Renal Disease

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Tubular & Interstitial Diseases

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tubular & Interstitial Diseases

- Most forms of tubular injury also involve the interstitium → so the two are discussed together.
- Diseases characterized by:

1. Inflammatory involvement of the tubules & interstitium (tubulointerstitial nephritis)
2. Ischemic or toxic tubular injury → acute tubular injury & the clinical syndrome of acute kidney injury.

Tubulointerstitial Nephritis

01 A group of inflammatory diseases that primarily involve the interstitium & tubules.

- Acute
- Chronic

02 Distinguished clinically from the glomerular diseases by the following hallmarks

- No nephritic or nephrotic syndrome
- The presence of defects in tubular function

03 Causes

- Bacterial Infections,
- Drugs
- Metabolic disorders
- Irradiation
- Immune reactions

Acute Pyelonephritis

01 A common suppurative inflammation of the tubules, interstitium & the renal pelvis, caused by bacterial infection.

02 Manifestation of urinary tract infection (UTI); UTI can involve: Lower (cystitis, prostatitis, urethritis), or upper (pyelonephritis) tracts or both.

03 The principal causative organisms in acute pyelonephritis are enteric gram-negative bacilli. Escherichia coli is by far the most common.

04 Other important organisms: Proteus, Klebsiella, Enterobacter, & Pseudomonas; uncommonly Staphylococci & Streptococcus faecalis

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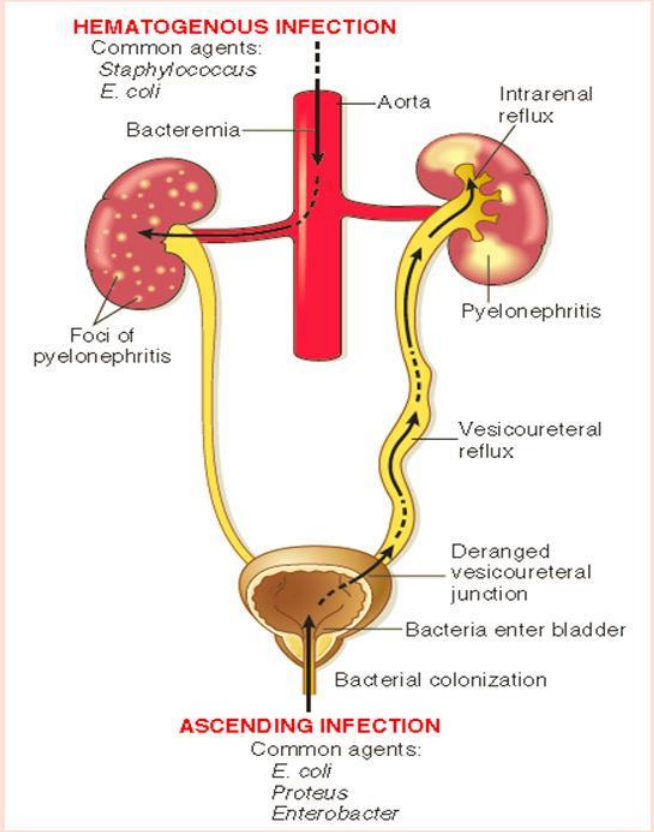
Urinary tract infection (UTI)

- Bacteria can reach the kidneys:

a) from the lower urinary tract (ascending infection)

b) through the bloodstream (hematogenous infection)

- The great majority of cases of pyelonephritis are associated with infections of the lower urinary tract, which are very common.
- Most infections of the lower urinary tract remain localized and do not spread to the kidney.



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)
5. Pregnancy ; pressure on the bladder &ureters from the growing uterus
6. Incompetence of the vesicoureteral orifice → vesicoureteral reflux (VUR), is an important cause of ascending infection. (20-40% of young children with UTI)

Vesicoureteral reflux (VUR)

