Chronic renal failur

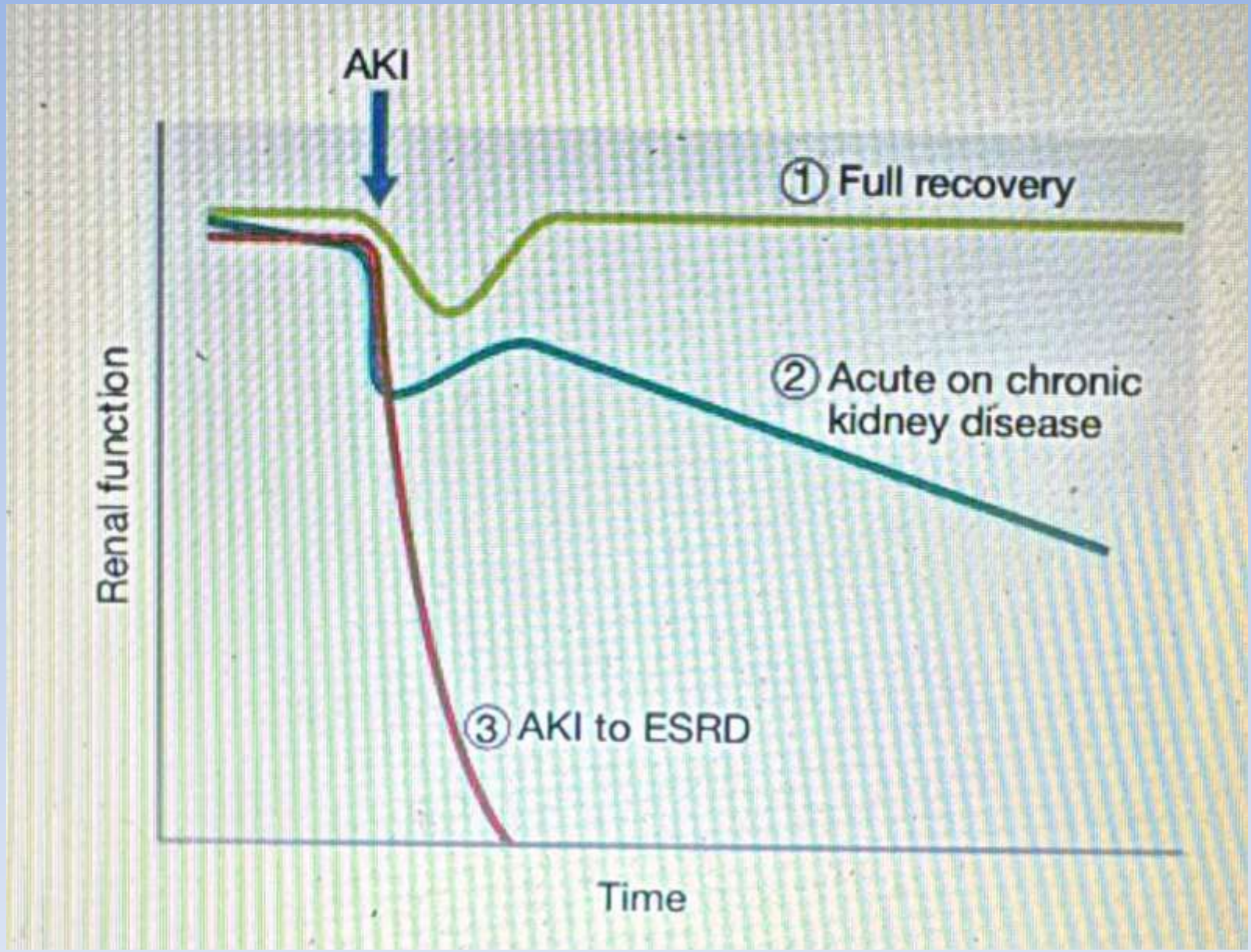
Definition

An irreversible deterioration in renal function that usually develops over a period of years . Initially, it manifests only as a biochemical abnormality but, eventually, loss of the excretory, metabolic and endocrine functions of the kidney leads to the clinical symptoms and signs of renal failure.

The prevalence of CKD stages 3–5 , are around 5%–7%, mostly affecting people aged 65 years and above . The prevalence of CKD in patients with hypertension, diabetes and vascular disease is substantially higher, and targeted screening for CKD should be considered.

In many cases the underlying diagnosis is unclear, especially among the large number of older patients with stage 3 CKD.

Renal biopsy is rarely undertaken since it is more risky and less likely to provide a histological diagnosis because of the severity of damage, and unlikely to alter management.


AKI
① Full recovery
② Acute on chronic kidney disease
③ AKI to ESRD
Renal function
Time

Stages of CKD

15.3 Stages of chronic kidney disease (CKD)

Stage[1]	Definition[2]	Description	Prevalence[4]	Clinical presentation[5]
1	Kidney damage[3] with normal or high GFR (>90)	Normal function	3.5%	Asymptomatic
2	Kidney damage and GFR 60–89	Mild CKD	3.9%	Asymptomatic
3A	GFR 45–59	Mild to moderate CKD	7.6% (3A and 3B combined)	Usually asymptomatic
3B	GFR 30–44	Moderate to severe CKD		Anaemia in some patients at 3B Most are non-progressive or progress very slowly
4	GFR 15–29	Severe CKD	0.4%	First symptoms often at GFR <20 Electrolyte problems likely as GFR falls
5	GFR <15 or on dialysis	Kidney failure	0.1%	Significant symptoms and complications usually present Dialysis initiation varies but usually at GFR <10

[1]Stages of CKD 1–5 were originally defined by the US National Kidney Foundation Kidney Disease Quality Outcomes Initiative 2002. In the 2013 Kidney Disease Outcomes Quality Initiative (K/DOQI) CKD guideline update, the suffices A1, A2 and A3 are recommended, indicating the presence of albuminuria of <30, 30–300 and >300 mg/24 hrs respectively, in view of the prognostic importance of albuminuria. [2]Two GFR values 3 months apart are required to assign a stage. All GFR values are in mL/min/1.73 m^2. [3]Kidney damage means pathological abnormalities or markers of damage, including abnormalities in urine tests or imaging studies. [4]From Hill NR, Fatoba ST, Oke JL et al. Global prevalence of chronic kidney disease – a systematic review and meta-analysis. PLoS One 2016; 11:e0158765. [5]For further information, see page 415.

Limitations of estimated glomerular filtration rate

1-It is based on serum creatinine, and so may overestimate actual GFR in patients with low muscle mass (e.g. those with cachexia, amputees) and underestimate actual GFR in individuals taking creatine supplements.

2-Creatinine level must be stable over days; eGFR is not valid in assessing acute kidney injury

3- eGFR is not valid in under-18s or during pregnancy

4- Ethnicity is not taken into account in routine laboratory reporting; the laboratory eGFR value should therefore be multiplied by 1.21 for Black people

Clinical presentation

-The typical presentation is for a reduced eGFR to be found incidentally during routine blood tests, often during screening of high-risk patients, such as those with diabetes or hypertension.

-An early symptom is nocturia, due to the loss of concentrating ability.

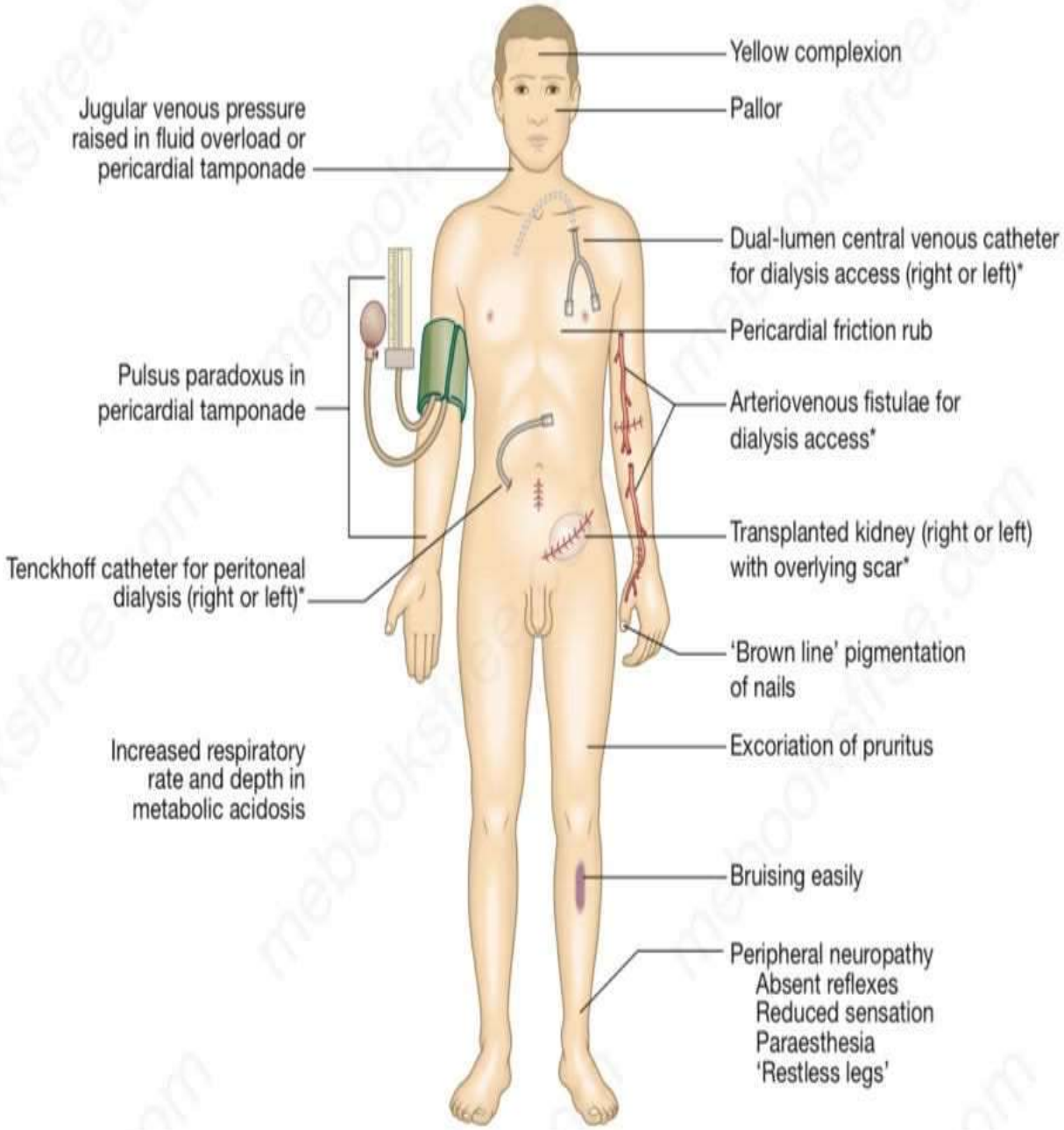
-Symptoms resulted from complications include:

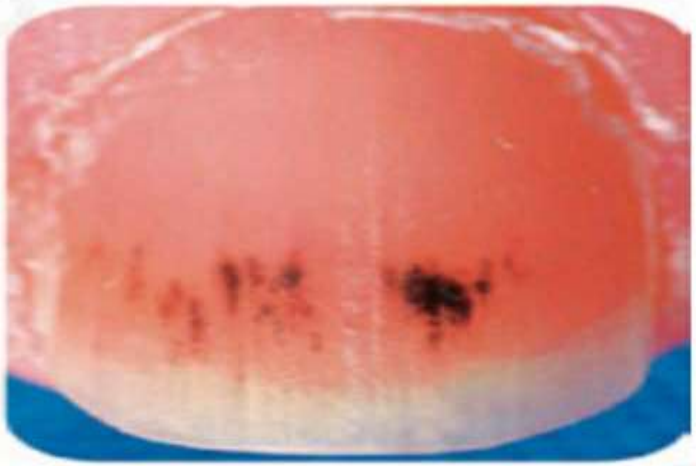
1- Tiredness or breathlessness, which may be related to anaemia or fluid overload.

2- uremic symptoms :pruritus, anorexia, weight loss, nausea, vomiting , hiccups , chest pain , confusion and muscle twitching .

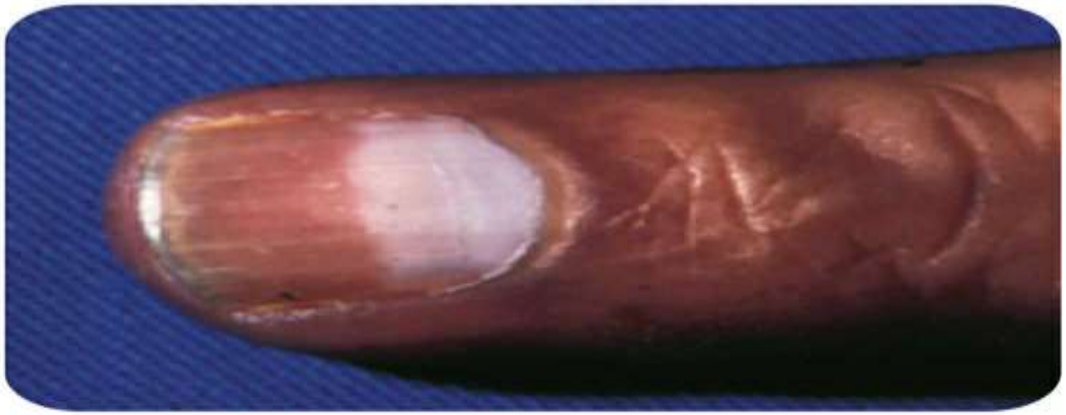
3-Deep (Kussmaul breathing) due to profound metabolic acidosis

-Symptoms and signs associated with the underlying cause , HTN , hematuria , polyuria,nocturia, anurea , frothy urine , abdominal pain , skin rash , joints pain ,jaundice (? Hemolysis),


Yellow complexion
Pallor
Jugular venous pressure raised in fluid overload or pericardial tamponade
Dual-lumen central venous catheter for dialysis access (right or left)*
Pericardial friction rub
Pulsus paradoxus in pericardial tamponade
Arteriovenous fistulae for dialysis access*
Transplanted kidney (right or left) with overlying scar*
Tenckhoff catheter for peritoneal dialysis (right or left)*
'Brown line' pigmentation of nails
Excoriation of pruritus
Increased respiratory rate and depth in metabolic acidosis
Bruising easily
Peripheral neuropathy
Absent reflexes
Reduced sensation
Paraesthesia
'Restless legs'



▲ Splinter haemorrhages



▲ 'Brown line' pigmentation of nails

Causes

15.28 Common causes of chronic kidney disease

Disease	Proportion	Comments
Diabetes mellitus	20–40%	Large racial and geographical differences
Interstitial diseases	20–30%	Often drug-induced
Glomerular diseases	10–20%	IgA nephropathy is most common
Hypertension	5–20%	Causality controversial, much may be secondary to another primary renal disease
Systemic inflammatory diseases	5–10%	Systemic lupus erythematosus, vasculitis
Renovascular disease	5%	Mostly atheromatous, may be more common
Congenital and inherited	5%	Polycystic kidney disease, Alport's syndrome
Unknown	5–20%	

Diabetic nephropathy

-Diabetic nephropathy is the most common cause of CKD in developed countries. In patients with diabetes may manifest as from (microalbuminuria) to dipstick-positive proteinuria, in association with evolving hypertension and progressive renal failure.

-Few patients require renal biopsy to establish the diagnosis,

>>> proteinuria/decline in renal function or the absence of microvascular disease in other organs, including retinopathy, should lead to suspicion that an alternative condition could be present.

-Management with ACE inhibitors and ARBs to slow progression. SGLT2 inhibitors, reduce cardiovascular mortality and progression of kidney disease at the expense of increased risk of genital infections.

Tubulo-interstitial diseases

Chronic interstitial nephritis :

>It may follow on from AIN that does not resolve

>Chronic ingestion of various toxins and drugs, such as lithium or non-steroidal anti-infammatory drugs (NSAIDs).

>Chronic metabolic and inflammatory diseases.

>In many patients, CIN presents at a late stage and no underlying cause can be identified.

Renal tubular acidosis may complicate CIN but is seen most often in myeloma, sarcoidosis, cystinosis, amyloidosis and Sjögren syndrome.

Typically, urinalysis is unremarkable and small kidneys are observed on ultrasound scan. Renal biopsy demonstrates infiltration of the renal parenchyma by lymphocytes, plasma cells and macrophages, with tubular atrophy and interstitial fibrosis.

Management is to identify and withdraw or treat the primary cause. Otherwise, treatment is supportive in nature, with correction of acidosis and hyperkalaemia; replacement of fluid and electrolytes, as required . Renal replacement therapy if irreversible renal damage has occurred.

18.19 Causes of chronic interstitial nephritis

Acute interstitial nephritis

- Any of the causes of acute interstitial nephritis, if persistent (see Box 18.18)

Glomerulonephritis

- Varying degrees of interstitial inflammation occur in association with most types of inflammatory glomerulonephritis

Immune/inflammatory

- Sarcoidosis
- Sjögren syndrome
- Chronic transplant rejection
- Systemic lupus erythematosus, primary autoimmune

Toxic

- *Aristolochia* in herbal medicines
- Lead
- Balkan nephropathy
- Chronic interstitial nephritis in agriculture communities (CKDu)

Drugs

- All drugs causing acute interstitial nephritis
- Tenofovir
- Lithium toxicity
- Analgesic nephropathy
- Ciclosporin, tacrolimus

Infection

- Consequence of severe pyelonephritis

Congenital/developmental

- Vesico-ureteric reflux: associated but causation not clear
- Renal dysplasias: often associated with reflux
- Inherited: now well recognised but mechanisms unclear
- Other: Wilson's disease, sickle-cell nephropathy, medullary sponge kidney (nephrocalcinosis)

Metabolic and systemic diseases

- Calcium phosphate crystallisation after excessive phosphate administration (e.g. phosphate enemas in patients with chronic kidney disease)
- Hypokalaemia

Papillary necrosis

The renal papillae lie within a hypoxic and hypertonic environment in the renal medulla that is why they are susceptible to ischaemic damage and canu nder go necrosis when their vascular supply is impaired as the result of diabetes mellitus, sickle-cell disease or long-term ingestion of NSAIDs.

The clinical presentation is variable. Some patients are asymptomatic and clinically silent, whereas others present with renal colic and renal impairment as necrosed papillae slough off and cause ureteric obstruction.

Investigations:

1-Urinalysis may be normal but more frequently haematuria and sterile pyuria are present with no significant proteinuria.

2-The imaging method of choice to make the diagnosis is CTU or intravenous pyelography

Management is based on relieving obstruction, where present, and withdrawal of the offending drugs.

Glomerulonephritis

Glomerulonephritis literally means ‘inflammation of glomeruli’, the term is often used more broadly to describe all types of glomerular disease, even though some of these (e.g. minimal change nephropathy) are not associated with inflammation.

Most types of glomerulonephritis are immun-mediated and several respond to immunosuppressive drugs.

In small-vessel vasculitis, no glomerular antibody deposition is observed (pauci-immune).

Glomerulonephritis is generally classiffed in terms of the histopathological appearances to :

1- Diseases typically presenting with nephrotic syndrome

2- Diseases typically presenting with mild nephritic syndrome

3- Diseases typically presenting with rapidly progressive glomerulonephritis

Proteinurea grades

15.9 Quantifying proteinuria in random urine samples

ACR[1]	PCR[2]	Typical dipstick results[3]	Significance
<3.5 (female) <2.5 (male)	<25	–	Normal
3.5–30	25–50	–	Moderately elevated albuminuria
30–70	50–100	+ to ++	Dipstick positive
70–300	100–350	++ to +++	Glomerular disease more likely; equivalent to >1 g/24 hrs
>300	>350	+++ to ++++	Nephrotic range: almost always glomerular disease, equivalent to > 3.5 g/24 hrs

[1]Urinary albumin (mg/L)/urine creatinine (mmol/L). [2]Urine protein (mg/L)/urine creatinine (mmol/L). (If urine creatinine is measured in mg/dL, reference values for PCR and ACR can be derived by dividing by 11.31.) [3]Dipstick results are affected by urine concentration and are occasionally weakly positive on normal samples.

Diseases typically presenting with nephrotic syndrome

1- Minimal change nephropathy:

-Can occur at all ages but it is the most common type of nephrotic syndrome in children .

It is caused by reversible dysfunction of podocytes. On light microscopy, the glomeruli appear normal but fusion of podocyte foot processes is observed on electron microscopy.

- Can be secondary to Atopy ,drugs, most commonly NSAIDs and haematological malignancies

-Treatment : High dose glucocorticoid therapy usually promotes rapid remission of nephrosis.Additional agents such as cytotoxics or calcineurin inhibitors may be needed in resistent cases .

-Glucocorticoid resistance in children warrants a biopsy to exclude an alternative diagnosis

- Prognosis: Minimal change disease typically does not progress to CKD but can present with problems related to the nephrotic syndrome and complications of treatment.

Diseases typically presenting with nephrotic syndrome

2-Focal segmental glomerulosclerosis:

Primary focal segmental glomerulosclerosis can occur in all age . Histological analysis shows sclerosis initially limited to segments of the glomeruli, which may also show positive staining for deposits of C3 and IgM on immunofluorescence. Since FSGS is a focal process, abnormal glomeruli may not be detected on renal biopsy if only a few are sampled, leading to an initial diagnosis of minimal change nephropathy.

Causes :

1- Primary > most common cause is unknown and typically present with abrupt onset of severe nephrotic syndrome/ common in people of West African descent /higher carriage rate of apolipoprotein L1 (APOL1) gene

2- Secondary to other diseases such as human immunodefficiency virus (HIV) renal disease (particularly in African Americans), morbid obesity , heroin abuse or chronic hypertension. In addition, it may reflect scarring from previous focal glomerular injury resulting from HUS, cholesterol embolism or vasculitis.

Present with more modest proteinuria than those with primary disease

Treatment :

1-Primary FSGS may respond to high-dose glucocorticoid therapy but the response is rarely as rapid as in minimal change disease. