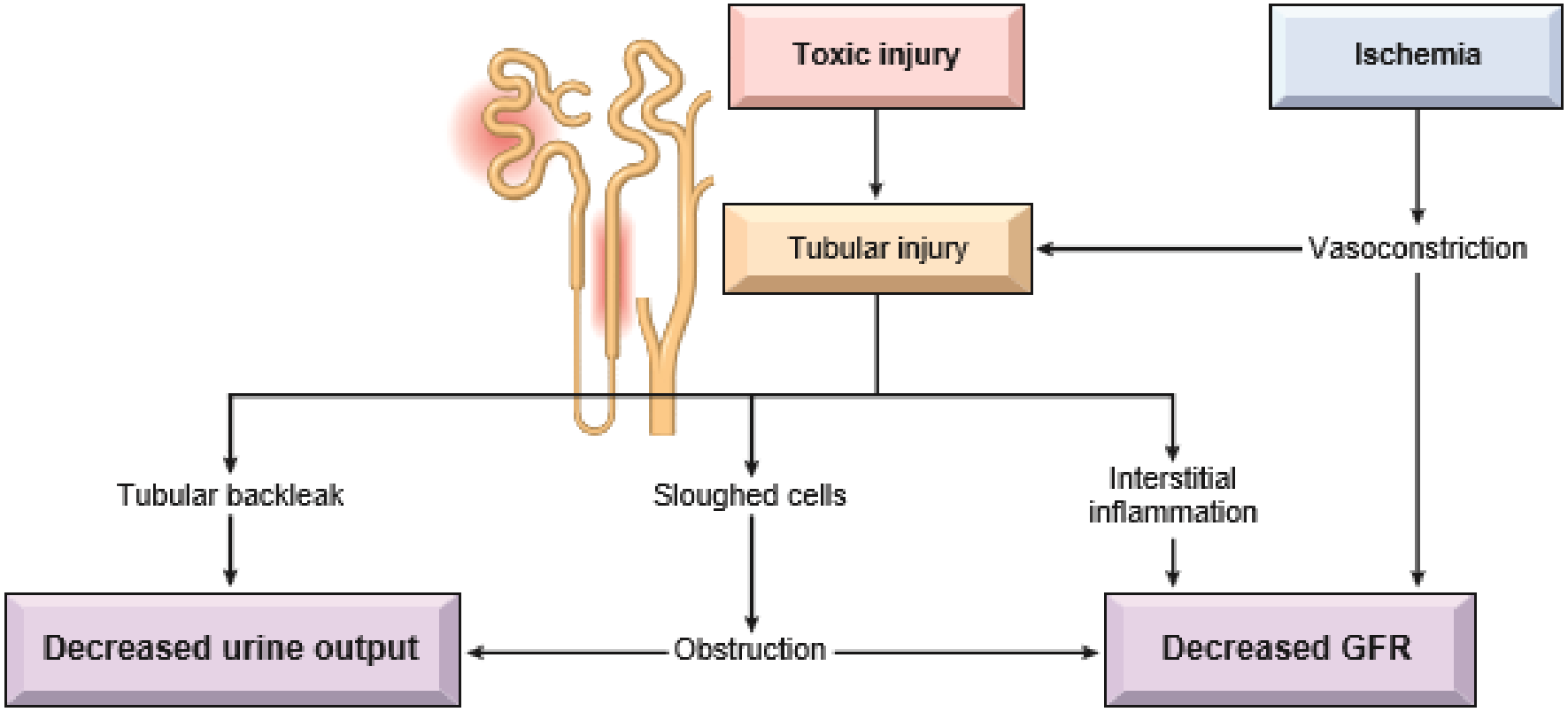
-Persistent and severe disturbance in blood flow

- Tubules are highly susceptible to ischemia and toxic damage due to

  High metabolic rate and high oxygen consumption rate

  Toxins are absorbed and concentrated by tubular epithelium.

- Mixed patterns of ATN also could be seen
  - Haemolytic crisis (Mismached blood transfusion) causing haemoglobinuria ,
  - Skeletal muscle injury – myoglobinuria


Toxic injury
Ischemia
Tubular injury
Vasoconstriction
Tubular backleak
Sloughed cells
Interstitial inflammation
Decreased urine output
Obstruction
Decreased GFR

Ischaemic ATI- Causes

Ischemia, due to decreased or interrupted blood flow.

