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# Pathology GUS

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# DISEASES AFFECTING TUBULES AND INTERSTITIUM



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# Topics covered in lecture:

**Urinary outflow obstruction: - Renal stones**

**- Hydronephrosis**

**Tubulointerstitial nephritis (TIN)**

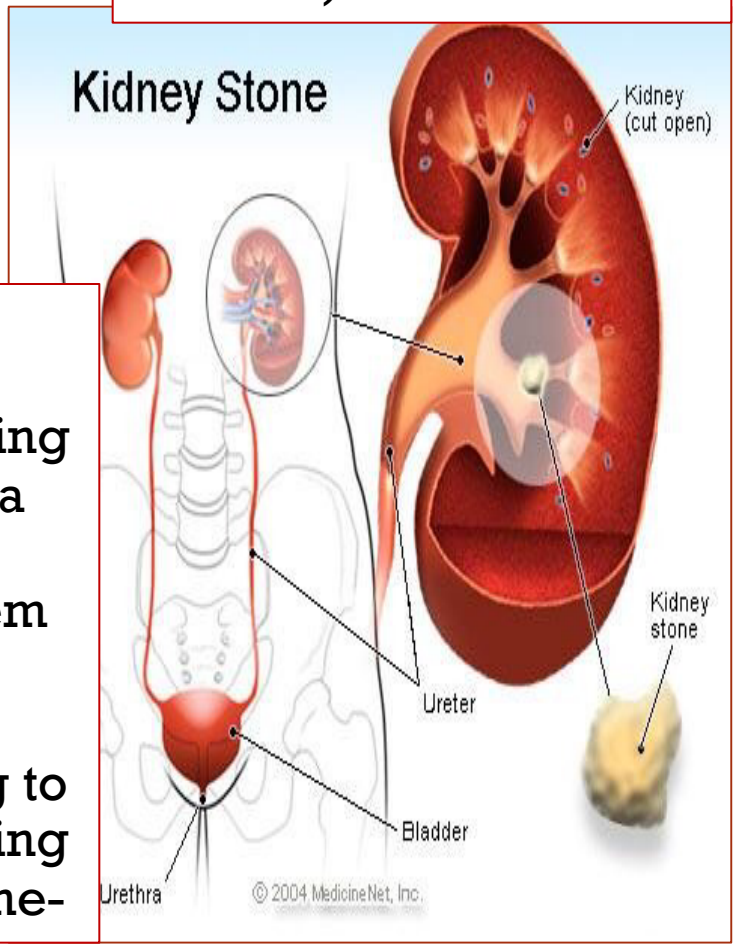
**Acute tubular injury (ATN)**

# URINARY OUTFLOW OBSTRUCTION

- **Renal Stones (*Urolithiasis*)**

- **stone formation; detected at any level in the urinary collecting system.**
- **Most common in kidney.**
- **(1%) of all autopsies.**
- **Symptomatic more common in men** or asymptomatic
- **Familial tendency toward stone formation**
- **unilateral in 80%**
- **Variable size**
- **Symptoms: painful hematuria, renal colic** ( severe pain in the loin and can radiate from the loin to the groin)

Renal stones are formed inside the kidney then can be located inside the urinary collecting system ( kidney, renal calyx , renal pelvis , ureters, urethra, urinary bladder)




The pain is because the stones are moving over the mucosa of the urinary collecting system , damage & trauma to the mucosa leading to pain and bleeding -seen in the urine-

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

Precipitation of crystals will be over the organic matrix

## ❖ Types are according to inorganic salt:

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

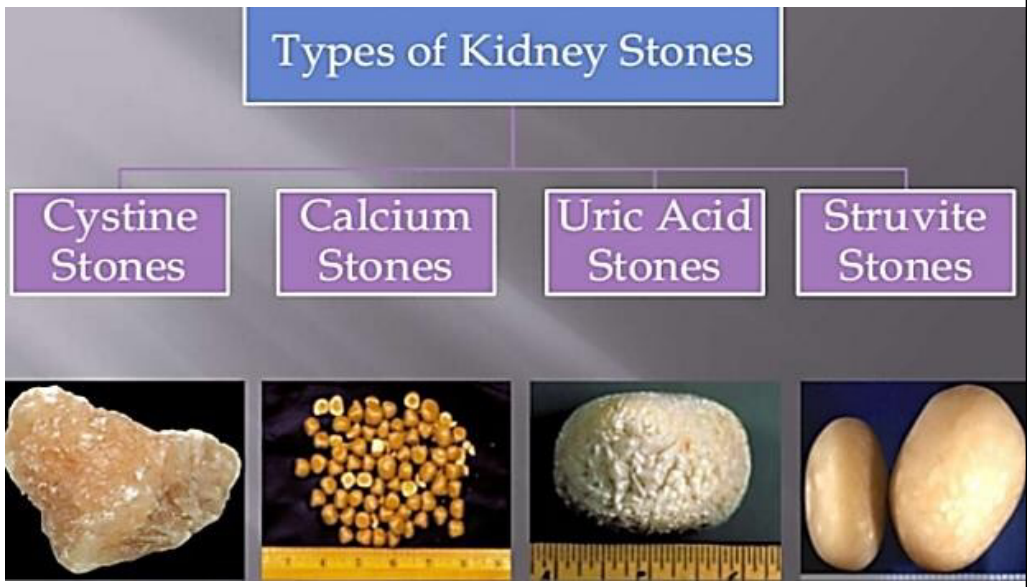
2 **Struvite (magnesium ammonium phosphate)** (<10%)

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

4 **cystine stones** (2%)

Renal Stones are usually diagnosed clinically

The type of stones is determined based on the morphology, radiology & chemical evaluation of the urine




Variable sizes , shapes and colors , some of them are radio opaque and some are not, could be small to be found in the urethra or the ureters

# Causes of Renal Stones

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

The solvent here is the urine & the solutes are the constituents of the stones , the urine can't solve more so perception occurs

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

Hypercalciuria will lead to supersaturation and stones formation

# 2-The presence of a nidus

Nidus ( organic matrix)

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

So patient with urinary tract infection may be more susceptible to renal stones

## 3-urine pH

It's found that formation of certain types of stones is favored according to the ph of the urine

- ***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

Increases the risk of having stones

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

Bacteria express urease enzyme that splits urea and forms ammonia ( alkaline urine)

Susceptible to struvite

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

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

Hyperuricemia = increased level of Uric acid in the blood

High cell turnover: cancer patients who are taking chemotherapy especially hematologic cancers

Hyperuricemia leads to hyperuricuria then uric acid stones

## 6- certain genetic/ metabolic abnormalities:

Abnormal absorption, secretion or excretion of certain metabolites

**e.g. cysteine stones…**

People with cysteine stone almost always have genetic abnormalities in the metabolism of cysteine —> accumulation of cysteine in urine —> cysteine stones

Patients are young because it's genetically determined and tend to recur

## The management

**Prophylaxis:** life style & diet

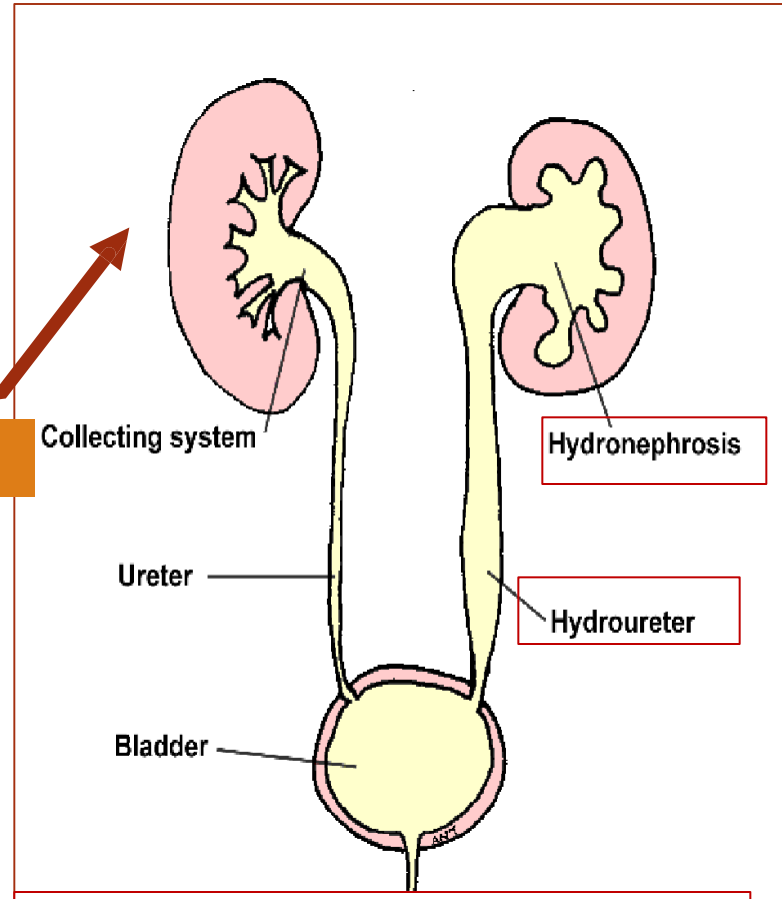
**Treatment** : depends on the size of the stones, very small stones can be passed with the urine and the patient could take drugs to facilitate this , if the stones are large we can do lithotripsy( تفتيت حصى )( ultrasound waves without invasive surgery or anesthesia) and the fragments of the stones can pass in urine, if the stones are very large or their place is critical, we could remove them by surgery

# Hydronephrosis

Hydro : water
Nephrosis: kidney

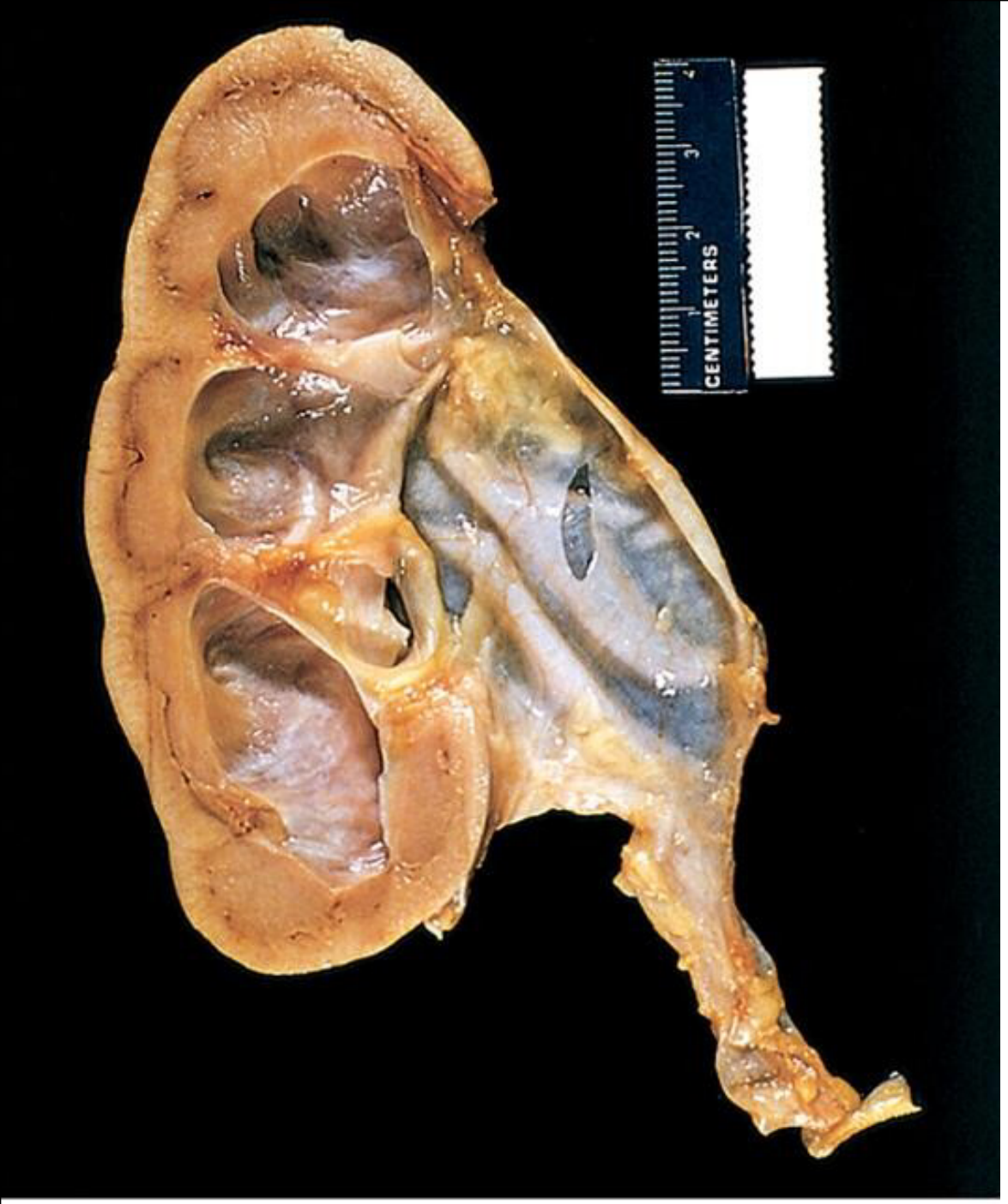
- **dilation of the renal pelvis and calyces due to (distal ) obstruction,accumulation of urine above the level of obstruction, with accompanying atrophy of kidney parenchyma.**
- **sudden or insidious**
- Acute or slowly evolving
- Acquired or congenital
- **Obstruction at any level from the urethra to the renal pelvis.**
- **Significance: if untreated, leads to renal parynchemal damage and dysfunction (pressure & compression)**