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

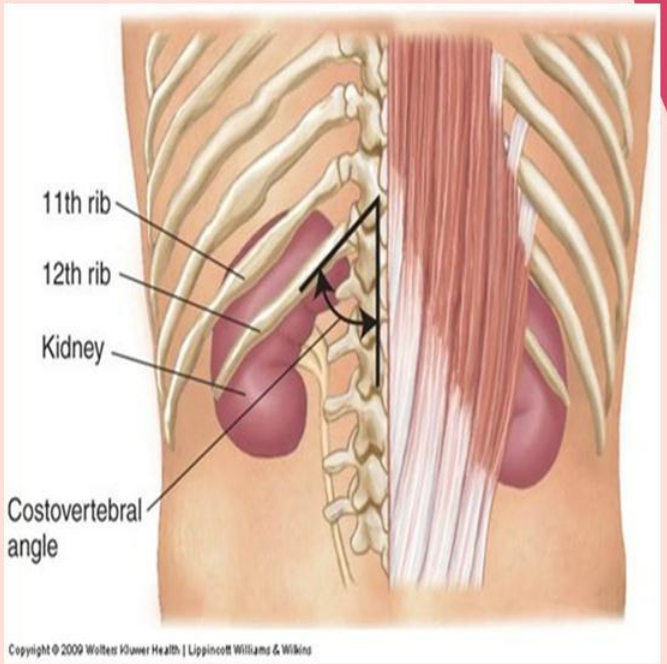
Pathogenesis:

- **In Children** usually a 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.
- VUR 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).

Acute pyelonephritis — Clinical

- Usually present with sudden onset of pain at the costovertebral angle
- Systemic signs of infection; chills, fever, nausea, malaise, & localizing urinary tract signs (dysuria, frequency, & urgency)
- Urine appears turbid → pus (pyuria).
- Usually unilateral → no renal failure.
- With predisposing factors → the disease maybe recurrent or chronic → more likely to be bilateral.



Chronic Pyelonephritis

01 A disorder in which chronic tubulointerstitial inflammation & scarring involve the calyces and pelvis

02 Chronic reflux–associated pyelonephritis is the most common cause of chronic pyelonephritis.

03 The hallmark of chronic pyelonephritis is scarring involving the pelvis or calyces, or both, leading to papillary blunting and marked calyceal deformities

04 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 & nocturia.

chronic pyelonephritis

Chronic Obstructive Pyelonephritis

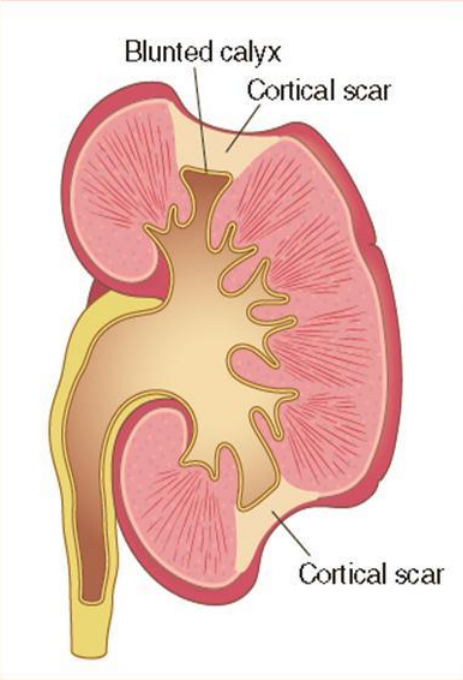
- obstruction predisposes to infection
- Recurrent infections superimposed on diffuse or localized obstructive lesions → recurrent renal inflammation & scarring→ chronic pyelonephritis.
- **Bilateral**, with congenital anomalies of the urethra (e.g., posterior urethral valves)
- **Unilateral**, in renal stones and unilateral obstructive lesions of the ureter.

