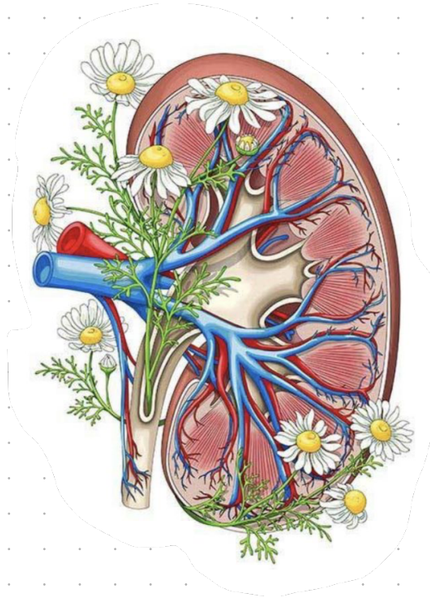
Pathology



Renal Disease

Tubular And Interstitial Disease (Lec 7)

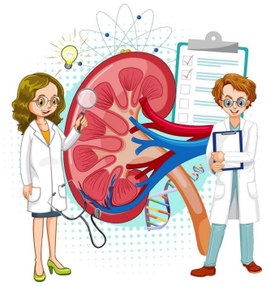
La Medica Academy
Study Smarter Not Harder

Done by : Saja Al-raggad

Tubulointerstitial Nephritis

- Most forms of tubular injury also involve the interstitium

→ so the two are discussed together.



- Diseases characterized by :

1- A group of inflammatory diseases that primarily involve the interstitium & tubules (Tubulointerstitial Nephritis)

Acute Chronic

2. Ischemic or toxic tubular injury
→ acute tubular injury & the clinical syndrome of acute kidney injury.

- Distinguished clinically from the glomerular diseases by :
  - No nephritic or nephrotic syndrome. (glomerular symptoms)
  - The presence of defects in tubular function. (tubular symptoms)
    - polyuria
    - nocturia
    - electrolytes
    - metabolic acidosis

- Causes:

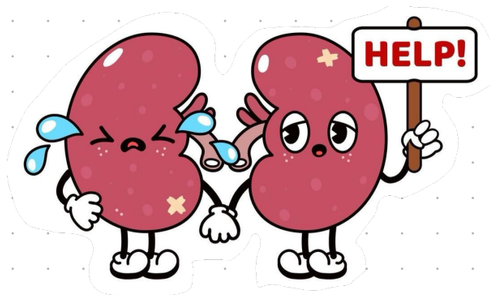
a. Bacterial infections
b. Drugs.
c. Metabolic disorders.
d. Irradiation.
e. Immune reactions.

1-Acute Pyelonephritis
2-Chronic Pyelonephritis
3-Drug-Induced Tubulointerstitial Nephritis

→ Main mechanism → inflammatory response

4-Acute Tubular Injury / Necrosis →

Main mechanism →
- indirectly due to prolonged ischemia
- directly due to toxin mediated damage



1-Acute Pyelonephritis

• A common suppurative inflammation of the tubules, interstitium & the renal pelvis

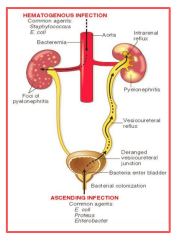
→ caused by bacterial infection (enteric gram- negative bacilli)

-Escherichia coli is by far the most common

Other important organisms:
– Proteus, Klebsiella, Enterobacter & Pseudomonas; uncommonly Staphylococci and Streptococcus faecalis.

Urinary Tract Infection UTI

▪ Manifestation → Lower (cystitis, prostatitis,urethritis), or upper (pyelonephritis) tracts or both.

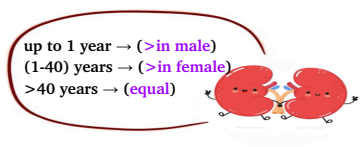


▪ Bacteria can reach the kidneys:

a) From the lower urinary tract (ascending infection).
-(Most common)
-remain localized and do not spread to the kidney.

b) Through the bloodstream (hematogenous infection).

➢ UTI risk factors:



1. UTI most commonly affects females; proximity of urethra to the rectum, the short urethra & trauma to the urethra during sexual intercourse.

