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Basic review of the renal diseases

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Abstract
Renal diseases (basic review) are to understand very easily for graduate, post graduate and post-doctoral ayush, dental, medical etc., students. I am reviewing main and important diseases in renal in day to day practical life for medical students and professionals. Diseases are glomerulonephritis, renal failure, nephritic syndrome, interstitial nephritis, poly cystic kidney disease.

Keywords: Renal diseases, causes, clinical features, investigation

Introduction
We have lot of diseases to explain in Renal. But only main/few diseases are reviewing for under graduate, post graduate and post-doctoral AYUSH, dental, medical, nursing etc., for entrance and main examination purpose.

Glomerulonephritis
Glomerulonephritis (GN) means "inflammation of glomeruli". It excludes glomerular diseases without cell proliferation or nephritic presentations, such as minimal change disease, membranous nephropathy, and focal segmental glomerulosclerosis that can, none the less, chronically compromise renal function. In primary glomerulonephritis, disease is almost entirely restricted to the kidneys (as in IgA nephropathy or post streptococcal glomerulonephritis) while in secondary glomerulonephritis it occurs in association with more diffuse inflammation (as in systemic lupus erythematosus or systemic vasculitis). Prompt diagnosis of glomerulonephritis is vital as patients with even mildly impaired renal function, hypertension, and urinary abnormalities may rapidly lose kidney function if not treated urgently [1, 2].
Nearly 200 years ago, Richard Bright first described glomerular disease, diagnosing proteinuria in his patients by using a candle to heat urine on a spoon to determine whether it precipitated with heat.Bright also first recognized the relationship of scarlatina (due to streptococcal infection) to subsequent glomerulonephritis in the 1800s. With the advent of immunopathology, studies of serum sickness models in rabbits by Germuth and Dixon provided seminal insights into the immune mechanisms that underlie most forms of glomerulonephritis [3-5].

Causes
Causes of glomerulonephritis are systemic vasculitis, SLE, good pasture's (anti GBM) disease, aggressive phase of other inflammatory nephritis, viral infection, bacterial endocarditiis, Lupus.

Types of glomerulonephritis
Post infectious endocapillary glomerulonephritis
Post streptococcal glomerulonephritis is the best known Example of end capillary glomerulonephritis, the most common form of acute glomerulonephritis seen after some bacterial, viral, fungal, and parasitic infections. Although this pattern of glomerular injury after a streptococcal infection remains an important cause of acute renal failure in the developing world [6].

