



DISEASES AFFECTING TUBULES, INTERSTITIUM, and collecting system

1

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Topics covered in lecture:

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Urinary outflow obstruction: - Renal stones
- Hydronephrosis

Tubulointerstitial nephritis (TIN)

Acute tubular injury (ATN)

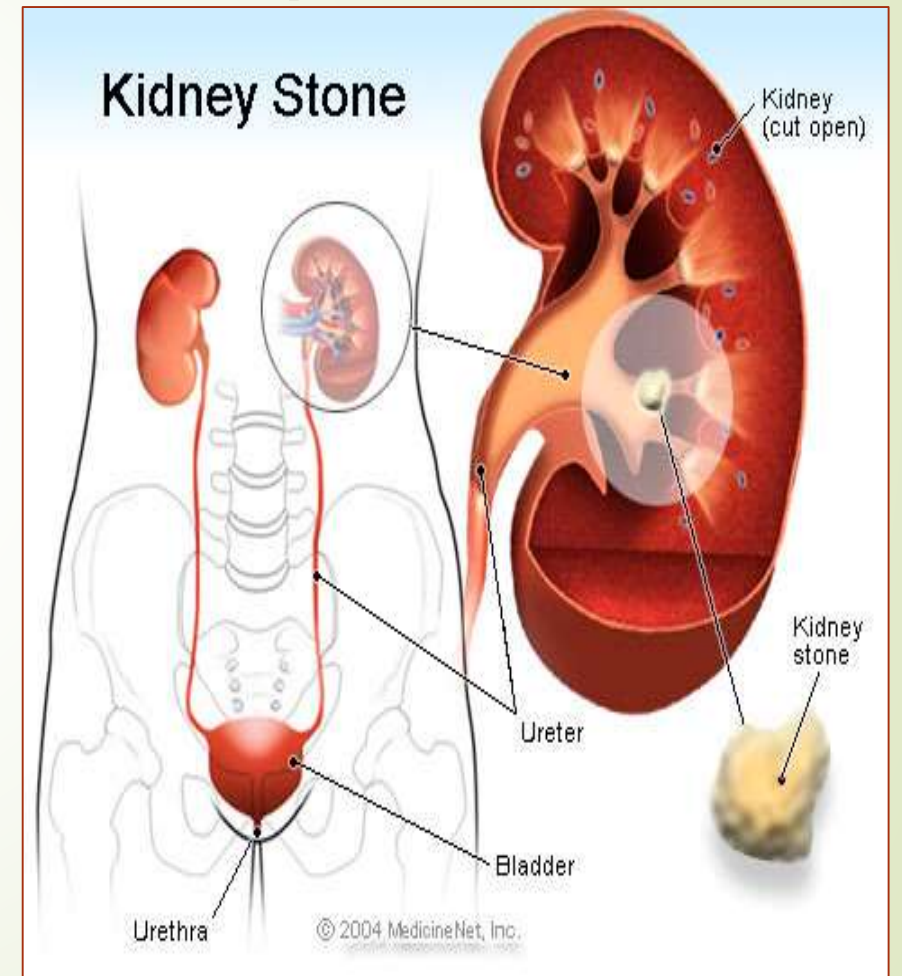
URINARY OUTFLOW OBSTRUCTION

3

- Renal Stones (Urolithiasis)

4

- stone formation; detected at any level in the urinary collecting system.
- Most common in kidney.
- (1%) of all autopsies.
- Symptomatic more common in men
- Familial tendency toward stone formation
- unilateral in 80%
- Variable size
- Symptoms: painful hematuria, renal colic



➔ Stone= inorganic salt (98%)+ organic matrix (2%)

5

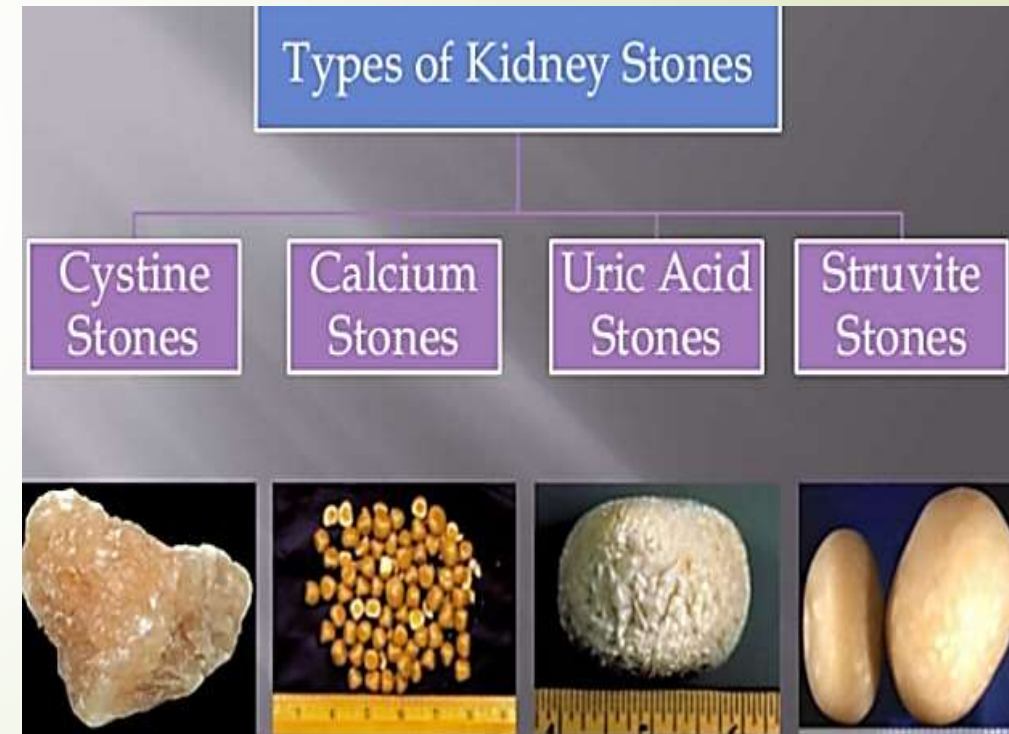
❖ Types are according to inorganic salt:

1- **calcium oxalate/ calcium oxalate+ calcium phosphate-- (80%) .**

2- **Struvite (magnesium ammonium phosphate) (<10%)**

3- **uric acid (6-7%)**

4- **cystine stones (2%)**



► Causes of Renal Stones

6

1-increased urine concentration of stone's constituents exceeds solubility in urine (supersaturation).

- 50% of *calcium stones* pts have hypercalciuria with no hypercalcemia.
- 5% to 10% → hypercalcemia and hypercalciuria.

➤ 2-The presence of a nidus

- Urates provide a nidus for calcium deposition.
- Desquamated epithelial cells
- Bacterial colonies

➤ 3-urine pH

- *Magnesium ammonium phosphate (struvite) stones occur with **alkaline** urine due to UTIs.*
- *Uric acid stones form in **acidic** urine (under pH 5.5).*



➔ 4-infections

e.g. urea-splitting bacteria (*Proteus vulgaris* and **staph**).

➔ 5- disorders causing hyperuricemia/ high cell turnover and:

e.g. gout; leukemias; tumor cell lysis following chemotherapy;
etc

➔ 6- certain genetic/ metabolic abnormalities:

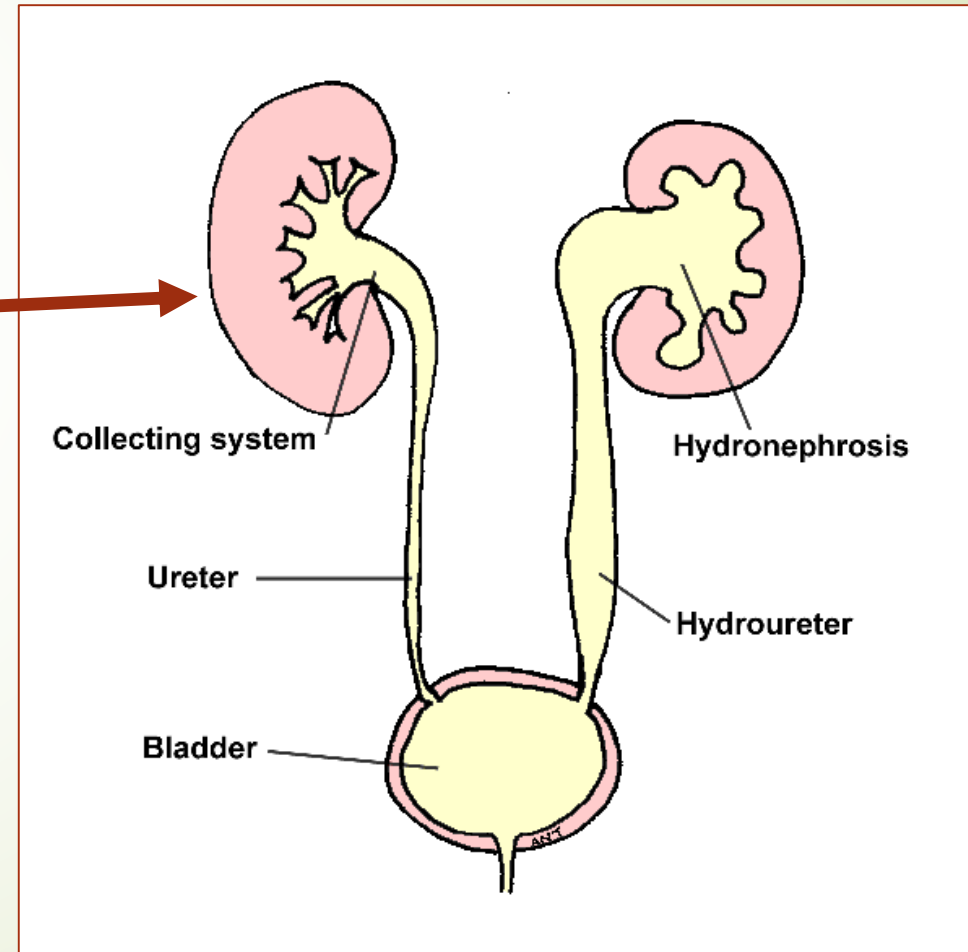
e.g. cysteine stones...

