**Renal Pathology**

**Dr. Methaq Mueen/ Lec 3**

**Diseases of tubules & Interstitium**

Group of diseases characterized by:

* **Inflammatory** involvement of tubules & Interstitium (tubulointerstitial nephritis).
* Acute tubular **necrosis** (ischemic or toxic renal injury).

**Tubulointerstitial nephritis**: characterized by

* Mainly affect tubules & Interstitium.
* Glomeruli are usually spared & only affected late in the disease.
* Most of cases are caused by bacterial infection.
* Some cases are due to drugs, hypokalemia, irradiation.
* tubulointerstitial nephritis can be either acute or chronic.

**Acute Tubular Necrosis:**

It is a clinicopathological entity characterized morphologically by destruction of tubular epithelium and clinically by acute renal failure.

**Pathogenesis(Causes of ATN)**

It can be caused by;  
1. Ischemia(this is due to shock)..  
2. Direct toxic injury of tubules (poisons like CCl4, drugs like gentamicin, radiation).

**Clinical features:**  
Clinical course of ATN It is highly variable, but in classical cases is divided into three phases:

**Initiating phase:**

* Last for 36 hours.
* Decrease renal output(mild oliguria) & rise in blood urea.

**Maintaining phase:**

From 2nd -6th day.

Urine output further fall (between 50cc to 400cc / day).

Features of Uremia, fluid overload.

Without treatment patient may die within this phase, while with good care the survival is the rule.

**Recovery phase:**

Steady increase in urine volume, reaching up to 3 liters per day over a period of 3 weeks.

Serious electrolytes imbalance( hypokalemia) due to tubular function dysfunction.

Increased susceptibility to infection.

**Urinary Tract Infection**  
UTI either lower UTI like cystitis, prostatitis, urethritis or Upper Pyelonephritis or both.

**Acute Pyelonephritis (PN):** It is a common suppuritive inflammation of kidney & renal pelvis caused by bacterial infection and In over 85% of cases, gram negative bacilli are responsible, the most common is E. coli, followed by Proteus, Klebsiella, and Enterobacter.

**Chronic PN,** is more complex disorder, bacterial infection plays a dominant role, but other factors (Vesicoureteral reflux, obstruction), are involved also in the pathogenesis.

**Pathogenesis of pyelonephritis (UTI):**• Routes of infection:

* Ascending infection (from lower urinary tract) ……. (Commonest).
* Hematogenous (by blood stream).

**Predisposing factors of UTI**:

1-Female > male (short urethra, urethral trauma during intercourse, close proximity of urethra to the rectum).

2-Congenital abnormality of urinary tract.

3-Urinary tract Catheterization.

4-Urinary tract obstruction (stone, tumors, & benign prostatic hyperplasia).

5-Vesicoureteric reflux disease (either congenital or Acquired).

6-Pregnancy.

7. Diabetes mellitus.

8. Immunodeficiency.

**Morphology of acute pyelonephritis:**

**Gross:** Kidney (single or bilateral) may be normal in size or enlarged.

Discrete, raised abscesses on the renal surface.

**MIC:**

The hallmark is patchy interstitial suppurative inflammation(large masses of neutrophils) within the renal parenchyma, tubular leukocyte casts and tubular necrosis.

Typically the glomeruli are resistant to the infection.

**Complications of acute pyelonephritis**:

* Necrotizing Papillitis:This is mainly seen in D.M, coagulative necrosis at the tip of papillae, indicate poor prognosis & end with renal failure.
* Pyonephrosis, when there is total or almost complete obstruction, especially when it is in the upper part of the urinary tract.
* Perinephric abscess.
* Septicemia.

**Clinical features,**

* Sudden onset of pain at costophrenic angle (renal angle), and systemic evidence of infection, such as fever , chills and malaise.
* There is also dysuria, frequency and urgency.
* GUE (Pyuria, bacteriuria),urine contains pus cells and leukocyte casts and bacteria   
  **Prognosis:**
* It needs treatment with antibiotics .
* The disease become chronic if there is predisposing factors & bilateral disease.

**Chronic Pyelonephritis :**

It is characterized by chronic tubulointerstitial inflammation and renal **scarring** associated with pathologic involvement of the calyces and pelvis.

It is an important cause of end-stage kidney disease.

* Predominantly interstitial inflammation & scarring of the renal parenchyma.
* Associated with grossly visible scarring & deformity of pelvicalceal system.
* **Divided into 2 types:**

1. Chronic obstructive pyelonephritis, which could be unilateral or bilateral.
2. Chronic reflux with pyelonephritis, which is the more common. It occurs early in childhood.  
     
   **Urinary Tract Obstruction (Obstructive Uropathy)**

Complications of obstruction:

* increases susceptibility to infection and to stone formation,
* and if unrelieved, it leads to permanent renal atrophy, termed hydronephrosis.

The obstruction may be sudden or insidious, partial or complete, unilateral or bilateral, and it may occur at any level.

The most common **causes of obstruction**  are:

1.Congenital anomalies, posterior urethral valves and urethral strictures.  
2. Urinary calculi.  
3. Prostatic hyperplasia.  
4. Tumors.  
5. Inflammation.  
6. Pregnancy.  
7. Functional disorders, neurogenic bladder.

**Pathogenesis**, even with complete obstruction, glomerular filtration persists for sometimes.This continued filtration leads to pelvicalyceal dilation, which leads in turn to renal atrophy and hydronephrosis

**Morphology,**

When the obstruction is sudden and complete, there is mild hydronephrosis, but if the obstruction is subtotal or intermittent, there is more severe hydronephrosis.

Depending on the level of urinary block, the ureter and the bladder may be affected too.

In advanced cases, the kidney may become transformed into a thin-walled cystic structure .  
**Chronic Pyelonephritis & Reflux Nephropathy**: characterized by

* More common form characterized by recurrent pyelonephritis associated with congenital Vesicoureteric reflux.
* Can be uni or bilateral diseases.

**Morphology of chronic pyelonephritis:**

**Gross:**

* Unequal contracted kidneys (sometime only one kidney is involved).
* The hallmark of Pyelonephritis is scarring involving the pelvis or calyces or both leading to blunting of papillary blunting & marked calyceal deformity.

**Mic:**

* Interstitial **fibrosis** (uneven).
* Inflammatory infiltrate (**lymphocytes**, plasma cells, & occasional Nutrophils).
* Dilated or contracted of tubules, with atrophy of lining epithelium.
* Many of **dilated tubules** contain pink, glassy appearing casts known as **Colloid Casts** that suggest appearance of thyroid tissue (**Thyroidization of renal tubules**),
* Glomeruli are usually spared, sometime there is focal glomerulosclerosis.

**Clinical Features:**

* Gradual onset of renal insufficiency.
* Hypertension

**Urolithiasis(urinary stones):**Is a stone formation at any level in the urinary collecting system. Most often arise in the kidney.

* The peak age at onset is 20-30 years. Male > female
* Some have familial tendency.

**Types of renal stones:**

according to chemical composition

1. Calcium oxalate or Calcium oxalate mixed with Calcium phosphate (75%).

2. Magnesium ammonium phosphate (15%).

3. Uric acid & cystine stones (10%).

**Causes of renal stones according to chemical types:**1. Calcium oxalate or Calcium phosphate

* Idiopathic hypercalciuria (50%)…….(abnormal absorption of Ca+2 & abnormal reabsorption of Ca+2 by the kidney).
* Hypercalcemia & Hypercalciuria (as in hyperparathyroidism, vitamin D intoxication, or sarcoidosis).
* Hyperoxaluria (increased Ca+2 reabsorption).
* Hyperuricosuria (urate act as favored nidus for calcium deposition).
* Unknown metabolic abnormality.

2. Magnesium ammonium phosphate (struvite).

* Renal infection (mostly Proteus {urea splitting bacteria}, Staphylococci), bacteria act as nidi for stones formation.

3. Uric acid stones

* Hyperuricemia.
* Hyperuricosuria
* Idiopathic

Note: in all types there is an organic matrix of mucoprotein form about 2.5% of weight of stones.

**Morphology of renal stones:**Unilateral stones in about 80% of patients

* Common sites of stone formation are renal pelvis, calyces, & bladder.
* The stones may have smooth contours or irregular external surface and on occasion they develop branches (stag-horn stones) branching stone, fill the renal pelvis & calyces and take a shape of the pelvicalyceal system ).

**Clinical features:**

* Symptomless like in staghorn stone.
* Renal colic & Uretric colic.
* Gross hematuria.

**Complications** are obstructive uropathy, recurrent UTI, ulceration ,bleeding

**Hydronephrosis**: dilatation of the renal pelvis & calyces, with progressive atrophy of the parenchyma, caused by obstruction to the outflow of urine.

It may occur at any level of urinary system from the urethra to the renal pelvis.

**Causes of Hydronephrosis:**

**1-congenital:**

* Atresia of the urethra.
* Aberrant renal artery compressing the ureter.
* Renal torsion.

**2. Acquired:**

* Foreign bodies: stones, necrotic papillae.
* Tumors: BPH, Carcinoma of prostate, bladder tumors (papilloma & carcinoma), Carcinoma of cervix.
* Inflammation: Prostatitis, Urethritis, Ureteritis.
* Nurogenic: Spinal cord damage with paralysis of the bladder.
* Normal pregnancy: mild & reversible.

**Morphology of Hydronephrosis:**

**1. Bilateral Hydronephrosis:** if the level of obstruction is below the URETER, lead to renal failure**.**

**2. Unilateral Hydronephrosis:** if the level of obstruction is above the URETER

display wide range of morphological changes, which vary with the degree & speed of obstruction.

**I. Subtotal or intermittent obstruction,**

* Kidney may be massively enlarged (20cm in length), & entirely distended pelvicalceal system.

Compressed & atrophied renal parenchyma.

* Obliteration of papillae & flattening of pyramids.

**II. When obstruction is sudden & complete,**

* GFR is reduced while dilatation is still slight.
* Unilateral or Bilateral hydroureter.

**Mic:**

* Tubular dilation follows by tubular atrophy & fibrous replacement of tubular epithelium with relatively sparing of the glomeruli.
* Eventually in severe cases the glomeruli become atrophic & disappear, converting the entire kidney into a thin shell of fibrous tissue.

**Clinical features:**

In case of bilateral complete obstruction:

1. Anuria.

2. Bladder distention (obstruction below the level of bladder).

3. Polyuria due to defect in tubular concentrating mechanisms & incomplete obstruction.

In case of unilateral hydronephrosis: Remain silent & diagnosed on routine examination as enlarged kidney.