PATHOLOGY

- SHEET NO. 5
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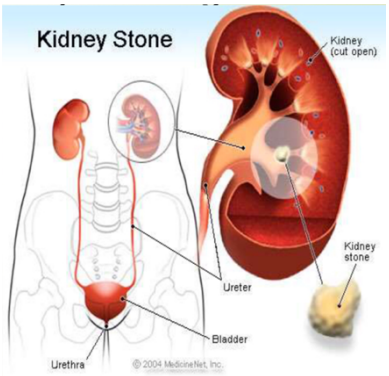
URINARY OUTFLOW OBSTRUCTION

Renal Stones (Urolithiasis)

one of the most common causes of urinary outflow obstruction and it means stone formation at any level in the urinary collecting system starting from the renal calyces and ending up at the level of urethra but the most common location is inside the kidney . Some studies indicate that (1%) of all autopsies discover cases of renal stones which lead us to 2 facts :

1. Renal stones can be a common medical issue

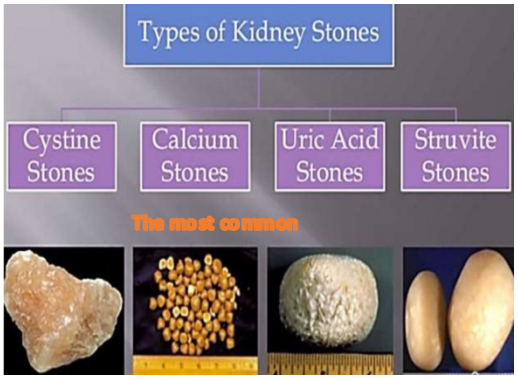
2. It could be completely asymptomatic in some patients (renal stones tend to be more Symptomatic in men)



- there are some familial tendency toward stone formation [which means that certain families might have several family members complaining & suffering from renal stones that might be recurrent]
- renal stones are usually unilateral in 80% with Variable size
- Symptoms: painful hematuria, renal colic المغص الكلوي

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

❖ **Types of renal stones** because it's the major part of the stone they are classified and named according to the inorganic component into 4 major types with different colors and different morphologies :



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

2- Struvite (magnesium ammonium phosphate inorganic salts) (<10%) as you can see in the picture they are large in size with smooth texture.

3- uric acid stones (6-7%) they have certain risk factors that will be discussed in this lecture .

4- cystine stones (2%) the least common type .

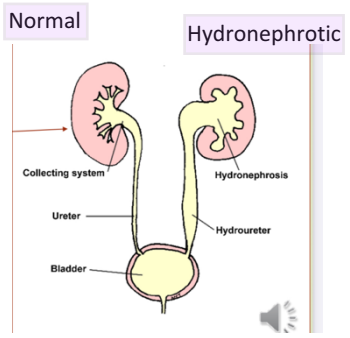
❖ **Causes of Renal Stones** , there are several precipitating factors that lead to formation of renal stones :

1. increased urine concentration of stone's constituents exceeds solubility in urine (**supersaturation**).
   - 50% of patients with **calcium stones** have hypercalciuria (increased concentration of calcium in urine) without hypercalcemia (increased concentration of calcium in blood) . This hypercalciuria with time will lead to super saturation of urine with calcium salts leading to precipitation of these salts forming calcium stones .
   - Only a small percentage of patients with calcium salts (5% to 10%) have hypercalcemia and hypercalciuria.
2. The presence of a nidus, urates provide a nidus for calcium deposition , so the nidus of a stone is the central part of it which is usually formed of organic materials like desquamated epithelial cells or some bacterial colonies . The formation and the presence of these things inside urine will encourage the formation of a renal stone
3. Urine pH; the formation of renal stones is favored at certain degrees of urine PH : like **Struvite**(magnesium ammonium phosphate) stones occur with alkaline urine that is produced by bacteria UTIs & **uric acid stones** that tend to form within acidic urine (under ph 5.5)
4. Infections : bacteria like (proteus vulgaris and staph) tend to split urea (into CO2 & NH3 ammonia) then form ammonium NH4 which forms alkaline urine encouraging the formation of alkaline stones
   haven't you noticed something? there's a link between urea splitting bacteria with alkaline urine and struvite stone
5. Disorders causing hyperuricemia/ high cell turnover and: e.g. gout; leukemia; tumor cell lysis following chemotherapy
   why cancer patient would develop renal stones? because cancer patients, especially hematological cancers, have very high cell turnover, so there are many cells dying, and when they die they increase uric acid
   *Hyperuricemia: increased uric acid concentration in the blood