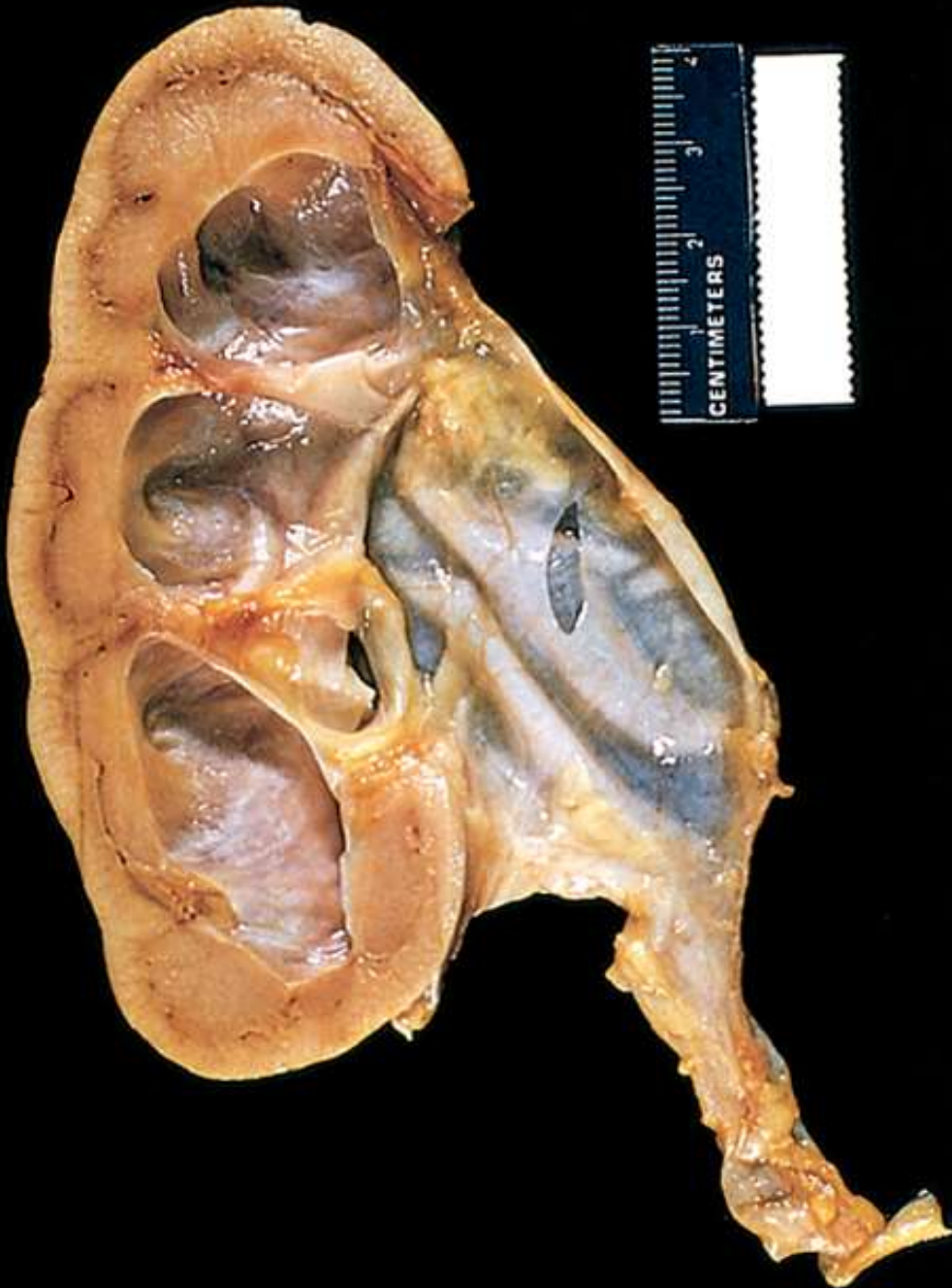
Hydronephrosis

9

- dilation of the renal pelvis and calyces due to obstruction, with accompanying atrophy of kidney parenchyma.
- sudden or insidious
- Obstruction at any level from the urethra to the renal pelvis.
- Significance: if untreated, leads to renal parenchymal damage and dysfunction

Normal kidney





Hydronephrosis of the kidney, with marked dilation of the pelvis and calyces and thinning of renal parenchyma.

The most common causes are

➤ **1- Congenital:**

examples

- Atresia of urethra
- Valve formations in ureter or urethra
- Aberrant renal artery compressing ureter
- Renal ptosis with torsion or kinking of ureter

2-Acquired:

- **Examples:**
- **Foreign bodies:** Calculi, necrotic papillae
- **Tumors:** prostatic hyperplasia, prostate cancer, bladder tumors, cervix or uterus cancer.
- **Inflammation:** Prostatitis, ureteritis, urethritis,
- **Neurogenic:** Spinal cord damage