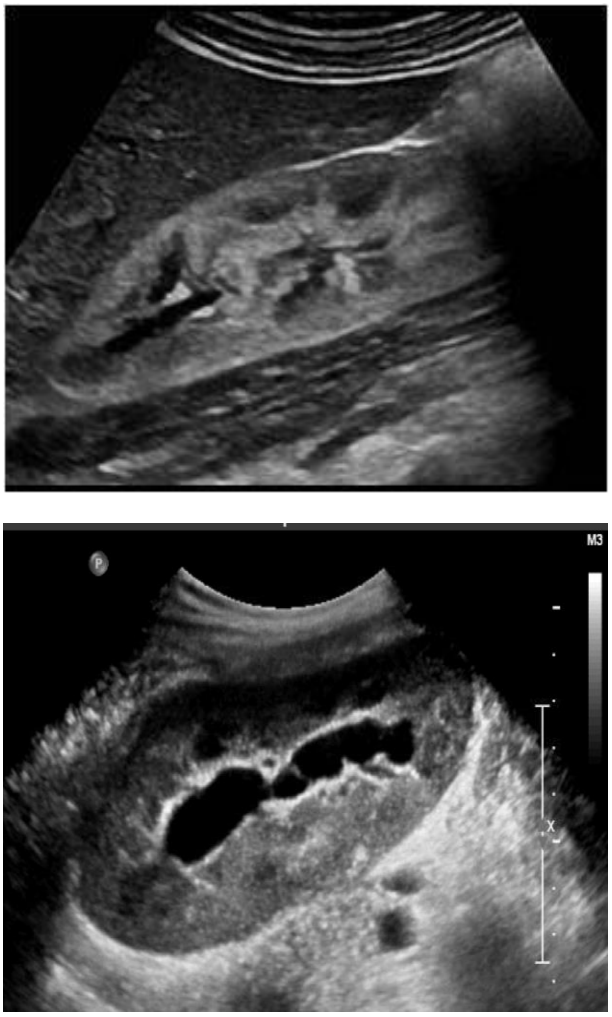


Fig 1: Glomerulonephritis ultrasound

Mesangio proliferative glomerulonephritis/ IgA nephropathy

IgA nephropathy is the commonest of all glomerulonephritides world-wide. Thus although only 4%–13% of patients present with acute nephritis. 9 Peak presentation is during the second and third decades showing a 2:1 male preponderance with attacks sometimes after infection. IgA nephropathy is the classic mesangioproliferative glomerulonephritis where cellular proliferation may be either diffuse or focal but affects predominantly the mesangium. Immunofluorescence shows paramesangial deposition of IgA (with some IgG and IgM) together with alternative pathway complement components, while electron microscopy shows mesangial dense deposits. Polymeric IgA1 is deposited in the kidney after overproduction of systemic IgA1 polymers (possibly in response to infection) together with impaired clearance through both the hepatic and the myeloid routes. In addition abnormal glycosylation of IgA may make it more prone to self-aggregate and form immune complexes with affinity for the mesangium. The disease is associated with a raised serum concentrations of IgA in 50% of patients, but serum complement levels are normal as complement activation is restricted to the kidneys alone.

Henoch schonlein purpura

However, as a small vessel vasculitis, HSP also has the systemic features of a purpuric rash largely affecting the lower limbs, arthritis or arthralgia, and abdominal pain sometimes in association with rectal bleeding. The disease is most commonly seen in those less than 20 years of age.

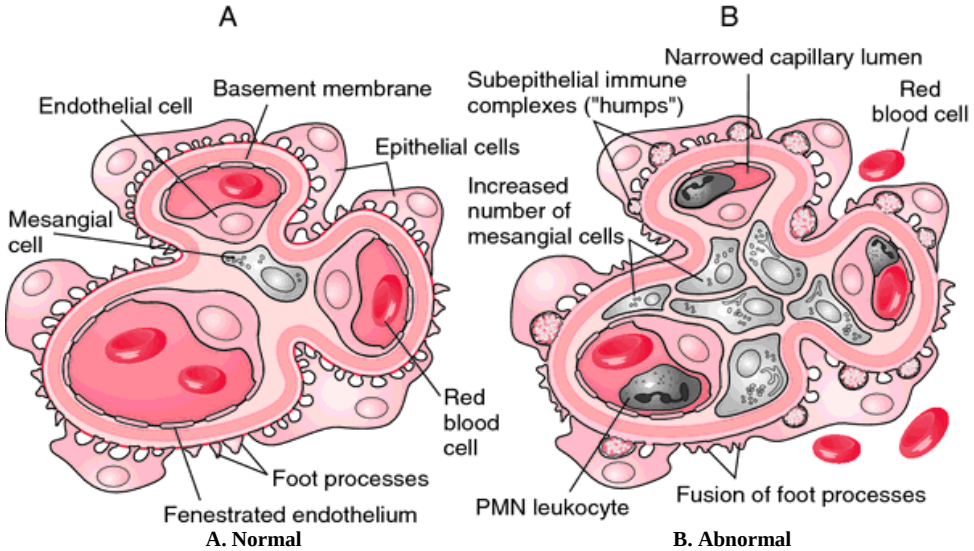
Rapidly progressive glomerulonephrtitis

The rapidly progressive glomerulonephritides are the most serious of all glomerulonephritides with the potential to destroy renal function within days. Although causes are heterogeneous, they are united by the histological finding of extensive crescents (a proliferation of parietal epithelial cells and mononuclear phagocytes with possible fibroblasts in Bowman's capsule) affecting more than 50% of glomeruli. Causes fall into three broad categories with different presentations, treatments, and prognoses. Biopsy shows a focal or diffuse proliferative glomerulonephritis with extensive crescents. The pathogenesis of vasculitis remains the focus of much research but direct immunoglobulin deposition in the glomerulus is not thought to play a significant part (hence the term pauci-immune). Serologically, however, these diseases are linked in about 90% of cases by the finding of antineutrophil cytoplasmic antibodies (ANCA).

Antibody staining is usually directed against the neutrophil cytoplasm in Wegener's with an antigen specificity for proteinase 3 on ELISA, whereas in microscopic polyangiitis it is generally perinucleur in pattern and is directed against myeloperoxidase. A direct causative role for ANCA in small vessel vasculitis remains controversial with experimental evidence pointing towards roles for neutrophils, macrophages, and T-cells in its pathogenesis.