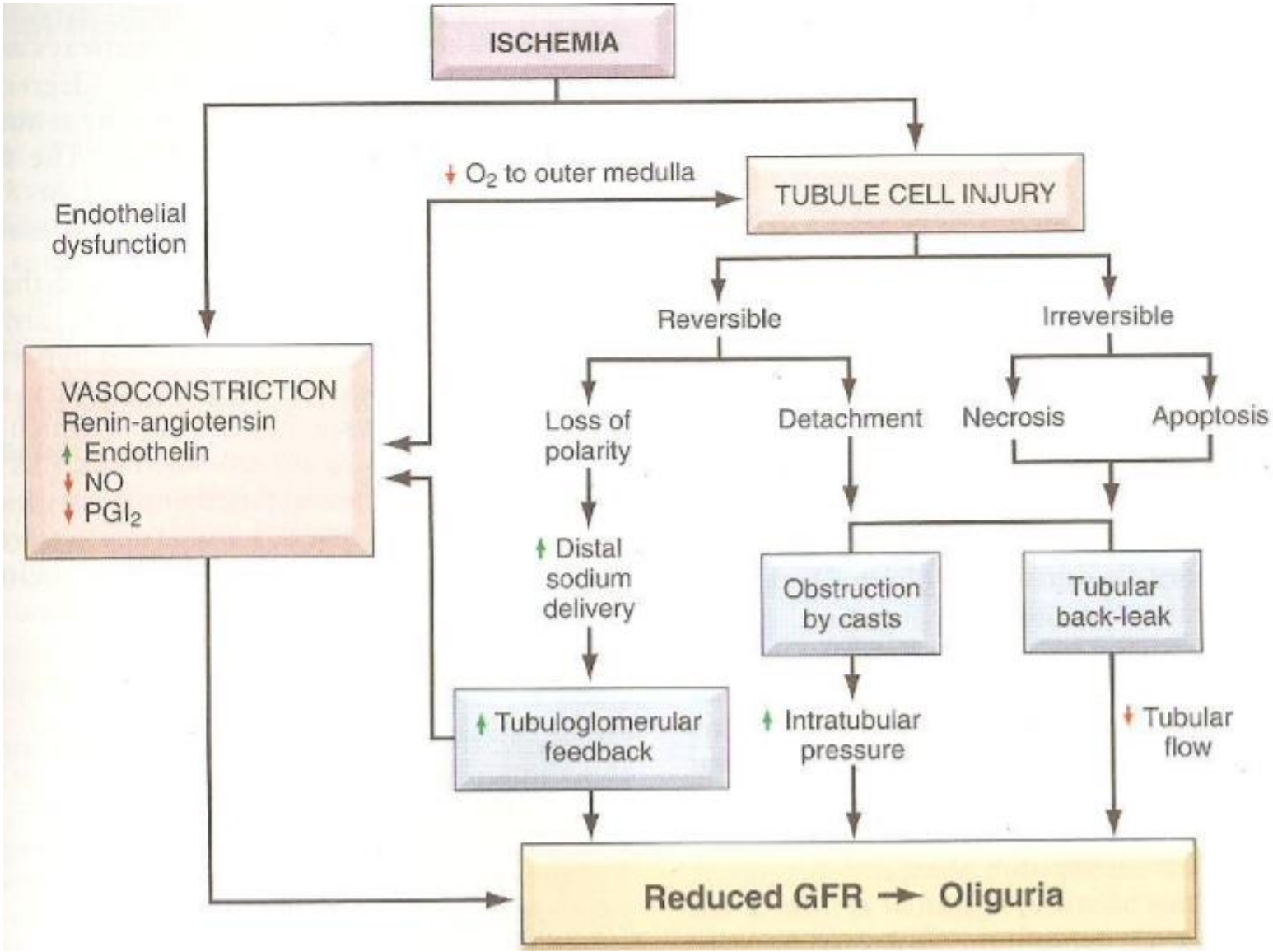
- Diffuse involvement of the intrarenal blood vessels