Tubulointerstitial Nephritis

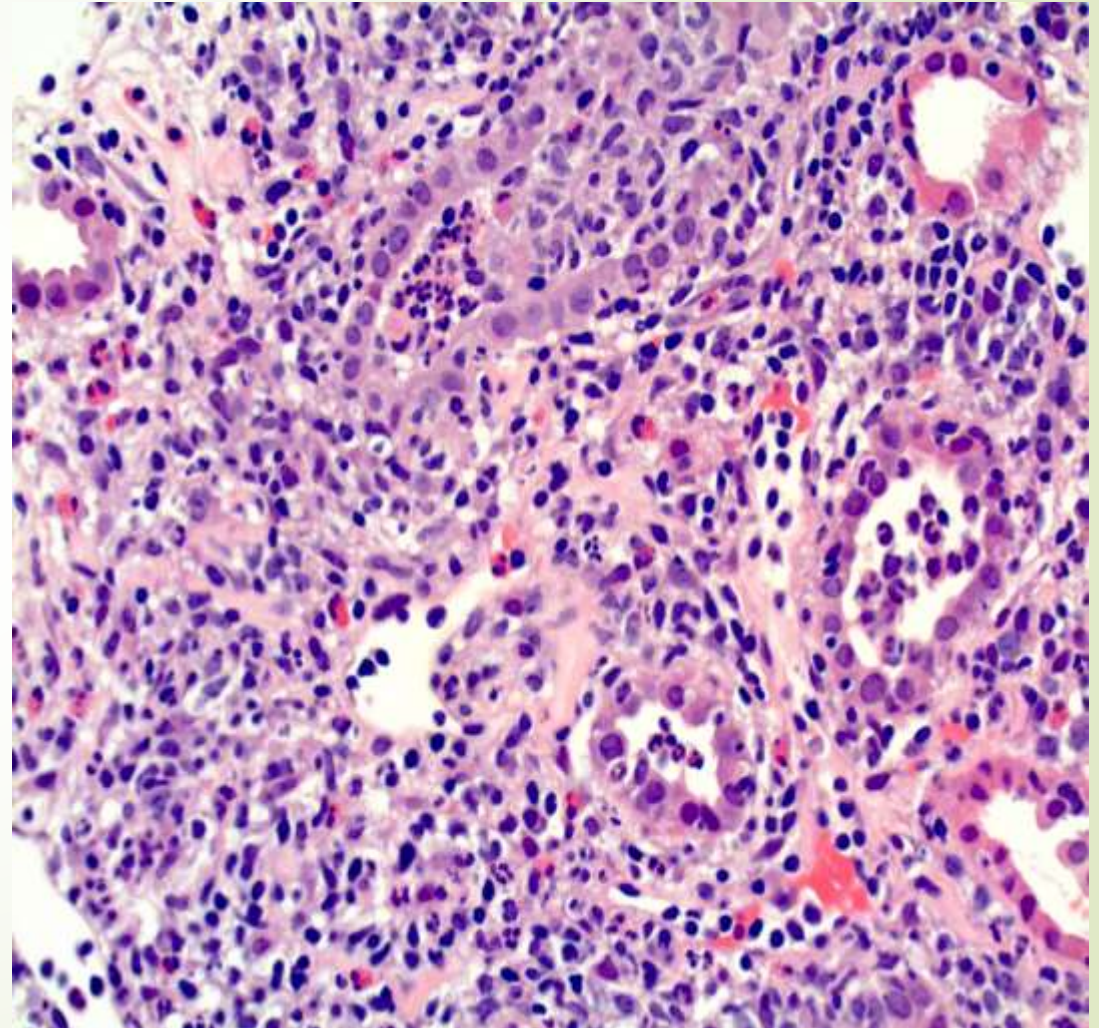
13

➤ Causes :

- 1- bacterial infection.
- 2- **drugs.**
- 3- metabolic disorders
- 4- physical injury (irradiation).
- 5- auto-immune reactions.