6. Certain genetic/ metabolic abnormalities: that leads to either abnormal abosrption or excretion of certain metabolites
e.g. cysteine stones... people with cysteine stones always have a genetic abnormality in the metabolsim of cysteine, so there's accumulation of cysteine amino acid in the urine so they'll develop cysteine stones. because it's a genetic problem, the patients are young, and those stones appear during childhood

Hydronephrosis

Hydro: water; nephrosis: related to the kidney

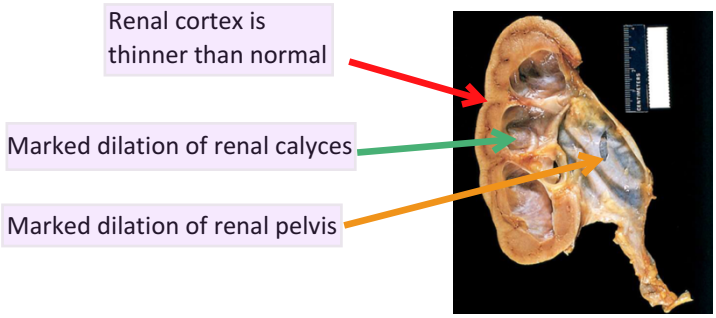


Dilation of the renal pelvis and calyces due to distal obstruction

Hydronephrosis production can be a sudden or insidious process an it can develop at any level from the urethra to the renal pelvis . The dilation will be proximal to the level of obstruction so if you have an obstruction at the level of urinary bladder or at the junction of the ureter with the urinary bladder the dilation will be proximal to it so the ureter would be dilated (hydroureter).

significance: if untreated, leads to renal parynchemal damage and dysfunction

As you can see in the picture the renal cortex and renal parenchyma of the kidney that is involved by hydronephrosis is becoming smaller in size and thickness which indicates that if hydronephrosis was left untreated it might lead to atrophy of renal parenchyma and impairment of the inner function

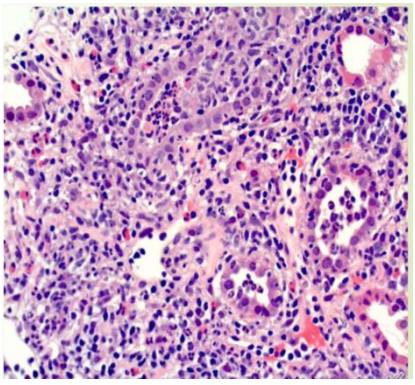


- Causes of hydronephrosis:

Congenital	Acquired
• Atresia of urethra	Foreign bodies: Calculi, necrotic apillae
• Valve formations in ureter or urethra	Tumors: prostatic hyperplasia, prostate cancer, bladder tumors, cervix or uterus cancer.
• Aberrant renal artery compressing ureter	Inflammation: Prostatitis, ureteritis, urethritis,
• Renal ptosis with torsion or kinking of ureter	Neurogenic: Spinal cord damage

Q. Is Hydronephrosis a type of renal cystic diseases? NO, it's totally another concept

Tubulointerstitial Nephritis



Also known as interstitial nephritis , as the name tubulointerstitial nephritis indicates inflammation of tubules & interstitium .

There are many causes for this disease such as : drugs , bacterial infection , metabolic disorders , physical injury (irradiation) , immune reactions .