  eg: microscopic polyangiitis, malignant hypertension, microangiopathies

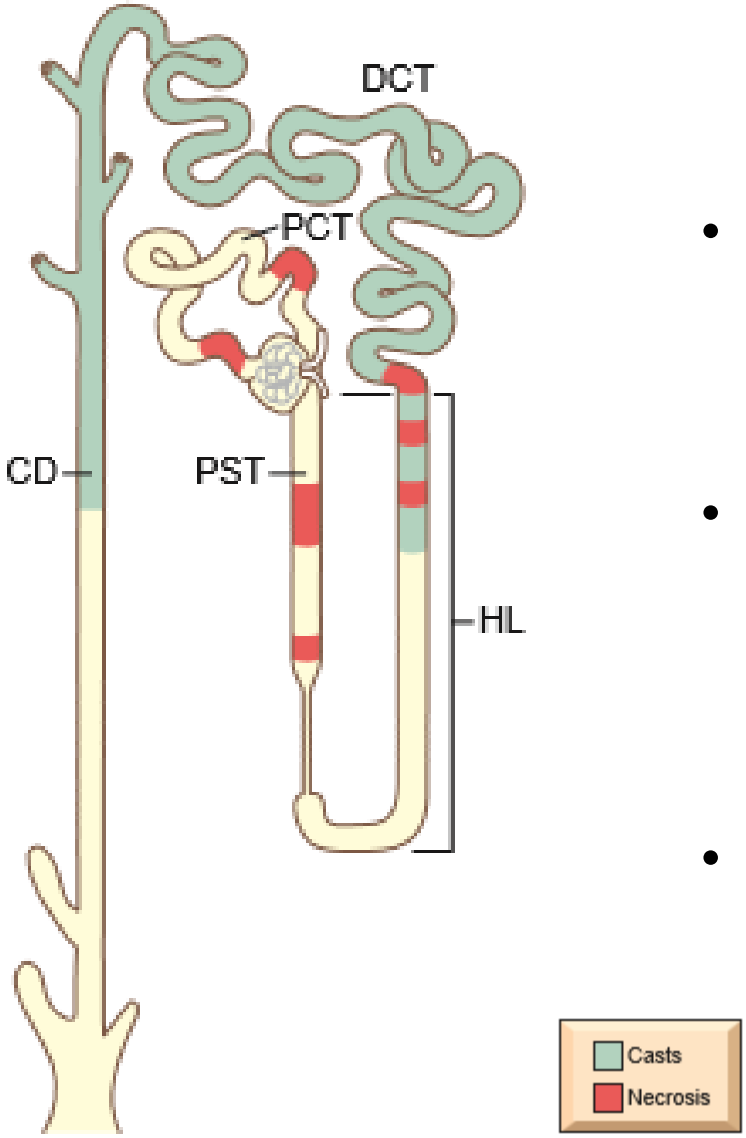
- systemic conditions

  Associated with thrombosis e.g, HUS, TTP,DIC
  Decreased effective circulating blood volume
  eg:hypovolemic shock

Pathogenesis ischaemic injury



Patterns of tubular damage



Ischaemic type

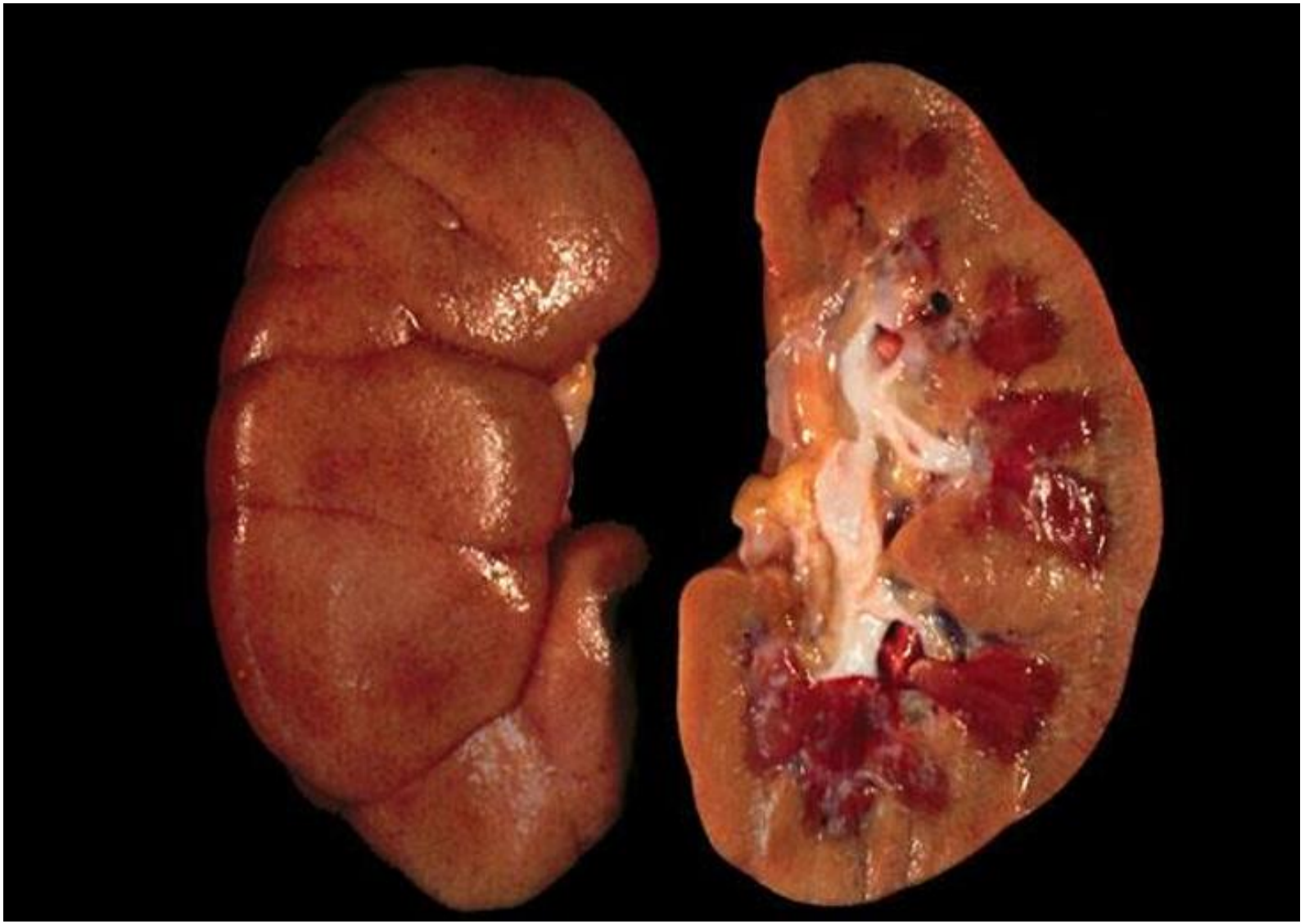
- Tubular necrosis is **patchy,** relatively short lengths of tubules are affected.
- **straight segments of proximal tubules (PST) and ascending limbs of Henle's loop (HL) in the medullla** are most vulnerable.
- lumens of the distal convoluted tubules (DCT) and collecting ducts (CD) contain casts

Ischaemic ATI

Macroscopy

- Kidneys mildly enlarged
- Cut surface bulges
- Cortex pale
- Medulla is congested

ATI -Macroscopy



Microscopy of ischaemic ATI

Tubules

- Dilated tubular lumens
- Multiple points with skip areas
  - Loss of PCT brush border
  - Swelling and vacuolation
  - Sloughing of epithelial cells
  - Flattened tubular epithelium
- Casts in DCT and collecting ducts : hyaline , granular , pigmented casts -Tamm-horsefall protein casts

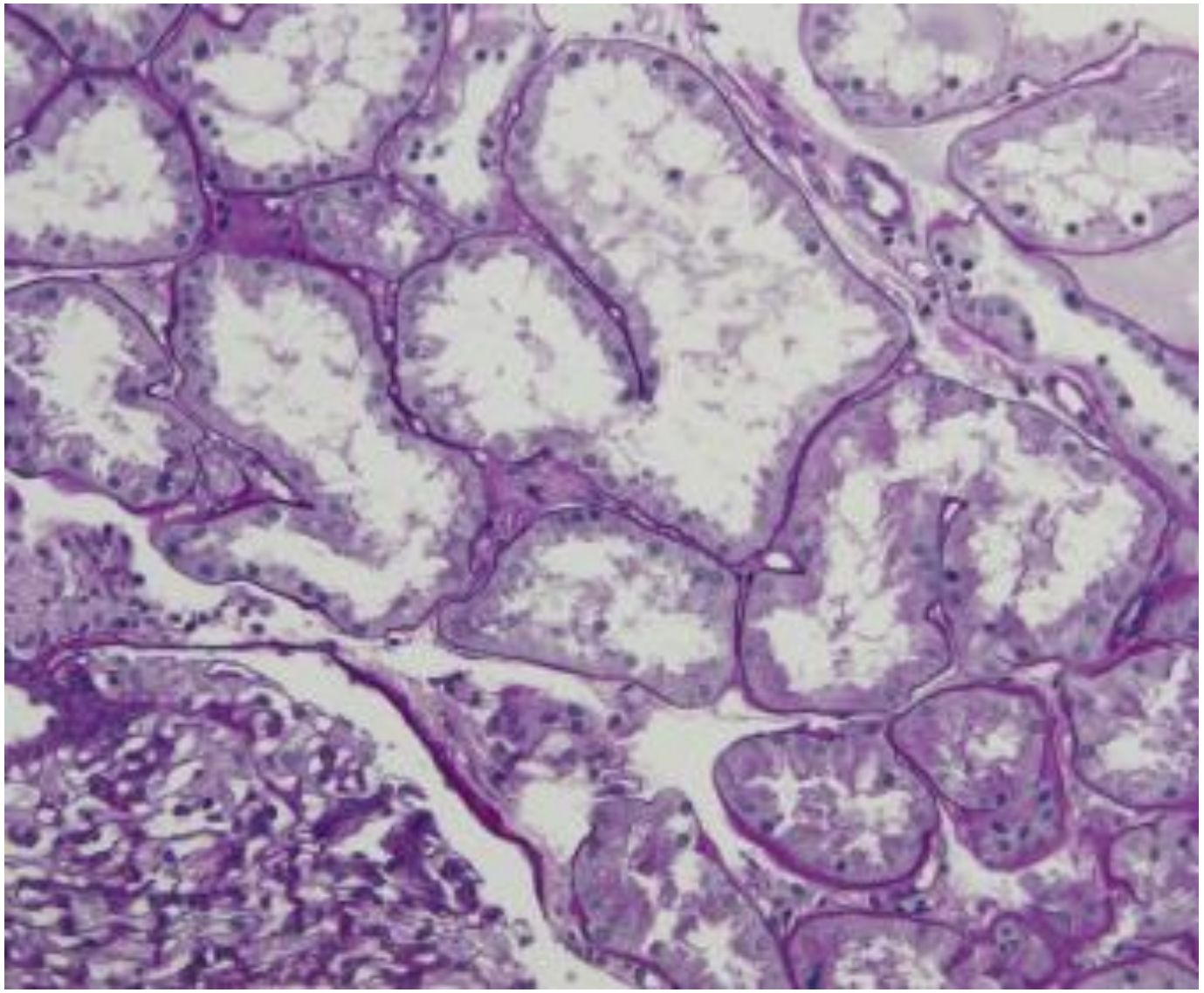
- With recovery - Regenerative changes with mitotic figures

Interstitium

- Oedema
- Inflammatory cells – lymphocytes , plasma cells , neutrophils.