➤ divided into :

- 1-acute
- 2-chronic



Drug-Induced Interstitial Nephritis

14

- Two forms:
- 1-Acute Drug-Induced Interstitial Nephritis
- 2- chronic Drug-Induced (Analgesic Nephropathy)
- Acute form of drug- induced TIN
- Most common drugs: synthetic penicillins (methicillin, ampicillin)
- Others: synthetic antibiotics; diuretics; NSAIDs; other drugs

➤ Pathogenesis of Acute Interstitial nephritis:

- **immune mechanism.**
 - IgE -mediated? type **I hypersensitivity**.
 - ? **T cell-mediated (type IV)** hypersensitivity reaction.

➤ Morphology

- interstitium : lymphocytes, plasma cells, macrophages, eosinophils and neutrophils
- glomeruli are normal

AIN- Clinical Course

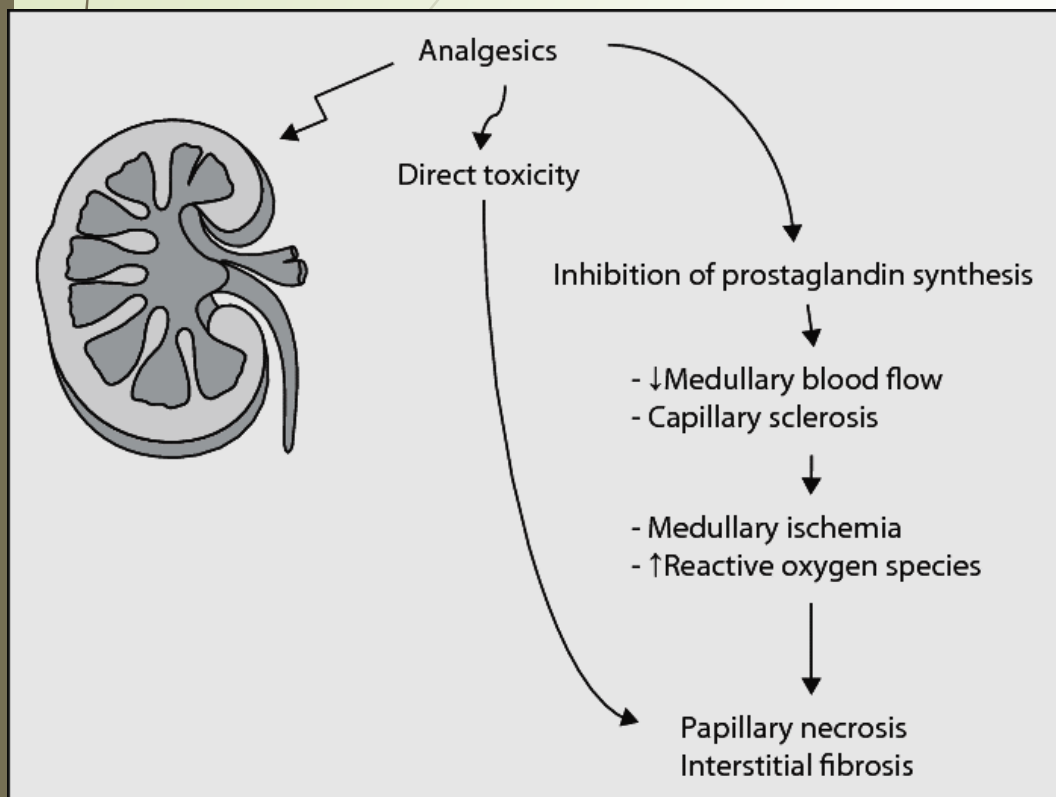
16

- ➔ 2-40 days after exposure to drug.
- ➔ **fever, eosinophilia & rash** (25%)
- ➔ **renal abnormalities:** hematuria, minimal or no proteinuria, and leukocyturia
- ➔ **withdrawal** of the offending drug is followed by **recovery**

Acute Interstitial Nephritis (AIN)



Analgesic Nephropathy: chronic drug-induced TIN



- Consumption of **large** quantities of analgesics over **long** periods may cause **chronic interstitial nephritis** often with **renal papillary necrosis**.
- **Aspirin and acetaminophen are common causes**
- **Pathogenesis** not entirely clear.
 - **covalent binding and oxidative damage**
 - **inhibition of prostaglandin synthesis**

