

## RENAL NOTES

### ACUTE TUBULAR NECROSIS

A rapid rise in creatinine following periods of hypotension is most commonly due to **acute tubular necrosis**. In ATN, urinalysis usually shows granular casts. Urine sodium is typically high due to tubular sodium loss, concentration is typically above 30 mmol/l. The urine to plasma osmolality ratio  $<1:1$ , the ability to concentrate urine is preserved despite sodium loss.

**Acute Tubular Necrosis** is associated with accelerated hypertension, hypotension, diabetes, liver failure, eclampsia, aminoglycosides, Cephalosporins, Cisplatin, Amphotericin and Ciclosporin.

**Haemodialysis** is useful for salicylates and NSAIDs, lithium, and in particular, Antifreeze poisoning. It is not useful for tricyclics, amiodarone and paraquat, paracetamol and digoxin, which is mostly tissue bound (use digoxin binding antibodies).

**Indications for urgent dialysis** are:

- uraemia
- pericarditis with effusion
- pulmonary oedema
- significant hyperkalaemia ( $>7$ ) with evidence of ECG changes
- rapidly rising urea and creatinine

In haemodialysis patients, sodium intake has to be moderated - high intake may cause fluid overload. Aluminium levels may accumulate in dialysis patients, so antacids containing aluminium should be avoided. PTH levels are usually high.

**Continuous Ambulatory Peritoneal Dialysis (CAPD):** Recent inguinal hernia surgery and history of perforated diverticular disease are relative contraindications. Large volumes of intraperitoneal fluid may compromise severe COPD. Patients with severe arthritis will not be able to manage peritoneal bag changes.

### NEPHRITIC AND NEPHROTIC SYNDROME

Infectious causes of acute **nephritic syndrome** are:

- staphylococcus
- pneumococcus
- v chickenpox
- malaria

Non infectious causes acute **nephritic syndrome**:

- Membranoproliferative glomerulonephritis
- IgA nephropathy
- Henoch-Schönlein purpura
- systemic lupus erythematosus
- mixed cryoglobulinemia
- Goodpasture's syndrome
- Wegener's granulomatosis

## **Proteinuria**

Microalbuminuria is protein >30 mg/l but dipstick testing can detect protein >300mg/l.

2+ proteinuria approximates to 1g/l of protein.

3+ proteinuria approximates to >3g/l.

The diagnosis of **nephrotic syndrome** comprises the triad of oedema, proteinuria >3g/d and hypoalbuminaemia. Hypercholesterolaemia is present in nearly all patients. Renal vein thrombosis and bacterial infections are also common.

Complications of **nephrotic syndrome** are :

hyperlipidaemia

hypoalbuminaemia

associated hypocalcaemia (Vit D binding protein Vitamin D lost in nephrotic urine)

prothrombotic tendency (eg renal vein thrombosis, DVT)

congestive cardiac failure

pneumococcal pneumonia

acute and chronic renal failure

## **GLOMERULONEPHRITIS**

Granular casts, red cell casts and selective proteinuria suggest **glomerulonephritis**.

**Minimal change nephrotic syndrome** is responsible for 90% of the cases of nephrotic syndrome in children less than 5 years of age. It also occurs in adults - approx 20%. The name is derived from the fact that the only detectable abnormality histologically is fusion and deformity of the foot processes under the electron microscope. Minimal Change Disease is steroid responsive and in general, does not lead to chronic renal failure. There is response to corticosteroids usually within the first month. 90% of patients with minimal change disease in the younger age group achieve remission after 8 weeks of steroids.

**Membranous glomerulonephritis / nephropathy** is characterised by subepithelial deposits of immune complexes in the glomerular basement membrane. It is a glomerular disease rather than a renal tubular acidosis. It is associated with malignancy (CLL, NHL), connective tissue disease (SLE, RA), infections (Hep B, malaria) and drugs (gold, penicillamine, captopril). **Membranous nephropathy** is the commonest cause of the nephrotic syndrome in adults, whereas in children it is minimal change disease. The renal biopsy with membranous nephropathy shows a thickened glomerular basement membrane and granular IgG + C3 on immunostaining.

Overall, 1/3 rapid decline, 1/3 respond to steroids and chlorambucil, 1/3 remit spontaneously. The goal of treatment is to minimize symptoms and slow the progression of the disease. Often, corticosteroids or immunosuppressive medications may be used to reduce symptoms and progression of the disorder.

Note: membranous GN is associated with Non-Hodgkin's lymphoma but Hodgkin's lymphoma is associated with minimal change GN.

**Focal Segmental Glomerulonephritis** In infective endocarditis, immune complexes form and may lead to **Focal segmental proliferative glomerulonephritis**. *ACE*

*inhibitors* usually reduce proteinuria and lipemia, and may slow the progression towards renal disease.