Membranoproliferative glomerulonephritis

This rare form of glomerulonephritis has enjoyed renewed interest after the discovery that a subtype of MCGN type I is associated with chronic hepatitis C infection. MCGN commonly presents as a nephrotic syndrome but in 16%–30% of patients the initial presentation is with acute nephritis. The disease can be subdivided into types I and II, with its idiopathic forms mostly seen in children and young adults with cases presenting at a younger age in type II than in type I disease, with a slight female preponderance. Type I MCGN shares some features with lupus nephritis, and a similar histological picture can also be seen with endocarditis and infected arteriovenous shunts. In type II MCGN, patients may have an associated partial lypodystrophy giving them a very gaunt facial appearance.



A. Normal **B. Abnormal**

Fig 2: Glomerulonephritis

Lupus nephritis

Renal involvement in systemic lupus erythematosus can present with proteinuria, haematuria, nephrotic syndrome, or with an acute nephritis. It is rarely the first manifestation of systemic lupus but usually occurs within five years and may be the first presentation leading to a definitive diagnosis.24 Patients (most commonly women in their 20s and 30s with a black preponderance) will frequently have suffered lethargy, arthralgia or arthritis, skin rashes, and the symptoms of pleurisy and pericarditis in the months before presentation.25 More than any other glomerulonephritis, lupus nephritis can change and evolve over time so that in a

patient with an initially benign glomerular lesion, a new presentation with acute glomerulonephritis should prompt repeat biopsy and if needed more aggressive treatment. High titres of antinuclear antibodies and antidouble stranded DNA antibodies together with low complement levels are helpful in a nephritic flare, although changes in such markers often precede the actual glomerular inflammation, sometimes by months [7].

Clinical features: Clinical features of glomerulonephritis are pink or cola coloured urine from red blood cells in urine, foamy urine due to excess protein (proteinuria), swelling evident in face, hand, feet and abdomen and hypertension.

Renal failure

Renal failure is failure of the excretory function of the kidneys, leading to retention of nitrogenous waste products of metabolism. Sudden and usually reversible loss of renal function, which develops over a period of days or weeks. An increase in plasma Creatinine concentration to more than 200 micro mol/l is often used as the biochemical definition [8, 9].

Causes

Causes of renal failure are pre renal, intrinsic renal, post renal and systemic diseases.

Pre renal are systemic (heart failure, shock), local (renal artery occlusion/ stenosis, diseases affecting arterioles), intrinsic renal are acute tubular necrosis/toxic/septic renal failure, glomerular disease- primary component of systemic disease, interstitial disease, in post renal are stones, inflammation, tumor, in systemic diseases are acting via one or more of these three categories.

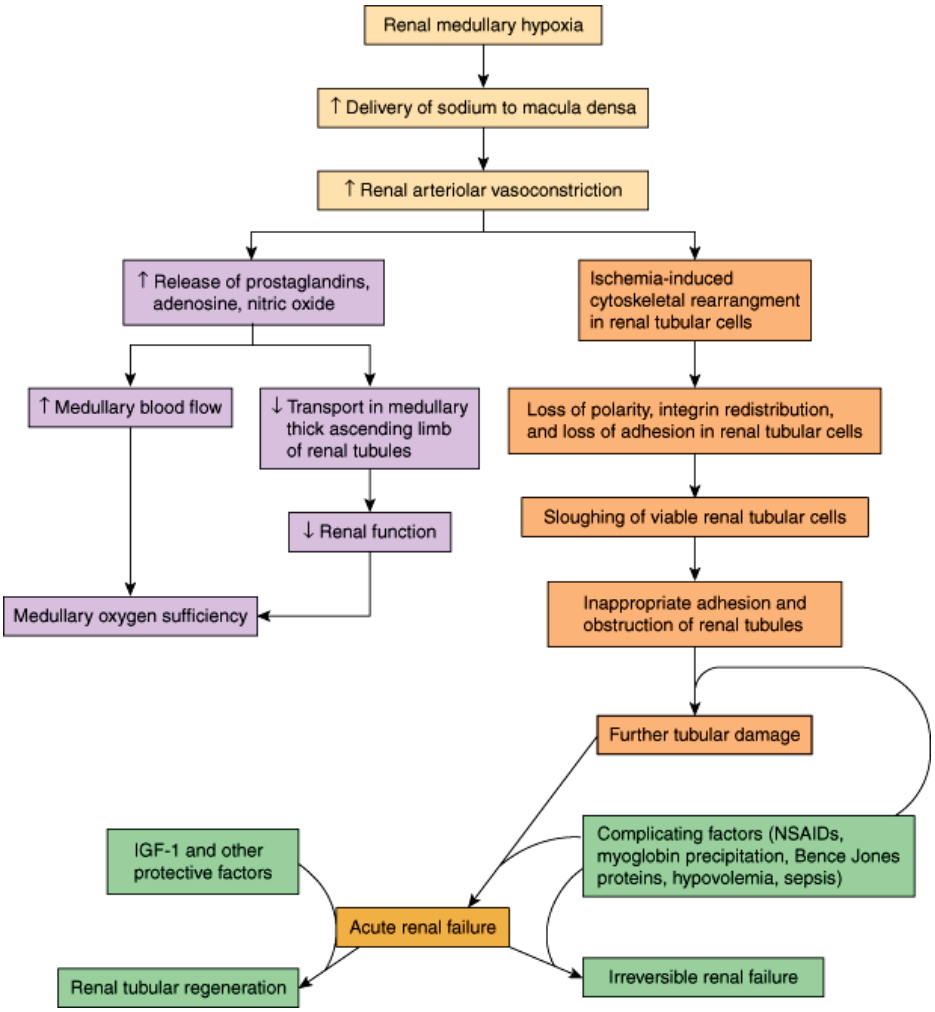


Fig 3: Pathogenesis of renal failure

Clinical features

Decreased urinary sodium concentration especially in septic patients. Decreased urine output, although occasionally urine output remains normal, fluid retention, causing swelling in your legs, ankles or feet, Shortness of breath, fatigue, confusion, nausea, weakness, irregular heart beat.

Chronic renal failure:

Chronic kidney disease (CKD) is recognized as a major health problem affecting approximately 13% of the United States population. Numbers of prevalent CKD patients will continue to rise, reflecting the growing elderly population and increasing numbers of patients with diabetes and hypertension. As numbers of CKD patients increase, primary care practitioners will be confronted with management of the complex medical problems unique to patients with chronic renal impairment. As well documented in the literature, the nephrologist rarely manages the medical needs of CKD patients until renal replacement therapy is required. In this chapter we will define CKD staging and discuss five complications associated with CKD: anemia, hyperlipidemia, nutrition, osteodystrophy, and cardiovascular risk [10].

Classification of CKD

- Stage 1: normal eGFR ≥ 90 mL/min per 1.73 m^2 and

persistent albuminuria
- Stage 2: eGFR between 60 to 89 mL/min per 1.73 m^2
- Stage 3: eGFR between 30 to 59 mL/min per 1.73 m^2
- Stage 4: eGFR between 15 to 29 mL/min per 1.73 m^2
- Stage 5: eGFR of < 15 mL/min per 1.73 m^2 or end stage renal disease

While anemia in CKD can result from multiple mechanisms (iron, folate, or vitamin B12 deficiency; gastrointestinal bleeding; severe hyperparathyroidism, systemic inflammation, and shortened red blood cell survival), decreased erythropoietin synthesis is the most important and specific etiology causing CKD associated anemia. Erythropoietin is a glycoprotein secreted by the kidney interstitial fibroblast and is essential for the growth and differentiation of red blood cells in the bone marrow. In CKD, tubular atrophy generates tubulointerstitial fibrosis, which compromises renal erythropoietin synthetic capacity and results in anemia. The anemia of CKD increases morbidity and mortality from cardiovascular complications (angina, left ventricular hypertrophy (LVH) and worsening heart failure) [11].

The term "CKD-associated mineral and bone disorders" comprises abnormalities in bone and mineral metabolism and/or extra-skeletal calcification secondary to CKD pathophysiology. Renal osteodystrophy is the spectrum of histological changes, which occur in bone architecture of patients with CKD. The kidney is the primary site for phosphate excretion and 1-α-hydroxylation of vitamin D. CKD patients develop hyperphosphatemia as a result of inadequate 1, 25 dihydroxy-vitamin D levels that reflect reduced synthesis from parenchymal scarring.