Vessels Vasa recta – Dilated with neutrophils

Glomeruli - No significant change



Ischemic acute tubular injury with dilated tubular lumens, tubular epithelial flattening, and loss of brush borders, with no significant interstitial inflammation and an unremarkable glomerulus (periodic acid–Schiff stain).

Prognosis of ischaemic ATI

Depends on –

- Severity of the renal failure
- Severity of the condition that precipitated the attack of ischaemic ATN
- Involvement of other organs
- Age of the patient

Medical school. world Rank 6

Karolinska Institute- Stockholm, Sweden

Nephrotoxic ATI

Causes

1)Ingested nephrotoxic chemicals

Heavy metals – Mercuric chloride , Barium chloride

Disinfectants Herbicides - Paraquet

2) Inhaled / cutaneously absorbed chemicals

Carbon tetrachloride , carbon monoxide

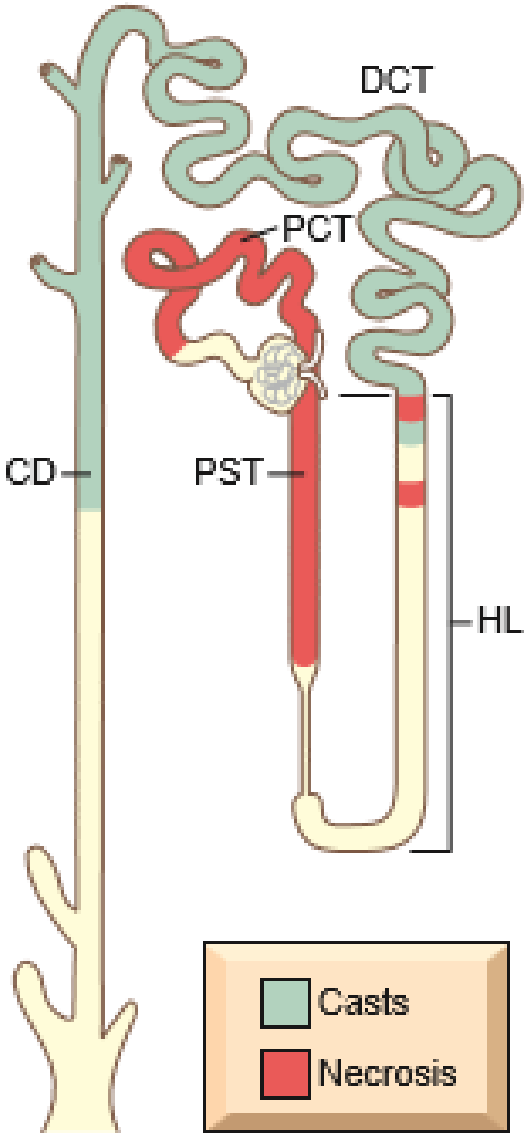
3)Animal venom – snake bite

4) Nephrotoxic therapeutic agents Antibiotics – Aminiglycosides Cisplatin Contrast media

Pathogenesis –Nephrotoxic ATI

- Due to direct damage of tubular epithelial cells
- Intra-tubular obstruction and back-leak are important in the pathogenesis of acute renal failure in nephrotoxic ATI

Patterns of tubular damage



Toxic type

- **Extensive necrosis** is present.
- **Commonly affect PCT**

(but necrosis of the distal tubule, particularly ascending HL, also occurs.)

- lumens of the distal convoluted tubules (DCT) and collecting ducts (CD) contain casts