Normal kidney




The obstruction is below the level of the ureter

Notice the cortical atrophy = renal dysfunction






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

# The most common causes are

## *1- Congenital:*

Anatomical abnormalities

***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:

obstruction either inside the urinary system or from outside

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

Loss of innervation of the sphincter ( neurogenic bladder) , the bladder continues accumulating urine without physiological process of voiding of urine and finally the pressure will expand the bladder and exerts a back pressure on the urinary system

# Tubulointerstitial Nephritis

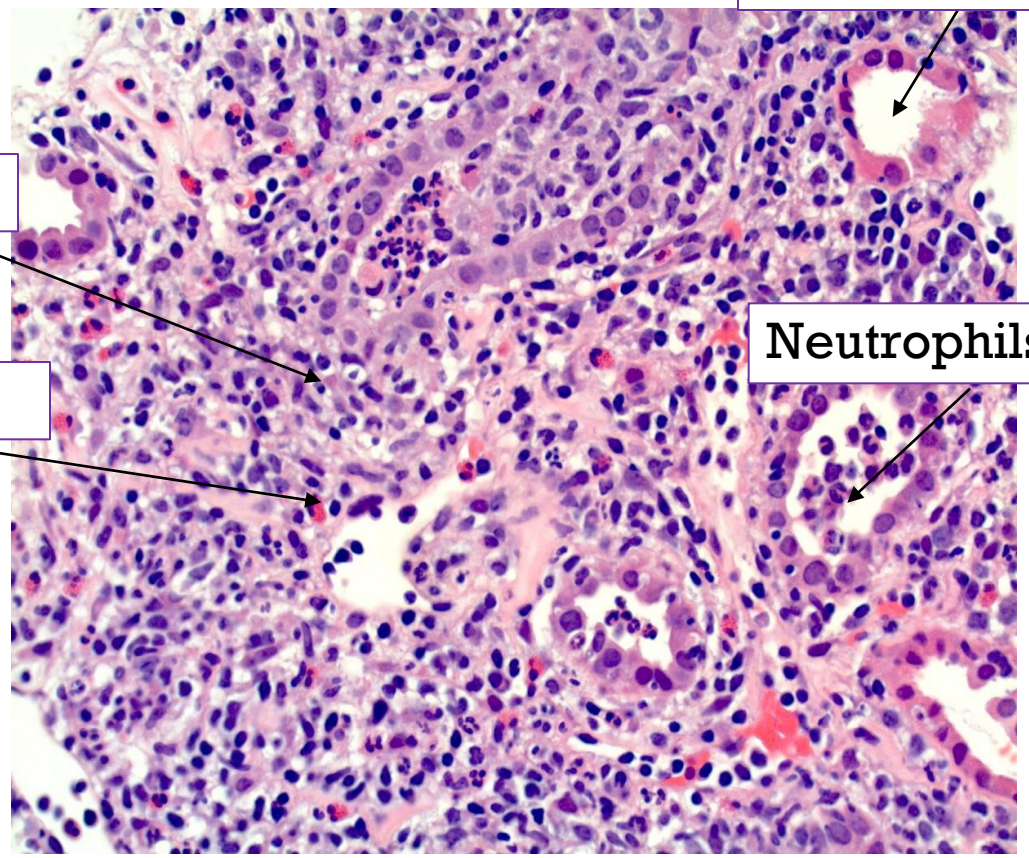
Tubulointerstitial = involves the tubules and the interstitium