2. Instrumentation, including catheterization & cystoscopy.

3. Obstruction; stones or BPH → stasis → natural defense mechanisms in bladder are overwhelmed.

4. Diabetes mellitus: the increased susceptibility to infection & neurogenic bladder dysfunction (stasis). (especially uncontrolled)

5. Pregnancy; pressure on the bladder Gureters from the growing uterus.

6. Incompetence of the vesicoureteral orifice → (VUR), is an important cause of ascending infection. (20-40% of young children with UTI).

➢ Vesicoureteral Reflux (VUR)

grades

presented with recurrent UTI

✓ It allows bacteria to ascend the ureter into the pelvis.

✓ Pathogenesis:

In Children

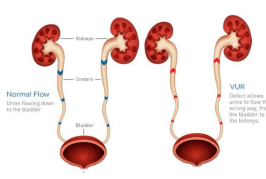
consequence of a congenital defect that results in incompetence of the ureterovesical valve.

Acquired

in individuals with a flaccid bladder resulting from spinal cord injury or with bladder dysfunction secondary to diabetes.

✓ results in residual urine after voiding in the urinary tract → favors bacterial growth.

Furthermore, VUR affords a ready mechanism where the infected bladder urine can be propelled up to the renal pelvis and further into the renal parenchyma through open ducts at the tips of the papillae (intrarenal reflux).



➢ Clinical:

– sudden pain at the costovertebral angle. (Flank pain)

– Systemic signs of infection; chills, fever, nausea, malaise and localizing urinary tract signs (dysuria, frequency, & urgency).

– With predisposing factors → the disease maybe recurrent or chronic → more likely to be bilateral.

– unilateral → no renal failure.

– Urine appears turbid → pus (pyuria).

2-Chronic Pyelonephritis

• A disorder in which chronic tubulointerstitial inflammation and scarring involves the calyces and pelvis.

hallmark of chronic Pyelonephritis → leading to papillary blunting and marked calyceal deformities.

• Chronic reflux-associated pyelonephritis is the most common cause of chronic pyelonephritis.

• Many patients come to medical attention late in the course

↓

If the disease is bilateral & progressive

↓

tubular dysfunction

↓

an inability to concentrate the urine

↓

polyuria and nocturia.

Chronic obstructive pyelonephritis	Chronic reflux-associated pyelonephritis
– Obstruction predisposes to infection. – Recurrent infections superimposed on diffuse or localized obstructive lesions → recurrent renal inflammation & scarring → chronic pyelonephritis. – Bilateral, with congenital anomalies of the urethra (e.g., posterior urethral valves). – Unilateral, in renal stones and unilateral obstructive lesions of the ureter.	– The most common cause of chronic pyelonephritis. – Superimposition of a UTI on congenital vesicoureteral reflux & intrarenal reflux. – Both the reflux & the renal damage may be unilateral or bilateral. – Bilateral → potentially lead to chronic renal insufficiency

➢ Morphology:

– Kidneys are irregularly scarred.

– If bilateral, the involvement is asymmetric.

(in chronic GN diffusely & symmetrically scarred).

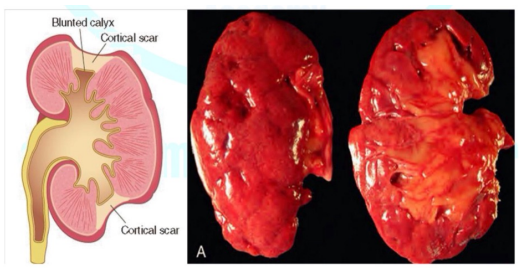
– Coarse, discrete, corticomedullary scars, blunted papillae

Note :

مش اي scarring تابع لهاذ المرض

Diffuse irregular → nephrotic & nephritis

irregular +Papillary blunting → Chronic Pyelonephritis



3-Drug-Induced Tubulointerstitial Nephritis

- occurs as an adverse reaction to any one of an increasing number of drugs.