Nephrotoxic ATI

Macroscopy

- Moderately enlarged
- Cortex pale
- Medulla is deep red

Nephrotoxic ATI

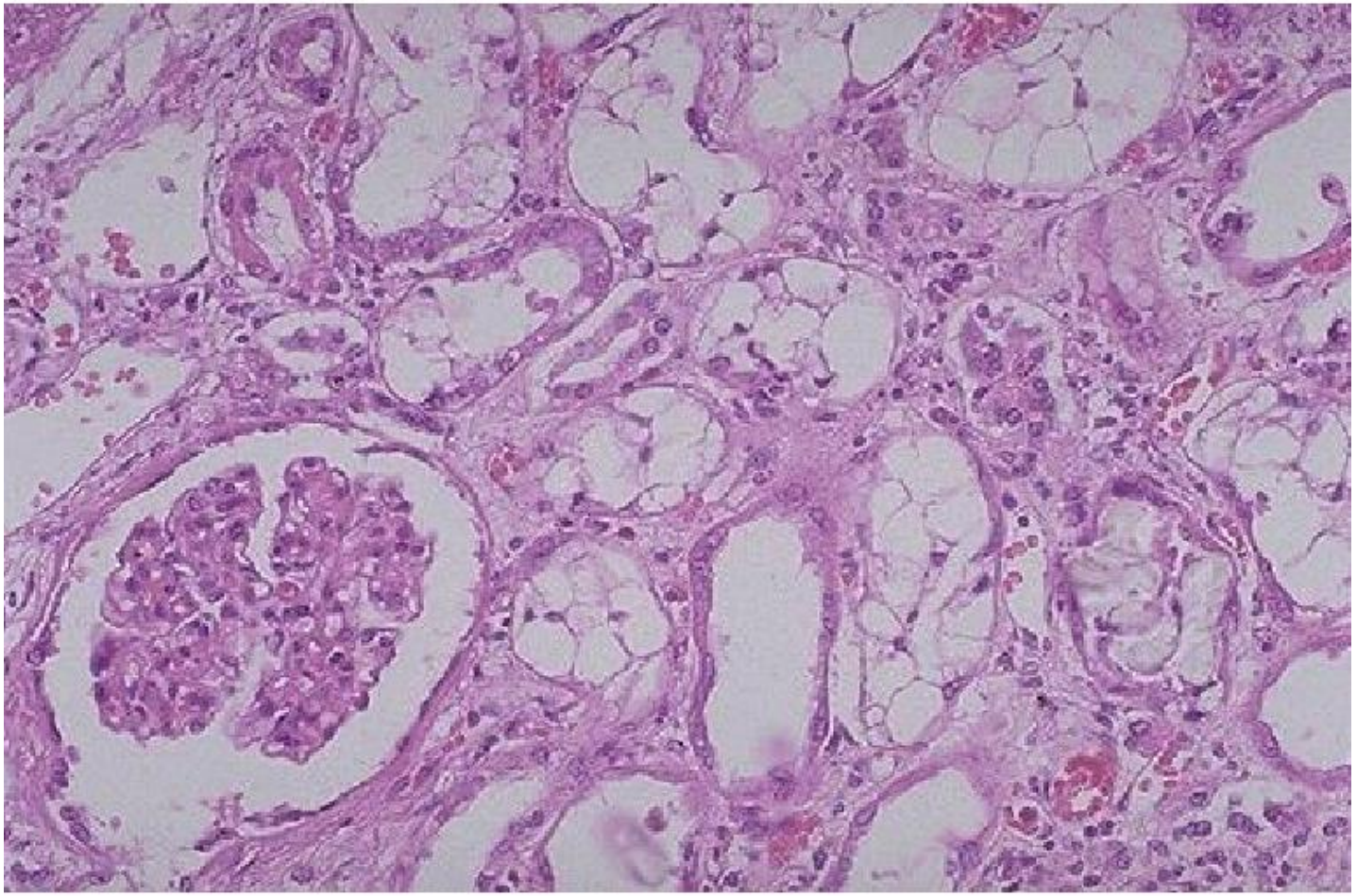
Microscopy

Different toxins affect different parts of the PCT.

Nonspecific changes(similar to ischaemic ATN) or
Specific changes in the tubular epithelium.

- **Carbon tetrachloride:** neutral lipid accumulation / fatty change in injured cells, followed by necrosis
- **Ethylene glycol:** ballooning and hydropic changes of proximal tubules, calcium oxalate crystals in tubular lumina
- **Hemoglobin / myoglobin:** numerous deeply pigmented, red-brown casts in distal and collecting ducts
- **Lead:** dark intranuclear inclusions and necrosis
- **Mercury:** large acidophilic inclusions
- **Vancomycin:** acute interstitial nephritis with lymphocytic and eosinophilic infiltrate and ATN

Nephrotoxic ATI



The tubular **vacuolization** and tubular **dilation** here is a result of the toxic effect of ethylene glycol poisoning

Clinical Course

The clinical course of AKI is highly variable, but the classic case may be divided into

1. Initiation phase
2. Maintenance phase
3. Recovery phase

The initiation phase

- About 36 hours

- The only indication of renal involvement is a slight decline in urine output with a rise in BUN.
- transient decrease in blood flow and declining GFR

The maintenance phase

Characterized by sustained decreases in urine output to between 40 and 400 mL/day (oliguria)

- salt and water overload
- BUN concentrations↑, hyperkalemia
- Metabolic acidosis
- Other manifestations of uremia.

The recovery phase

- steady increase in urine volume that may reach up to 3 L/day.
- The tubules are still damaged, so large amounts of water, sodium, and **potassium** are lost in the flood of urine

- Eventually, renal tubular function is restored and concentrating ability improves.
- BUN and creatinine levels begin to return to normal.

- Subtle tubular functional impairment may persist for months, but most patients who reach this phase eventually recover completely.

