# Al-Mustaqbal University College


# Pathophysiology 3rd stage

# Disorders of Renal System

# Part 3

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## Nephrotic Syndrome

Nephrotic syndrome is the loss of 3.5 g or more of protein in the urine per day.

Under normal circumstances, virtually no protein is lost in the urine.

Nephrotic syndrome usually indicates severe glomerular damage.

Diabetic nephropathy is the most common cause of nephrotic syndrome.

In individuals who do not have diabetes, different glomerular diseases may account for the disorder.

Loss of plasma proteins into the urine leads to sodium retention, hypoalbuminemia, and hypoimmunoglobulinemia.

Thromboembolic complications are common.

Clinical manifestations include Four main symptoms of nephrotic syndrom:

- Proteinurea.
- Hypoalbuminemia
- Edema.
- Hyperlipidemia (elevated plasma lipids) is associated with hypoalbuminemia, perhaps as a hepatic response to low levels of albumin.

- Increased susceptibility to infections (caused by hypoimmunoglobulins) and generalized edema.

**Treatment consists of mechanisms to reduce proteinuria.**

These mechanisms include a soy-based protein, low-fat diet, with salt restrictions.

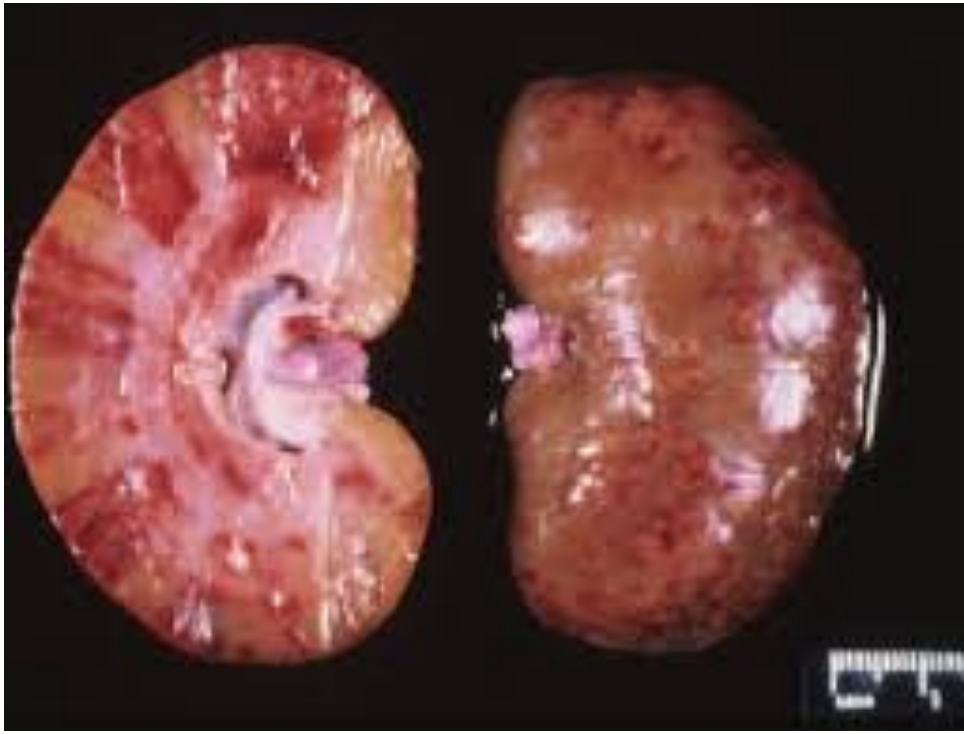
Angiotensin-converting enzyme (ACE) inhibitors reduce proteinuria and have become a mainstay of treatment.

Diuretics may be prescribed to increase fluid loss.

Protein supplements may be provided to prevent malnutrition unless renal failure is suspected, in which case they are contraindicated as protein worsens renal failure.

# Pyelonephritis

Pyelonephritis is inflammation of the parenchyma and lining of renal pelvis of kidney



## Etiology:

Gram negative organism like "E.coli (common)"
Gram positive organism like Staph.saprophyticus,
Virus (Rare)
Parasite

## Pathogenesis:

In the majority of UTIs bacteria establish infection by ascending from the urethra to the bladder.

Continuing ascent up the ureter to the kidney is the pathway for most renal parenchymal infections.