Nephritis = inflammation

This appears in all cases of tubulointerstitial nephritis

## Causes :

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




Inflammatory cells ( leukocytes) are attacking >> damage in the interstitium and the tubules.
All types of leukocytes ( neutrophils, eosinophils, plasma cells , lymphocytes) are present

**divided into :** According to duration of the process

- 1-acute — Days to weeks
- 2-chronic — More than 6 weeks

# Drug-Induced Interstitial Nephritis

- **Two forms:**
- **1-Acute Drug-Induced Interstitial Nephritis**
- **2- chronic Drug-Induced (Analgesic) Nephropathy**

- **Acute form of drug- induced TIN**

Abnormal immune response against the medication ( allergy)

- **Most common: synthetic penicillins (methicillin, ampicillin)**
- **Others: synthetic antibiotics; diuretics; NSAIDs; other drugs**

# Pathogenesis of Acute Interstitial nephritis:

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

## Morphology

**interstitium : lymphocytes and macrophages, eosinophils and neutrophils**

**glomeruli are normal**

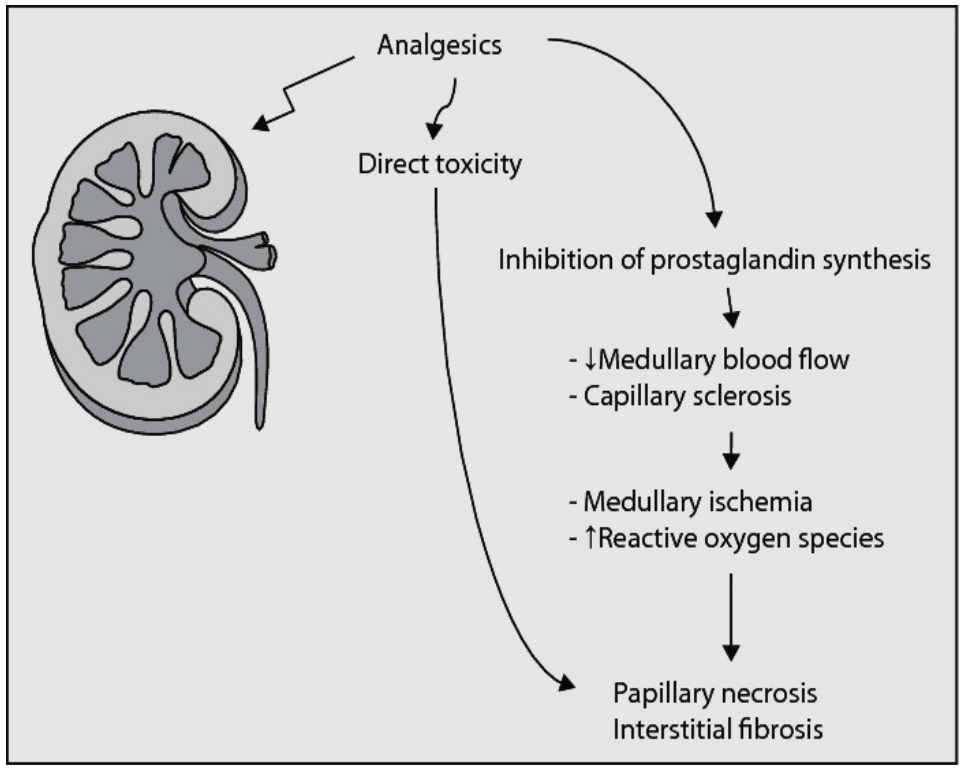
# AIN- Clinical Course

- **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**

After taking the history urine analysis and CBC test are done

Leukocytes in urine Indicating the immune response

# Analgesic Nephropathy: chronic drug- induced TIN




- Cancer patients, chronic rheumatological disease patients need analgesics for long periods of time
- Analgesics abusers

(Are susceptible to analgesic nephropathy )

- Consumption of **large** quantities of analgesics over **long** periods (years) 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**

This will lead to relative status of vasoconstriction and because of chronic duration this will lead to ischemia in renal parenchyma and interstitial fibrosis and tubular atrophy —> renal dysfunction

# *Clinical Course of chronic IN*

- Progressive renal impairment, chronic renal failure, hypertension….