Prognosis-ATI

- Depends on the initiating event and damage to other organs
- With modern therapy - 95% recovery

Rank3

University of Cambridge, UK

Renal papillary necrosis

Causes

- Diabetes mellitus
- Acute obstructive pyelonephritis
- Analgesics
- Sickle cell anaemia

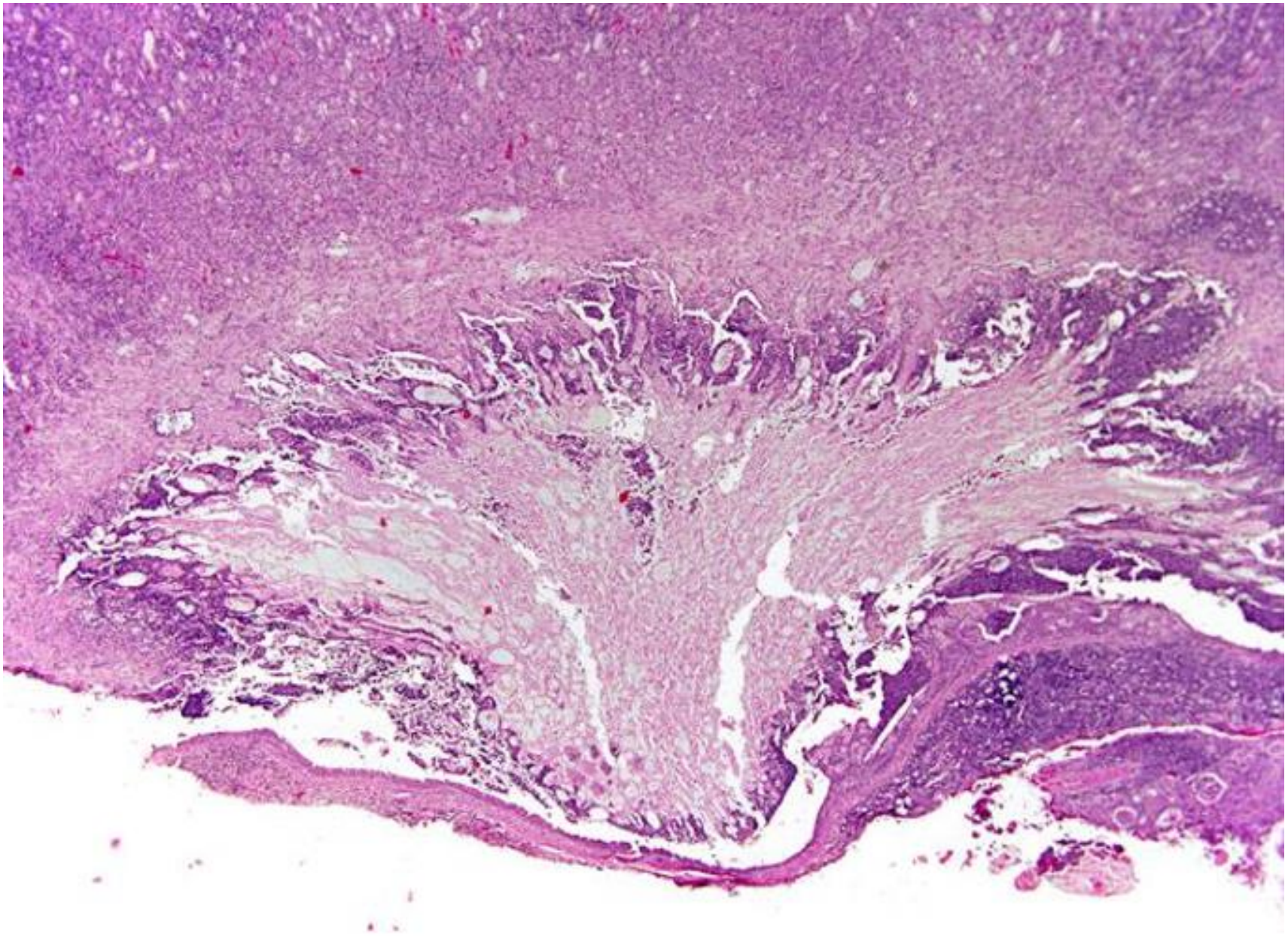
Macroscopy –

- Kidneys of normal size
- Distal 1/3 of the papillae surrounded by a cream zone
- Tip of the papillae may shed
- Changes of the primary cause would be evident

Renal papillary necrosis

Microscopy

- Necrosis of papillae
- Necrosed papillae separated from the adjacent tissue by a band of neutrophils
- With analgesics – tubular atrophy and interstitial fibrosis occur



Renal cortical necrosis

One of the rare causes of ARF/AKI

Traditionally, this term is applied to bilateral, confluent, ischaemic necrosis involving almost all the renal cortex

(sparing subcapsular, deep juxtamedullary zones and sparing the medulla)

The pathogenesis of renal cortical necrosis is unclear.