- (idiosynchratic) in some patients { not expected / not dose-related

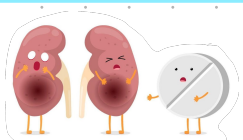
- Pathogenesis is immune reaction: (hapten reaction)

– Immediate (Type 1) hypersensitivity reaction.
– T cell-mediated (Type 4) hypersensitivity reaction.

hapten → جزيئات صغيرة ما بتعمل immune reaction

(hapten + large protein) → Complex can trigger immune reaction

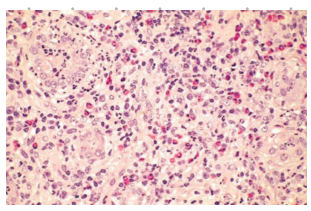
- Drugs :



a. Penicillins (methicillin, ampicillin).
b. Other antibiotics (rifampin).
c. Nonsteroidal anti-inflammatory agents.
d. Diuretics (furosemide).
e. Proton pump inhibitors (omeprazole).

➢ Morphology LM :

–The abnormalities are in the Interstitium → pronounced edema & infiltration by mononuclear cells, principally lymphocytes & macrophages.



–Eosinophils & neutrophils may be present, in large numbers.

➢ Clinical :

– The disease begins about 15 days after exposure to the drug.

* الذي نعالم ، نقدر الشخص المرض من خلالهم ① ② ③

– Fever, eosinophilia (transient), rash (~25%), and renal abnormalities.

– Urinary findings include hematuria, minimal or no proteinuria & leukocyturia (+/-eosinophils).

– Acute kidney injury with oliguria ~ 50% of cases (more in older age).

– Clinical recognition is imperative → withdrawal of the offending drug is followed by recovery → but renal function may take several months for to return to normal.

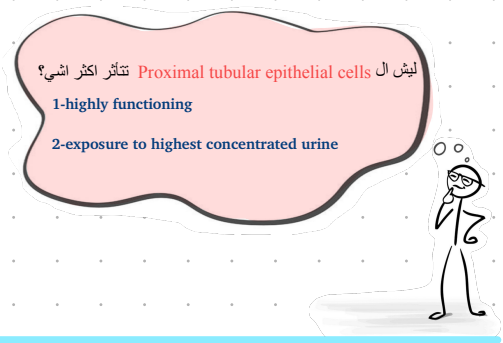
4-Acute Tubular Injury / Necrosis

- The most common cause of acute renal failure.

- Damage to tubular epithelial cells & an acute decline in renal function.

• Pathogenesis :

–Proximal tubular epithelial cells are particularly sensitive to hypoxemia and also are vulnerable to toxins.



• Prognosis :

– It is a reversible condition, 95% recover if properly and promptly treated.

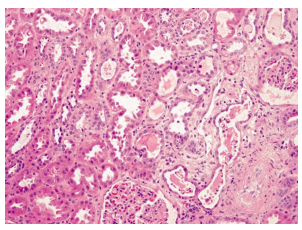
– varies depending upon the severity and nature of Injury, also comorbid conditions.

•Presentation :

↓ GFR ↑ serum creatinine

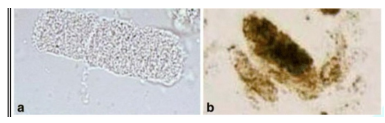
➢ Morphology :

– Blebbing, vacuolization, & detachment of tubular cells from their underlying basement membranes with sloughing of cells into the urine & proteinaceous casts.



عبارة عن tubular epithelial cells الي انجرحوا وصار فيهم necrosis &damage

-epithelial casts
-Muddy brown cast



➢ Clinical :

– initially is dominated by the inciting medical, surgical or obstetric event.

– Manifestations of:
acute kidney injury, oliguria & ↓ ↓ GFR, electrolyte abnormalities, acidosis & signs and symptoms of uremia & fluid overload.

• Two forms of ATl: differ in underlying causes:

Ischemic ATI	Nephrotoxic ATI
– A period of inadequate blood flow. – In a setting of hypotension/shock. – Conditions; severe trauma, blood loss, acute pancreatitis & septicemia. Mismatched blood transfusions & other hemolytic crises.	Caused by: – Poisons, including heavy metals(mercury) – Organic solvents (carbon tetrachloride). – Drugs such as gentamicin & other antibiotics, & radiographic contrast agents.