- A complication of analgesic abuse is:

Very rare

increased incidence of *transitional-cell carcinoma* of the renal pelvis

# Acute Tubular Necrosis / injury (ATN/ ATI)

**characterized morphologically by damaged tubular epithelial cells**
**and clinically by acute suppression of renal function.**

***It's is the most common cause of acute renal failure.***

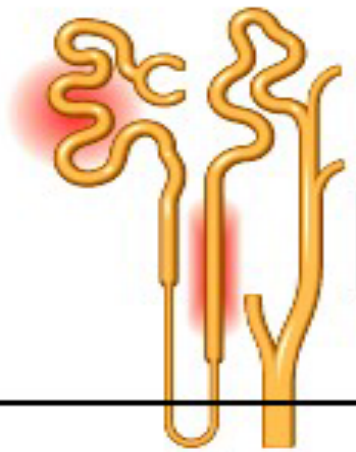
- **ATN is a reversible condition if treated properly and quickly.**

- **Clinical manifestations: electrolyte abnormalities, acidosis, uremia, signs of fluid overload, often oliguria.**
- **Proximal tubular epithelial cells are particularly sensitive to hypoxemia and toxins**

Acute renal failure ( oliguria, uremia, deterioration of consciousness, abnormal kidney function test, high urea and creatinine)

# Acute Tubular Necrosis (ATN/ ATI)

Also if a toxic agent is directly damaging the tubules , the same cascade




The fluid will go back to the interstitium

Reduction of blood flow

Necrotic cells

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

Will be translated as uremia

# ✓ ATI Types:

## 1- ischemic ATN :

Anything that leads to severe reduction in blood supply

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

## 2- nephrotoxic ATN

**poisons including heavy metals (e.g., mercury)**

**organic solvents (e.g., carbon tetrachloride)**

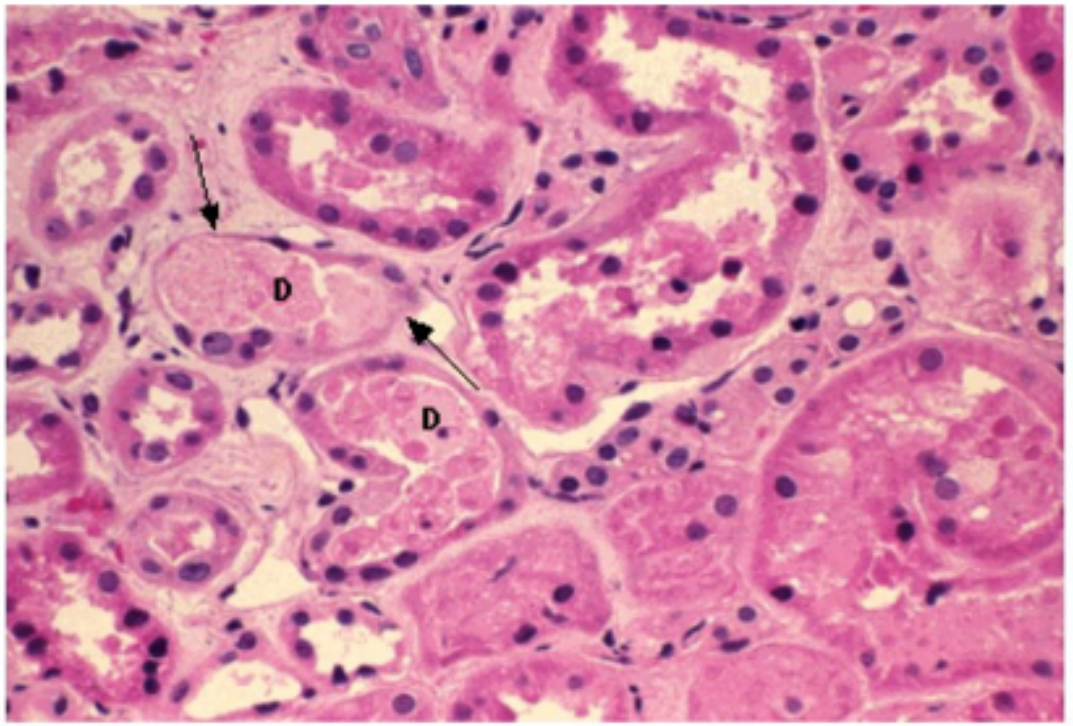
**drugs such as gentamicin and other antibiotics, and radiographic contrast agents.**

Not very important

# ATN

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

And loss of the apical brush borders




**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 ( Treating the shock, blood supply, fluids , treating the toxic agents )
- In those with preexisting chronic kidney disease, complete recovery is less frequent