**Mesangio Capillary Glomerulonephritis** occurs in post streptococcal infection and caused by immune complexes depositing sub endothelially (capillary). The two most common variants are type I MCGN and type II MCGN (also called dense deposit disease). Type I is much more common than type II, which is a rare disease. MCGN is characterized by capillary basement membrane thickening and mesangial cell proliferation. It are associated with low levels of C3. Mesangiocapillary glomerulonephritis is a significant cause of nephrotic syndrome in children (accounts for about 8% of cases) and adults (accounts for about 14%).

Immune complex deposition is predisposed to by C3 nephritic factor rise in MCGN type II, which stabilises C3bBb and activates the complement pathway. In post streptococcal glomerulonephritis, oliguria, proteinuria and haematuria occurs.

**Diffuse proliferative glomerulonephritis** is the commonest glomerulonephritis in SLE. There is mesangial and endothelial cell proliferation, polymorphonuclear cell infiltrate and granular subepithelial deposits of C3. It also carries the worst prognosis with progression towards renal failure.

The currently recommended therapy is pulse intravenous corticosteroids in combination with pulse cyclophosphamide continued for at least 12 months after remission. Newer regimes include combinations of prednisolone and mycophenolate

## **RENAL TUBULAR ACIDOSIS**

**Urine pH** is determined by H<sup>+</sup> concentration. Urine is more alkalotic on a vegetarian diet. In type I RTA, the ability to develop a hydrogen ion gradient across the distal nephron is impaired so that the urine pH is never < 5.5.

In **Renal Tubular Acidosis**, the defect is in excretion of acid in Type I RTA and absorption of bicarbonate in Type II.

Nephrocalcinosis occurs in **type I distal RTA** due to less acid urine –acidification of urine is more difficult in type I. Inability to reduce the urinary pH below 5.4 is typical of Type I RTA.

In contrast, phosphate handling is worse in **type II proximal RTA** e.g. Fanconi syndrome (phosphaturia, aminoaciduria, glycosuria) and osteomalacia occurs. Hypokalaemia is a feature of renal tubular acidosis. Bicarbonate wasting in the proximal tubules is the primary problem. Expired tetracycline use is a cause of proximal type II RTA.

## **RENAL STONES**

**Calcium oxalate and urate stones** are a common association with bowel resection due to hyperabsorption of oxalate and concentrated urine. **Calcium oxalate** stones are the commonest kind of stones. **Calcium phosphate** stones are the second commonest and account for 20%.

**Uric acid stones** (5% of all stones) are associated with high purine metabolism, chronic diarrhoea, gout.

**Cystinuria** is a disorder of proximal tubular cells. Amino aciduria (COAL – cystine, ornithine, arginine, lysine) – causes **cystine stones** (accounts for 1% of all stones). Proteus splits urea into ammonia, causing alkaline urine. They predispose to **struvite stones** (magnesium ammonium phosphate).

**Radiopaque stones** are: Calcium oxalate, calcium phosphate, triple phosphate, cystine stones.

**Radiolucent stones** are: Uric acid, xanthine stones.

## MISCELLANEOUS

**IgA nephropathy** or Berger's disease is a clinical/pathological entity defined by the presence of macroscopic or microscopic hematuria and mesangial IgA deposits. Signs and symptoms include proteinuria, nephrotic syndrome, acute nephritis, malignant hypertension, chronic renal failure, and acute renal failure.

Proteinuria is typically within the mild range. There is a 2:1 male predominance. Findings on renal biopsy are characteristic. In all patients, IgA is present and is deposited mainly in the mesangium of the glomerular tuft. Other immunoglobulins and complement, especially C3, are often found in a mesangial pattern.

Although there is no cure, progression towards ESRF occurs usually in about 10-20 years, quicker if hypertension were present (which should be treated with an ACE inhibitor).

**Analgesic nephropathy** is usually a result of prolonged or chronic ingestion of analgesics, especially over-the-counter (OTC) medications that contain phenacetin or acetaminophen and nonsteroidal antiinflammatory drugs (NSAIDs) including aspirin or ibuprofen. The ingestion may have been excessive over a period of years. This frequently occurs as a result of self-medication, often for some type of chronic pain.

There is interstitial nephritis and renal papillary necrosis, eventually leading to acute renal failure or chronic renal failure. There may be haematuria but minimal or no proteinuria.

**Adult Polycystic Kidney Disease** : Inheritance is autosomal dominant. There is a mutation on the short arm of chromosome 16 (there are 16 alphabets in 'polycystic kidney'). Genetic linkage analysis can be done as well (but less practical) to screen for PKD1 mutation on chromosome 16 and a PKD2 mutation on chromosome 4.

5% of patients with APKD have intracranial aneurysms and 20% have mitral valve prolapse, and even abdominal hernias. Pancreatic cysts occur in 10% of patients. Ultrasonography with the criteria of more than 2 cysts in < 30 years age group is diagnostic of adult polycystic kidney disease.