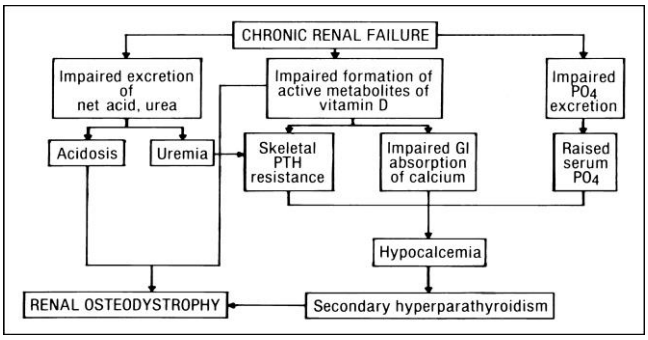


Fig 4: Chronic Renal Failure

Hypertension is a traditional cardiovascular risk factor which contributes to the cardiovascular risk associated with CKD. Szcech and colleagues demonstrated that patients with hypertension are at increased risk for new or recurrent cardiovascular events in individuals with stage 2–3 CKD. CKD patients are more likely to develop congestive heart failure (CHF). Bibbins et al evaluated the association between CKD and new-onset CHF in African and Caucasians Americans . Dyslipidemia is a major risk factor for cardiovascular morbidity and mortality and is common among patients with CKD. As patients progress through the stages of CKD, nutritional requirements are altered and metabolism of protein, water, salt, potassium, and phosphorous are affected[12].

Nephrotic syndrome

When substantial amount of protein are lost in the urine, a series of secondary phenomena occur. Evidence of fluid retention or oedema and more than 3.5 g of proteinuria per day. The disease that cause nephritic syndrome always affect the glomerulus and tend to be non inflammatory or subacute examples of inflammatory glomerulonephritis [13].

It is caused by increased permeability through the damaged basement membrane in the renal glomerulus especially infectious or thromboembolic. It is the result of an abnormality of glomerular permeability that may be primary with a disease specific to the kidneys or secondary to congenital infections, diabetes, systemic lupus erythematosus, neoplasia, or certain drug use. Nephrotic syndrome is an important chronic disease in children. The estimated annual incidence of nephrotic syndrome in healthy children is two to seven new cases per 100,000 children younger than 18 years of age. More common in boys than girls in younger age groups, but once adolescence is reached there is no significant difference between genders. Increased incidence and more severe disease seen in African American and Hispanic populations [14].

Causes

Primary cause: Minimal change nephropathy, focal glomerulosclerosis, membranous nephropathy, hereditary nephropathies. Non inflammatory glomerulonephritis – minimal change nephropathy, focal and segmental glomerulosclerosis (FSGS), membranous nephropathy, proliferative/inflammatory glomerulonephritis – mesangiocapillary glomerulonephritis (MCGN), subacute prolifertive nephritis, systemic lupus erythematosus (SLE), diabetic nephropathy and amyloidosis.

Infection: HIV, hepatitis B virus, human immunodeficiency virus, hepatitis C, cytomegalovirus, toxoplasmosis, parvovirus B1, amyloidosis and paraproteinemias, preeclampsia

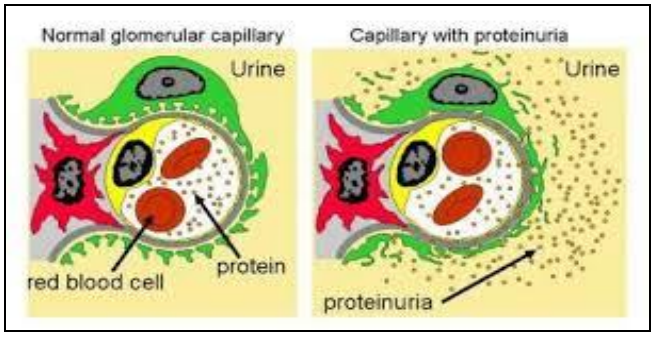


Fig 5: Nephrotic syndrome

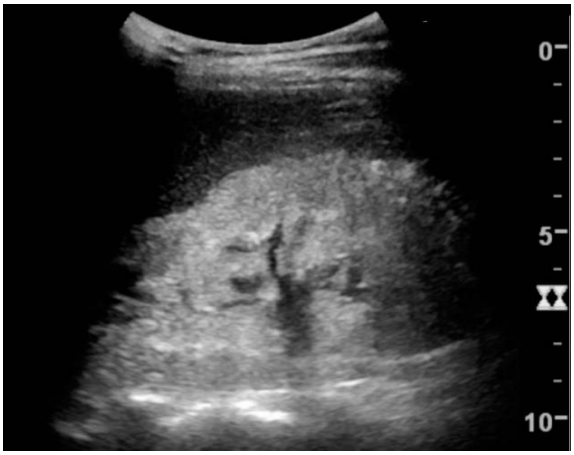
Pathophysiology

The glomerular capillaries are lined by a fenestrated endothelium that sits on the glomerular basement membrane, which in turn is covered by glomerular epithelium, or podocytes, which envelops the capillaries with cellular extensions called foot processes, these processes interdigitate with special cell cell junctions called the slit diaphragm which together forms the glomerular filter. Normally, larger proteins (greater than 69 kD) are excluded from filtration. Destruction of podocytes above a critical mass also leads to irreversible glomerular damage. Proteinuria that is more than 85% albumin is selective proteinuria. Albumin has a net negative charge, and it is proposed that loss of glomerular membrane negative charges could be important in causing albuminuria.

Nonselective proteinuria, being a glomerular leakage of all plasma proteins, would not involve changes in glomerular net charge but rather a generalized defect in permeability.
Mutations in several podocyte proteins have been identified in families with inherited nephrotic syndrome; a plasma factor may alter glomerular permeability, especially in patients with the steroid-resistant nephrotic syndrome and lastly altered T-lymphocyte polarized immune responses, in that the T-cells could result in the production of a permeability factor. Increased plasma levels of IgE, IgG4, and association with atopy suggest type II cytokine bias in patients with MCNS.In vitro studies suggest that podocytes express receptors for IL-4 and IL-13, the activation of these receptors might disrupt glomerular permeability resulting in proteinuria. No particular cytokine triggers the nephrotic syndrome.
Many of the complications of nephrotic syndrome can be linked to dysregulated lipid metabolism and dyslipidemia. These abnormalities include elevated plasma levels of cholesterol, triglycerides, and the apolipoprotein B; decreased lipoprotein lipase activity in the endothelium, muscle and adipose tissues; decreased hepatic lipase activity, and increased levels of the enzyme PCSK9. Also, there is an increase in the plasma levels of immature HDL particles and reduced cholesterol efflux [15].

Clinical features
Clinical features of nephrotic syndromes are oedema accumulates predominantly in the lower limb in adults, extending to the genitalia and lower abdomen as it gets more severe. In morning, the upper limbs and face may be more affected. In children, ascites occurs early and oedema is often seen only in the face. Blood volume may be normal, reduced or increased.

Investigation
Urine test: Urine samples over 24 hours (for an accurate measure), proteinuria (3 g protein)is diagnostic. Lipiduria, the presence of free lipid or lipid within tubular cells, within casts, or as free globules, suggests a glomerular disorder.
Blood tests: The serum albumin level is classically low in nephrotic syndrome, serum albumin often is < 2.5 g/dL. Creatinine concentrations vary by degree of renal impairment. Total cholesterol and triglyceride levels are typically increased. Serologic studies: The role of testing for secondary causes of nephrotic syndrome.



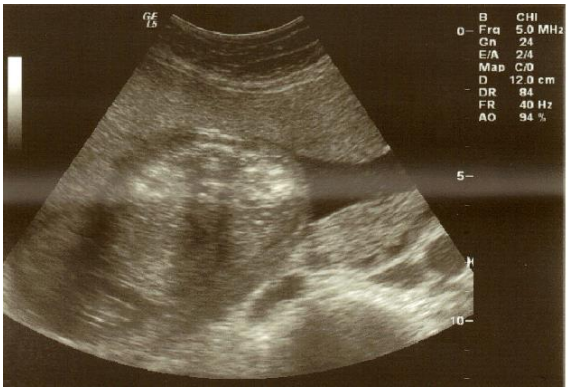


Fig 6: Nephrotic syndrome ultrasonography

Ultrasonographic: Individuals with a single kidney may be prone to developing focal glomerulosclerosis, having only one kidney is also a relative contraindication to kidney biopsy. Ultrasonography also demonstrates renal echogenicity. Increased renal echogenicity is consistent with intrarenal fibrosis
Renal biopsy: indicated for the following: congenital nephrotic syndrome, children older than 8 years at onset, steroid resistance, frequent relapses or steroid dependency, significant nephritic manifestations.

Different diagnosis
The differential diagnosis includes
- Hepatic: insufficiency, hepatocellular cirrhosis, Budd-Chiari syndrome
- Digestive: exudative enteropathy, lymphangiectasia, malnutrition
- Cardiac: hereditary angioneurotic edema
- Immune: anaphylaxis

Complications
- Generalized edema
- Respiratory distress
- Sepsis
- Peritonitis
- Thromboembolism
- Failure to thrive

Patient education
Advise to take low salt diet intake.

Interstitial nephritis
It is divided in to acute and chronic interstitial nephritis
Acute interstitial nephritis: it is refers to acute inflammation within the tubule interstitium. Acute interstitial nephritis (AIN) is an under recognized and under diagnosed cause of acute kidney injury (AKI). It is estimated to account for 15 – 20% of cases of AKI; it is the reported diagnosis in 2.8% of all kidney biopsies, and 13.5% of biopsies done specifically for acute renal failure. Considerable evidence implicates antigen initiated cell-mediated injury in the pathogenesis of AIN. Drugs account for 70% of all cases, with over 150 different agents incriminated. The remaining cases are due to infections, autoimmune diseases, and rarely idiopathic. Early tribulations and classifications notwithstanding, most diseases of the kidney continued to be considered as tubulopathies rather than glomerulopathies

through the first decades of the 20th century. It is within this context that the pathologic diagnosis of "acute interstitial nephritis" (AIN) was described in 1898 by William Thomas Councilman (1854 – 1933), then pathologist in chief at the Brigham Hospital [16, 17].

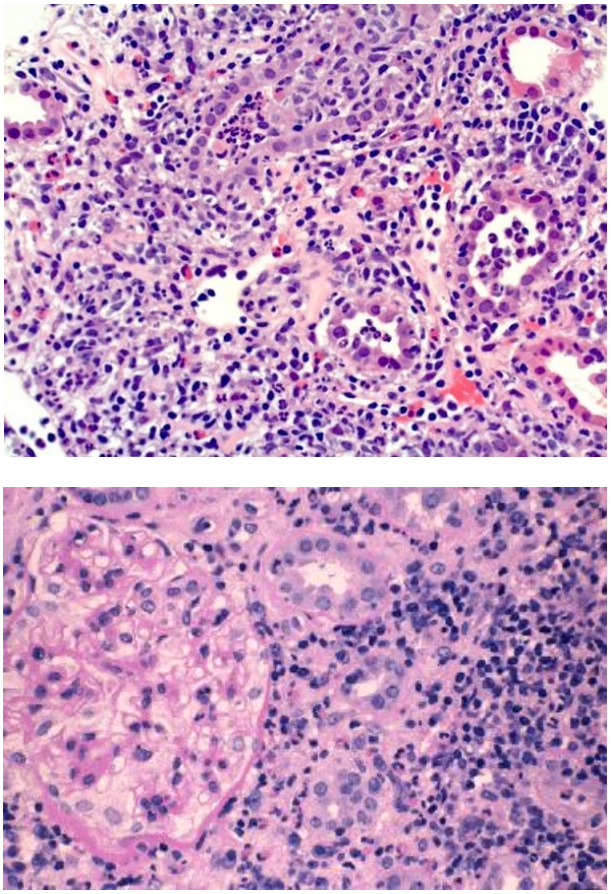


Fig 7: Interstitial Nephritis

Causes

Drugs: penicillins, NSAIDs, allopurinol, frusemide.

Infections: leptospirosis, tuberculosis, pyelonephritis, cytomegalovirus, hantavirus.

Systemic disease: Sarcoidosis, sjogren's syndrome, myeloma.

Renal biopsies show intense inflammation with polymorphonulcer leucocytes and lymphocytes surrounding tubules and blood vessels and occasional eosinophils (figure 7).

Investigations

Laboratory markers of tubular dysfunction are evident before decrements in filtration rate and consequent increments in blood urea nitrogen (BUN) and serum creatinine levels. The principal hallmarks of glomerular disease (salt retention, oedema, hypertension) are characteristically absent. The early diagnosis of acute interstitial nephritis by detecting tubular dysfunction is central to its diagnosis at a potentially reversible stage.