According to the duration of the process and the manifestations of the disease we can divide it into 2 types :

1. Acute
2. Chronic

- This picture shows us the presence of significant inflammatory infiltrates that are attacking the tubules as well as the interstitium including different types of leukocytes like eosinophils , lymphocytes , neutrophils and macrophages .

Now we will discuss one type of tubulointerstitial nephritis which is **Drug-Induced Interstitial Nephritis**

According to the duration of the process, (drug induced interstitial nephritis) can be divided into :

1-Acute Drug-Induced Interstitial Nephritis :

Associated most commonly with the use of synthetic penicillins (methicillin , ampicillin) , other medications including other synthetic antibiotic , some diuretics , NSAIDs as well as other drugs

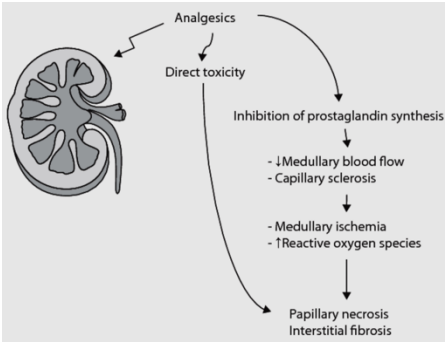
- **Pathogenesis of Acute Interstitial nephritis:** it is an immunologic mechanism ,some say that it is related to type 1 hyper sensitivity reactions while others say that type 4 hypersensitivity reactions (T cell-mediated) might play a rule as well
- **Morphology**
  The presence of leukocytes within the interstitium and tubules including lymphocytes , macrophages , eosinophils , neutrophils . The glomeruli are usually spared from this condition
- **Acute form of drug induced IN- Clinical Course**
  It usually begin 2 to 40 days after exposure to the drug , they include :

1. fever 😜 , eosinophilia , rash (25%)
2. Renal abnormalities : mainly in the form of hematuria , minimal or no proteinuria and leukocyturia which means the presence of leukocytes within urine

This condition is of an acute onset and usually recovery develops soon following withdrawal of the offending medication .

2- chronic (Analgesic) drug induced nephropathy:

As the name indicates the major offender of this disorder are the analgesics , the clinical setting of this condition is the consumption of large quantities of analgesics over a long period of time leading to chronic interstitial nephritis along with renal papillary necrosis .



- Aspirin and acetaminophen are common causes
- Pathogenesis is not entirely clear but is said to be related to :
  - Covalent binding and oxidative damage
  - Inhibition of prostaglandin synthesis

So they can have direct toxicity that leads to renal papillary necrosis and interstitial fibrosis but at the same time the major effect is through inhibition of prostaglandin synthesis leading to vasoconstriction and reduces medullary blood flow and cause capillary sclerosis with time this will lead to ischemia and to production of reactive oxygen species and with the progression of the disease and continuous using of those medications over a long period of time this will also add to papillary necrosis and interstitial fibrosis

- Clinical course of chronic interstitial nephritis , it is usually variable and usually accompanied by progressive renal impairment and then 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)

Another term for this disease is acute tubular injury, it is characterized **morphologically** by damaged tubular epithelial cells and **clinically** by acute suppression of renal function. In fact acute tubular injury is the most common cause of acute renal failure worldwide. 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 maybe more than any other part in the kidney .