Seen in

- Pregnancy with haemorrhage
- Septicaemia
- Severe trauma
- Postoperative shock
- Severe acute rejection of renal transplant

Macroscopy –

- Moderately enlarged Kidney
- Almost the entire cortex is pale yellow
- If the patient survives the cortex is thinned-out and patchily calcified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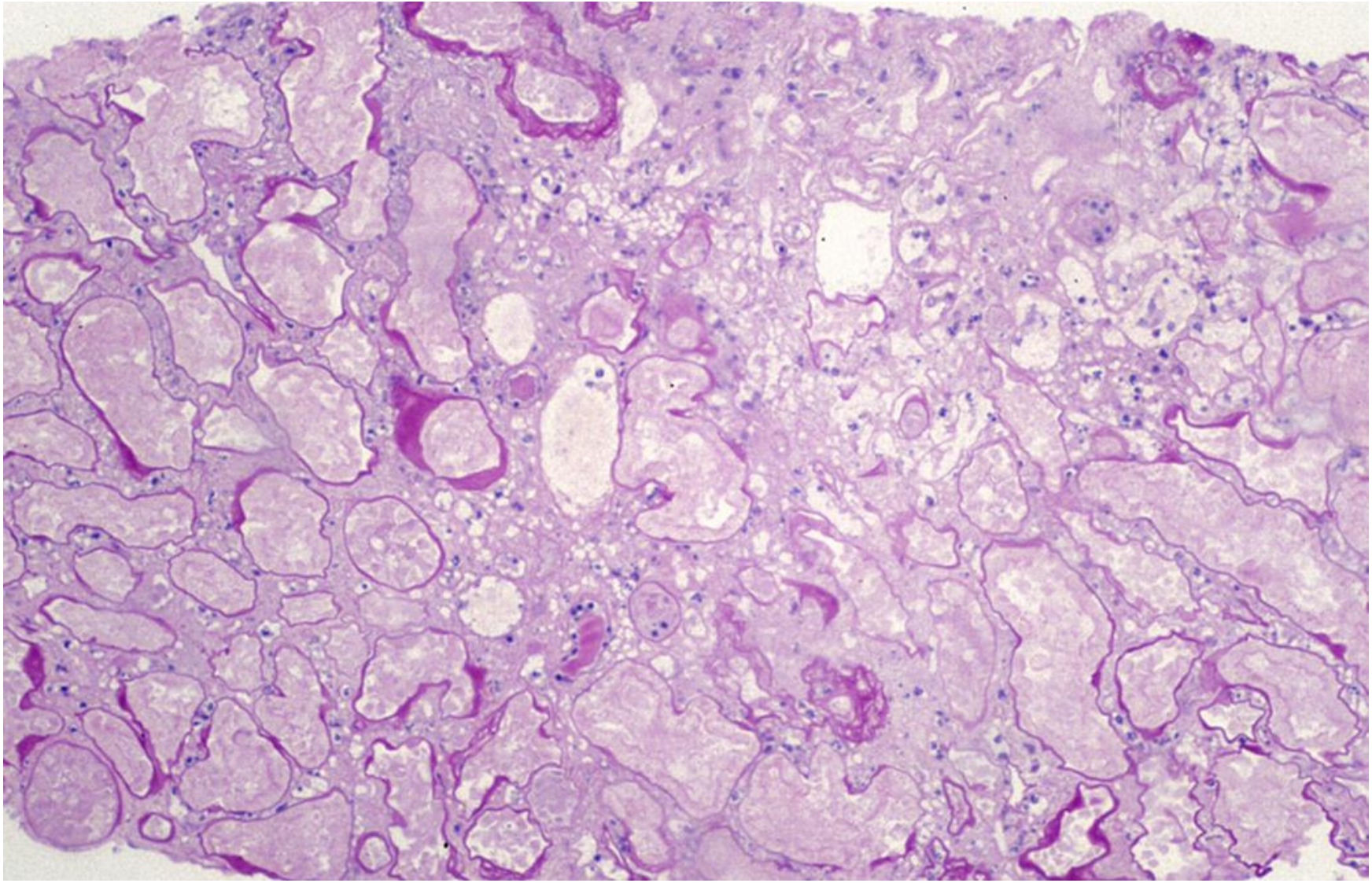
Microscopy –

- Patchy or diffuse cortical involvement coagulative, ischaemic necrosis of **glomeruli and tubules.**
- Tubules lined by cells devoid of nuclei
- +/-Arteries and arterioles contain thrombi
- +/- Intraglomerular thrombi
- Haemorrhage within glomeruli
- Parenchymal tissue in cortico- medullary zone is spared



Cortical necrosis with frank tubular necrosis with ghost-like outlines of cells without discernible nuclei, characteristic of coagulative necrosis (periodic acid–Schiff stain).

C) Post renal causes-AKI

Mechanical obstruction of the urinary collecting system, including the renal pelvis, ureters, bladder, or urethra, results in obstructive uropathy or postrenal AKI.

Eg:

- Stone disease
- Strictures
- Intraluminal, extraluminal, or intramural tumors
- Thrombosis or compressive hematomas

Summary

- Acute renal failure results from several causes
- Acute tubular necrosis is the commonest cause of acute renal failure
- ATN is a reversible condition and complete recovery is possible with timely and proper management of the condition

Rank 1

University of Oxford-UK

Rank-1

Harvard,USA (Boston, Massachusetts)