Clinical Course of chronic IN

- Progressive renal impairment, chronic renal failure, hypertension....
- A complication of analgesic abuse is: **increased incidence of transitional-cell carcinoma** of the renal pelvis

Acute Tubular Necrosis (ATN/ ATI)

- ▶ characterized morphologically by damaged tubular epithelial cells and clinically by acute suppression of renal function.
- ▶ ***It is the most common cause of acute renal failure.***
- ▶ **ATN is a reversible condition if treated properly and quickly.**
- ▶ **Clinical manifestations: electrolyte abnormalities, acidosis, uremia, signs of fluid overload, often oliguria.**
- ▶ Proximal tubular epithelial cells are particularly sensitive to hypoxemia and toxins

Acute Tubular Necrosis/ Injury (ATN/ ATI)

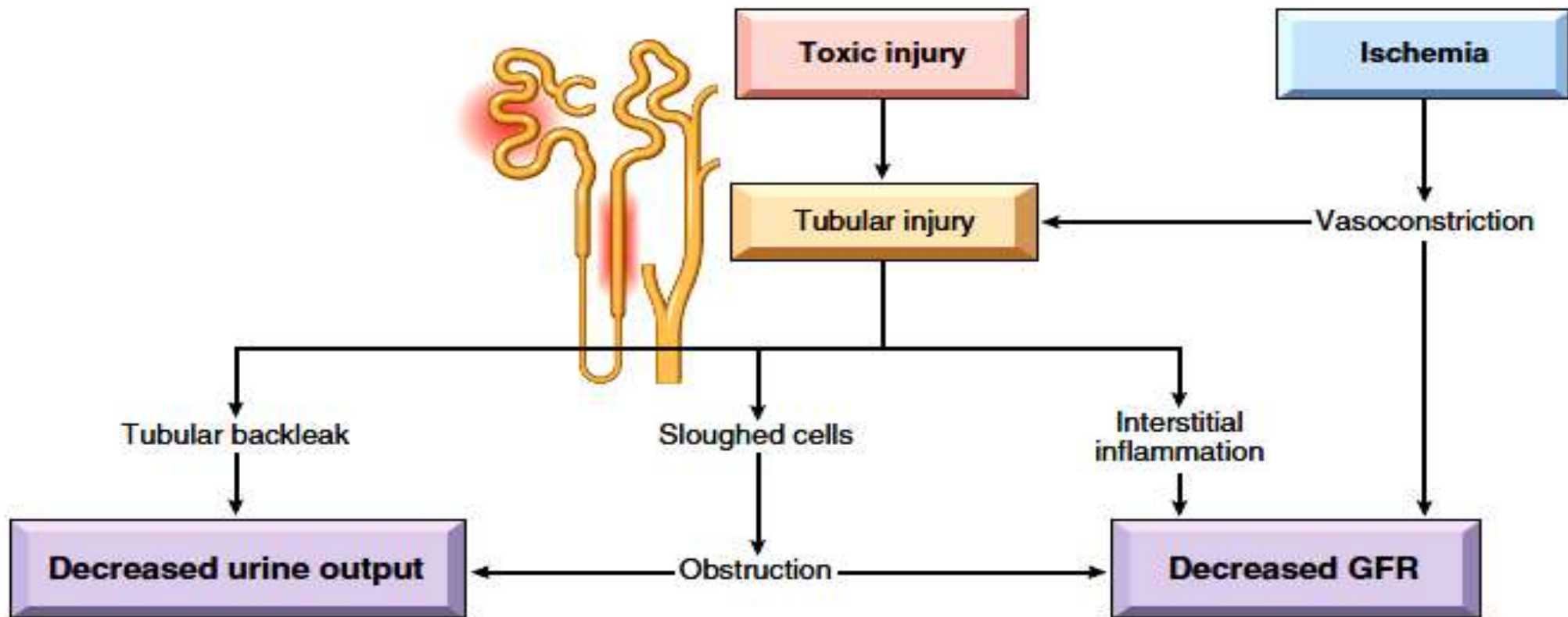


Fig. 14.16 Postulated sequence in ischemic or toxic tubular injury.