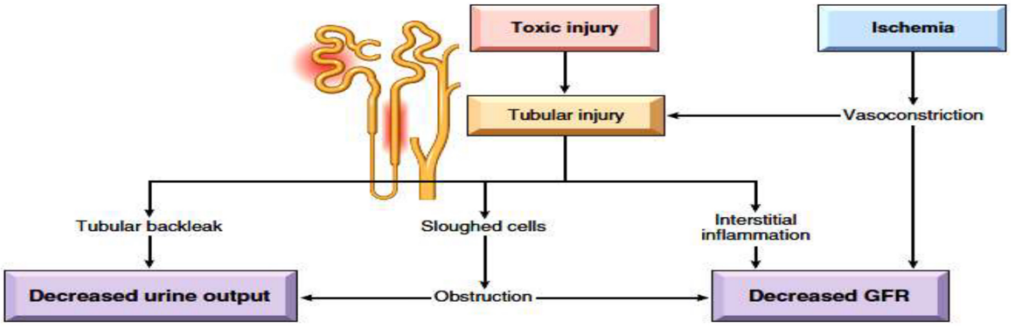


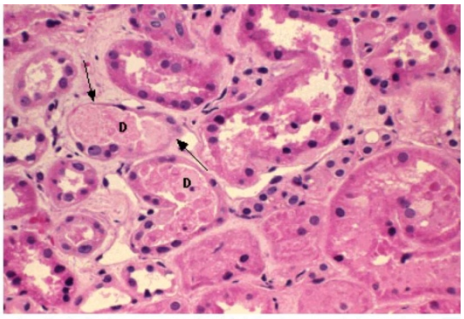
Fig. 14.16 Postulated sequence in ischemic or toxic tubular injury.

- ❖ **The causes are toxic injury & ischemic injury (the most common)**

- ○ Ischemia leads to vasoconstriction which leads to decrease GFR and this will be translated into acute renal failure and it is associated with shock (e.g. severe trauma; acute pancreatitis; septicemia; mismatched blood transfusion, hemolytic crises, myoglobinuria, etc...)
- ○ The second type which is less common is nephrotoxic ATN that is related to certain nephrotoxic material that is introduced into the kidney such as : poisons including heavy metals (e.g., mercury) , organic solvents (e.g., carbon tetrachloride) , drugs such as gentamicin and other antibiotics, and radiographic contrast agents.

- ○ The toxic injury that is produced by certain medications or certain substances would lead to acute tubular necrosis that is accompanied by interstitial inflammation
- ○ injured tubules will have sloughed cells that will block and cause obstruction at the level of tubular lumen
- ○ The injured tubules will lack the basement membrane so there will be back-leak from substances and toxins within urine into the tubular vascular bed
- ○ All these together will lead to decrease GFR as well as reduction of urine output giving us the clinical picture of ATI

- This picture shows a case of ATN the proximal renal tubules are showing different manifestations and evidences of Acute injury including the presence of sloughing epithelial cells in the lumen of tubule & flatting of the epithelial cells . epithelial cell injury with blebbing at the luminal pole, detachment of tubular cells from their underlying basement membranes, and granular casts



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

The most important thing to remember about ATI is that it can be a reversible process if it was treated properly and quickly .

Tubular epithelial cells have good capability of repair and regulation so with proper management , gradual clinical improvement with the gradual tubular regeneration would be the case in most cases

- repair and tubular regeneration —> gradual clinical improvement
- With supportive care, patients who survive have a good chance of recovering renal function
- those with preexisting chronic kidney disease or abnormal renal function for whatever underlying cause may not show complete recovery from acute tubular necrosis.

Past Papers

1- All of the following can lead to hydronephrosis, except ONE:
a. Atresia of urethra .
b. PKHDI mutations.
c. Ptosis of renal pelvis.
d. Prostatic hyperplasia .
e. Spinal cord damage.

2- All are correct regarding acute drug-induced tubulointerstitial nephritis, except one :
a. Characterized by fever, skin rash and eosinophilia .
b. Develops within days to weeks following drug exposure.
c. Causes hematuria without significant proteinuria .
d. Increased risk of urothelial carcinoma of the renal pelvis .
e. Hypersensitivity reactions may be implicated.

3- "Struvite" renal stones are composed of :
a. Magnesium ammonium phosphate.
b. Calcium phosphate.
c. Cystine crystals .
d. Uric acid crystals.
e. Calcium oxalate.

4- Pathogenesis of analgesic nephropathy :-
a. T-cell mediated
b. Inhibition of PG synthesis
c. Type I hypersensitivity reaction
d. Non-covalent binding to enzymes

Answers:
1. B 2. D 3. A 4. B

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