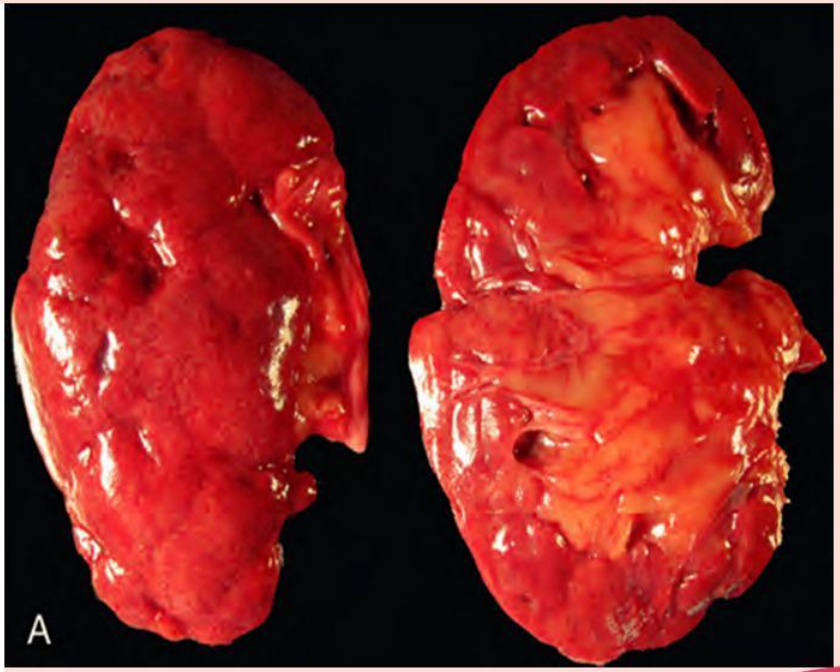
Chronic Reflux–Associated Pyelonephritis

- **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.

Chronic Pyelonephritis - Morphology

- Kidneys are irregularly scarred;
- If bilateral, the involvement is asymmetric. (in chronic GN diffusely & symmetrically scarred).
- Coarse, discrete, corticomedullary scars, blunted papillae





Drug-Induced Tubulointerstitial Nephritis

01 Acute drug-induced TIN occurs as an adverse reaction to any one of an increasing number of drugs.

02 Pathogenesis is immune reaction

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

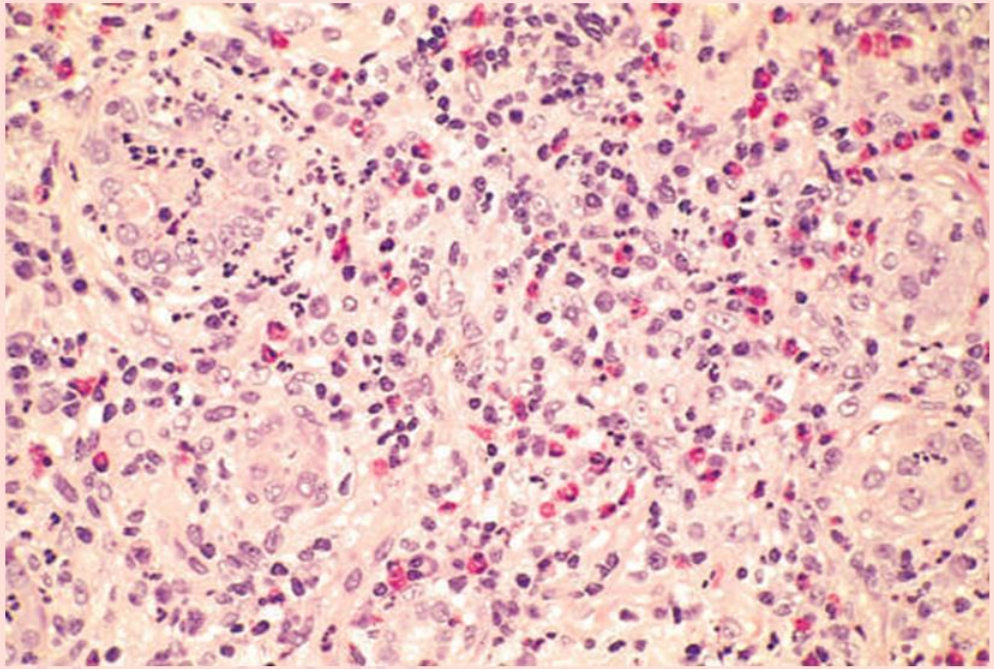
03 Drugs associate/w TIN

- penicillins (methicillin, ampicillin)
- other antibiotics (rifampin)
- nonsteroidal anti-inflammatory agents
- Diuretics (furosemide)
- proton pump inhibitors (omeprazole)

Drug-Induced Tubulointerstitial Nephritis

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.



Drug-Induced Tubulointerstitial Nephritis

Clinical

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

Acute Tubular Injury/Necrosis

01 About the Disease

Damage to tubular epithelial cells & an acute decline in renal function
The most common cause of acute renal failure

02 Pathogenesis

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

03 Prognosis

It is a reversible condition, 95% recover if properly and promotly trated

04 Presentation

Manifests clinically as decreased GFR with concurrent elevation of serum creatinine

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Two forms of ATI: differ in underlying causes:

Ischemic ATI

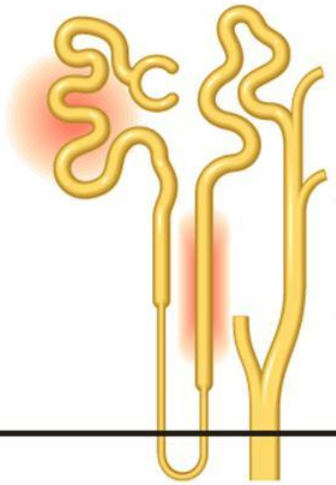
- A period of inadequate blood flow
- In a setting of hypotension/ shock.
- Conditions; severe trauma, blood loss, acute pancreatitis & septicemia. Mismatched blood transfusions & other hemolytic crises,

Nephrotoxic ATI

caused by;

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

Acute Tubular Injury



Toxic injury

Ischemia

Tubular injury

Vasoconstriction

Tubular backleak

Sloughed cells

Interstitial inflammation

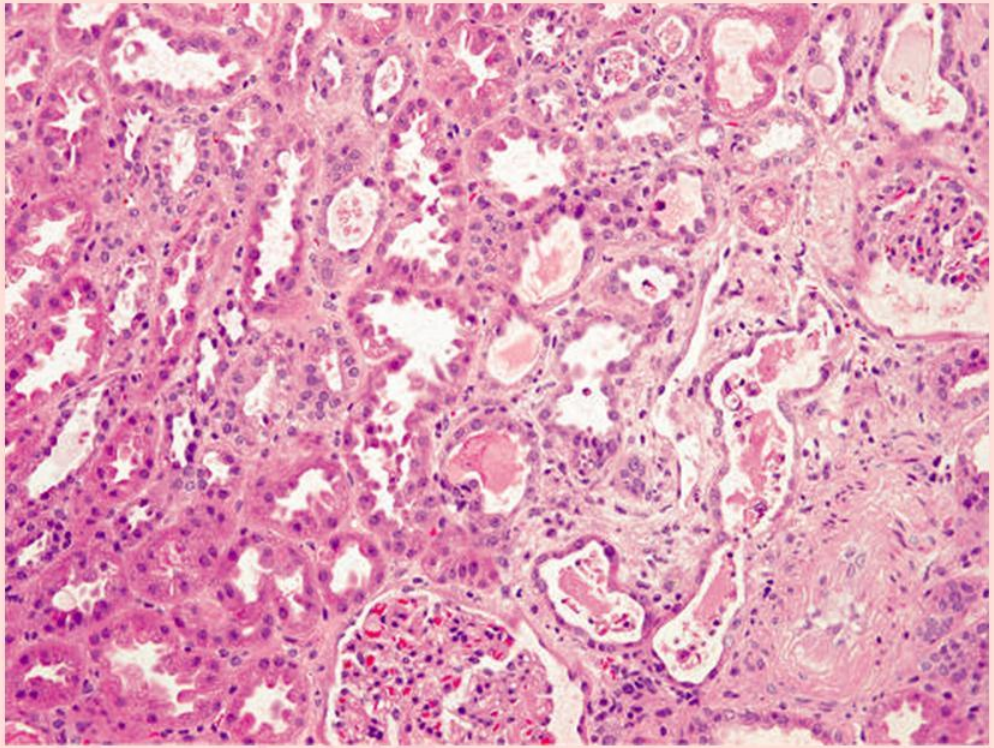
Decreased urine output

Obstruction

Decreased GFR

Acute Tubular Injury -Morphology -LM

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



Acute Tubular Injury - Clinical

- The clinical course 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.
- Prognosis varies depending upon the severity & nature of Injury, also comorbid conditions

Question?

Thanx!

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