➤ ATI Types:

21

1- ischemic ATI :

- most common

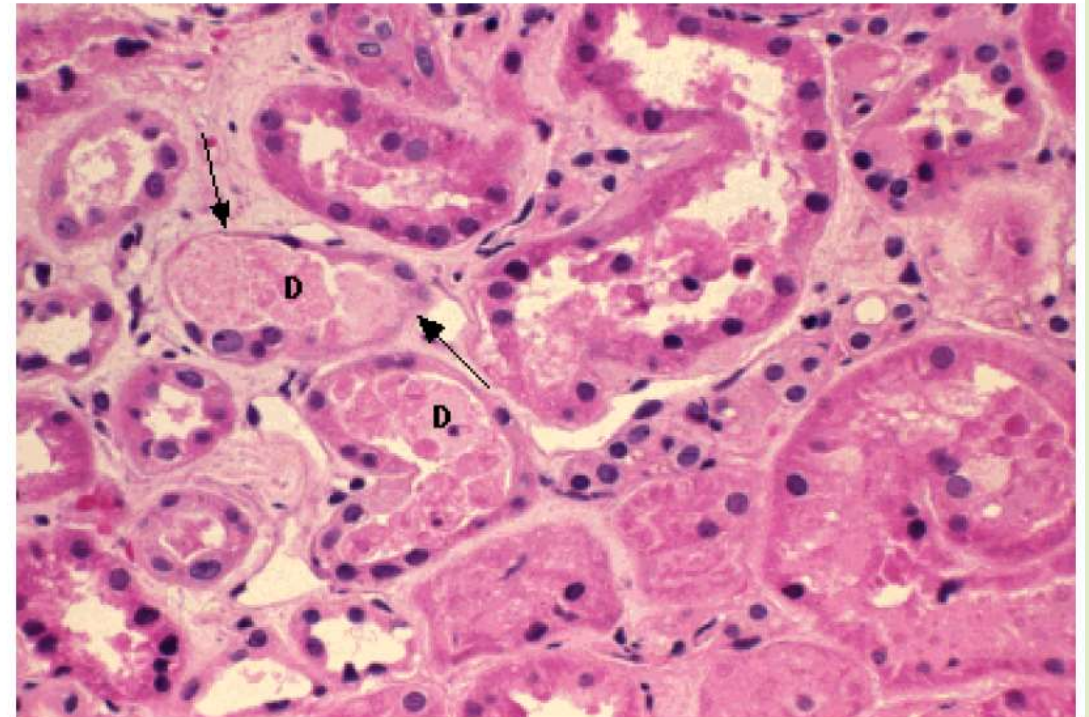
- *associated with shock (e.g. hypotensive shock, severe trauma; acute pancreatitis; septicemia; mismatched blood transfusion, hemolytic crises, myoglobinuria, etc...)*

2- nephrotoxic ATI

- **poisons** including heavy metals (e.g., mercury)
- **organic solvents** (e.g., carbon tetrachloride)
- **drugs** such as gentamicin and other antibiotics, and radiographic contrast agents.

Acute tubular epithelial cell injury with blebbing at the luminal pole, detachment of tubular cells from their underlying basement membranes, and granular casts

ATN



Acute tubular necrosis Light micrograph in acute tubular necrosis showing focal loss of tubular epithelial cells (arrows) and partial occlusion of tubular lumens by cellular debris (D). Courtesy of Helmut Rennke, MD.

ATI- management

- ▶ repair and tubular regeneration → gradual clinical improvement
- ▶ With supportive care, patients who survive have a good chance of recovering renal function
- ▶ In those with preexisting chronic kidney disease, complete recovery is less frequent