## Clinical Feature

**Mild pyelonephritis:**

- low-grade fever with or without lower-back or costovertebral-angle pain

**Severe pyelonephritis**:

- High fever “picket-fence” 72hr
- Nausea
- vomiting
- flank and/or loin pain

## Laboratory Diagnosis:

## The Urine Dipstick Test:

Rapid diagnostic test
Appearance of WBC in urine test for nitrite & leukocyte esterase
(family Enterobacteriaceae, in detected in urine PMN)
Negative outcome, its not sufficient for pregnancy women

## Urinalysis:

WBC in Cast shape due to of pyelonephritis
No WBC, No Infection

## Treatment:

Fluoroquin1olones (oral ciprofloxacin) the first- line therapy for acute uncomplicated pyelonephritis

Oral TMP-SMX

If the pathogen's susceptibility is not known and TMP SMX is used an initial IV l -g dose of ceftriaxone is recommended

or acarbapenem. Combinations of a ß-Iactam and a ß-Iactamase inhibitor

# Hypertensive Glomerular disease

1- Renal failure may occur with progressive high-pressure damage to the renal capillaries, the glomeruli.

With glomerular injury, blood flow to the functional units of the kidney, the nephrons, is impaired, and these can become hypoxic and die.

With damage to the glomerular membranes, proteins will be lost in the urine, decreasing the plasma colloid osmotic pressure and contributing to edema, which is often seen with long-standing hypertension.

2- Secondary Hypertension: An example of secondary hypertension is renal vascular hypertension, which develops as a result of renal artery stenosis.

This condition may be congenital or a result of atherosclerosis.

Renal artery stenosis reduces blood flow to the kidney, leading to activation of renal baroreceptors, stimulation of renin release, and production of angiotensin II.

Angiotensin II increases blood pressure directly by increasing TPR, and indirectly by increasing aldosterone synthesis and sodium reabsorption.

If repair of the stenosis is possible or the affected kidney is removed, blood pressure returns to normal.

# Drugs Induced Kidney Disease

- The heart pumps approximately 25% of cardiac output into the kidneys
- Any drug in the blood will eventually reach the highly vascularized kidneys May potentially cause drug-induced renal failure

- If the drug is primarily cleared by the kidney, the drug will become increasingly concentrated as it is moves from the renal artery into the smaller vasculature of the kidney

- The drug may be filtered or secreted into the lumen of the renal tubules

- The concentrated drug exposes the kidney tissue to far greater drug concentration per surface area

- Drug-induced kidney failure is a major adverse event associated with multiple medication classes
- Medications as diverse as OTC analgesics (ibuprofen, acetaminophen), antibiotics and chemotherapy agents can cause kidney damage
- Medication use accounts for 2% of hospital admissions for acute renal failure and up to 15% of admissions into intensive care

# NSAIDs

- Selective cyclooxygenase (COX-2) inhibitors cause similar renal dysfunction
- COX-2 exists as a constitutive enzyme in the thick part of the ascending loop of Henle and in the renal medulla
- COX-2 causes natriuresis and diuresis Inhibition of COX-2 by selective COX-2 inhibitors, such as celecoxib and rofecoxib
- causes renal dysfunction particularly in patients who are salt depleted or haemodynamically unstable.

# Cisplatin

- Nephrotoxicity is the major dose-limiting toxicity for cisplatin.

- Platinum compounds are believed to mediate their cytotoxic effects through their interaction with DNA”

- Inaddition  low concentrations of cisplatin preferentially result in apoptotic cell death while at higher concentrations necrosis ensues.

ACEIs and ARBs cause ARF

Stopping the medication should resolve the renal failure. Restarting the drug at a lower dose may be possible.

Statin nephrotoxicity: Rare but serious cases of rhabdomyolysis acute tubular necrosis Muscle pain, dark urine, electrolyte abnormalities and renal failure. Recognizing the process as drug-induced renal failure and stopping the drug is essential.

## Drugs of Abuse

- Cocaine and heroin.
- Cocaine use can cause renal artery thrombosis (clotting), severe hypertension and interstitial nephritis.
- long-term cocaine use can lead to chronic renal failure.
- Long-term tobacco use also increases the risk of kidney cancer.

# Finally

- Many drugs cause AKI
- Age (particularly over 65 years), pre-existing renal impairment, comorbidities such as diabetes mellitus, heart failure, liver cirrhosis and hypovolaemia. All increase the risk of drug-induced AKI.
- Addressing potential risk factors
- understanding of the mechanisms of nephrotoxicity involved

# Reference: Corwin , Pathophysiology, 3rd Edition