Chronic interstitial nephritis

It is defined as a "chronic inflammation within the tubule interstitium".

Causes: chronic glomerular disease, immune/inflammatory disease, tumors (myeloma), drugs (NSAIDs, analgesic nephropathy), metabolic/congenital (wilson's disease, hypokalaemia, medullary sponge kidney hypercalcluria, sickle cell nephropathy), toxins (lead, Chinese herbs, balkan nephropathy).

Clinical features

Hypotension, polyuria, sodium and water depletion. Patients present in adult life with chronic renal failure, hypertension and small kidneys.

Polycystic kidney disease

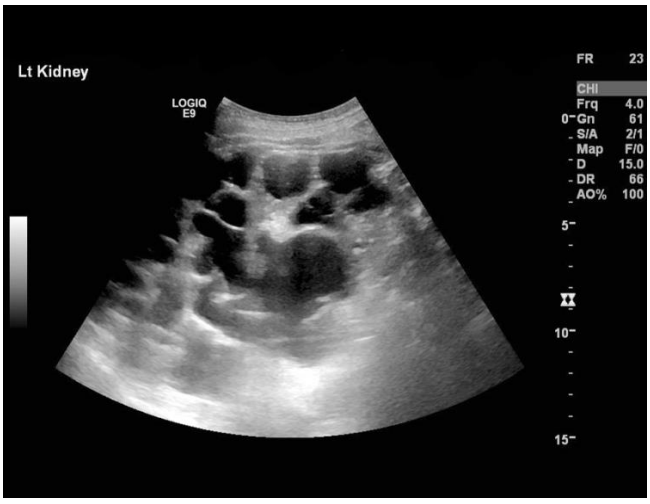
Polycystic kidney disease (PKD) is an inherited disorder characterized by cystic expansion of the kidneys producing progressive kidney enlargement and renal insufficiency, in addition to various extrarenal manifestations. The disease can be inherited in autosomal dominant and recessive forms. Autosomal dominant polycystic kidney disease (ADPKD) is characterized by slow but progressive enlargement of the kidneys with renal failure occurring by the fifth to sixth decade of life. Polycystic kidney disease (PKD) is the most common genetic cause of kidney failure in adults and children. PKD is characterized by progressive cystic dilation of the renal tubules, which results in nephromegaly and often culminates in end stage renal disease. The disease occurs in approximately 1:800 to 1:1,000 people and accounts for 2.5% of all cases of end stage renal disease. In patients with polycystic kidney diseases (PKDs), the kidneys contain multiple fluid filled cysts, although other organs may also be affected [18].

Pathology

Small cysts of proximal tubular epithelium are present in infancy and enlarge at a variable rate. In full developed adult polycystic kidney disease the kidneys are asymmetrically enlarged and contain numerous cysts. These differ in size and are surrounded by a variable amount of parenchyma which often shows extensive fibrosis and arteriolosclerosis [19].

Clinical features

Hypertension, which may or may not be associated with deterioration of renal function. Vague discomfort in loin or abdomen due to increasing mass of renal tissue, acute loin pain or renal colic due to haemorrhage in to a cyst, haematuria, urinary tract infection, renal failure [20, 21].



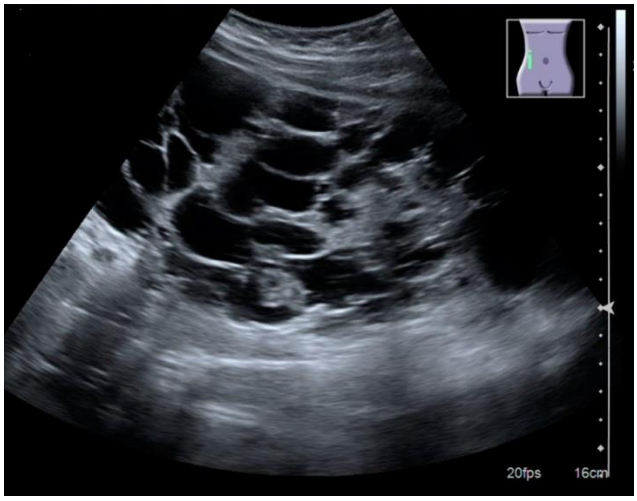


Fig 8: Polycystic kidney disease ultrasonography

Investigations

The diagnosis is made on the basis of clinical features, family history and ultrasound (figure 8)**.**

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