Flank pain and haematuria occur and there is increased risk of infections. Cysts form primarily from collecting ducts. About 50% of patients reach end stage renal failure at age 50.

**Amyloid** : Nephrotic syndrome and renal vein thrombosis can occur in **amyloid renal disease**. Congo red staining shows apple green birefringence with polarised light in **amyloidosis**. AL amyloid may respond to cytotoxic therapy and resolution of proteinuria may occur.

**Alport syndrome** encompasses a group of heterogeneous inherited disorders involving the basement membranes of the kidney and frequently involving the cochlea (nerve deafness) and the eye (visual disturbance). Inheritance can be autosomal dominant, recessive or X linked recessive. These disorders are the result of mutations in type IV collagen genes.

Gross haematuria is the commonest presentation, along with visual disturbance and deafness. Renal impairment and nephrotic syndrome may develop later in life

**Bartter's syndrome** is hypokalaemic alkalosis due to hyperaldosteronism. The defect is due to reduced resistance to angiotensin II.

**Liddle's syndrome** is a rare condition in which there is hypokalaemic alkalosis but low aldosterone levels are found. It is seldom necessary to treat metabolic alkalosis by acidification, fluids often help to correct it.

Causes of **nephrogenic Diabetes Insipidus** are-

hypercalcaemia

hypokalaemia

sickle cell disease

lithium carbonate

amyloidosis

myeloma

malnutrition

analgesic nephropathy

pregnancy

damecloxycline

methicillin

**Diabetic nephropathy** In type I diabetes, there is a 50% chance of progressing towards ESRD. In type II diabetics, there is a 15% chance of doing so.

**Familial hypocalcaemic hypercalcaemia (FHH)** due to a mutation in the calcium receptor. Familial hypocalcaemic hypercalcaemia (FHH) or familial benign hypercalcaemia is an autosomal dominant inherited disorder of calcium metabolism. It is characterized by lifelong asymptomatic hypercalcaemia associated with a relative hypocalcaemia and a tendency to hypermagnesaemia. The biochemical features of this disorder are difficult to distinguish from mild primary hyperparathyroidism. Several patients have had parathyroidectomy for hyperparathyroidism with no effect on calcium levels.

**Henoch Schonlein purpura (HSP)** causes a rash around the trunk and polyarthrits. It is associated with renal failure caused by a glomerulonephritis which is similar to Ig A glomerulonephritis causing macroscopic haematuria.

**Multiple myeloma:** Proteinuria is present in 90% of patients and abnormal light chains (Bence Jones protein) are found in 80% of patients. At diagnosis, the creatinine level is elevated in 50% of patients. Proximal tubules are increasingly damaged by the large protein load, and large obstructing casts frequently form within the tubules. The combination of interstitial fibrosis and hyaline casts surrounded by epithelial cells or multinucleate giant cells constitutes myeloma kidney.

Additionally, hypercalcemia and hypercalciuria as well as hyperuricemia contribute to kidney damage. Renal amyloidosis (usually lambda light chains) and light chain deposition disease (usually kappa light chains) occurs. Cryoglobulinaemia is uncommon but may cause a membranoproliferative glomerulonephritis

**Sarcoidosis** : Renal involvement occurs infrequently in children and adults with **sarcoidosis**. Renal disease can be attributed to granulomatous interstitial infiltration or to disorders of calcium homeostasis, including hypercalcemia and hypercalciuria with or without nephrocalcinosis and nephrolithiasis. Clinically, variable renal disease occurs in 5-10% of adult cases. The clinical manifestations in reported cases of renal granulomatous sarcoidosis include proteinuria, leukocyturia, hematuria, concentration defect, hypertension, and renal failure.

**von Hippel Lindau disease** is transmitted as an autosomal dominant condition. Affected individuals may have renal cysts, Clear cell renal cell carcinoma (CCRCC), retinal angiomas, central nervous system haemangioblastoma, pheochromocytoma.

**Wegener's granulomatosis**: Sinusitis can arise from involvement of the nasal tract and sinuses in the Wegener's pattern of the disease. Often a patient with systemic vasculitis will have a long history of indolent disease, but will then present late with severe aggressive disease. Serum anti-neutrophil cytoplasmic antibodies (ANCA) and antibodies against the ANCA antigens myeloperoxidase and proteinase 3 may be positive.

**Renal vein thrombosis** can present with nephrotic syndrome, haematuria, loin pain and worsening renal failure. Treatment is with heparin/warfarin.

**Rhabdomyolysis** causes myoglobinuria, which must be differentiated from haematuria. Causes of rhabdomyolysis are falls, drugs (metals, gasoline, alcohol), viral infections & malaria. rhabdomyolysis causes myoglobinuria, which must be differentiated from haematuria.

Ultrasound is a good method of detecting **renal scars**. DMSA, which is taken up by tubular cells can be used to detect scars (as opposed to DTPA which is filtered by the glomerulus and not taken up by tubular cells, hence not good for detecting scarring).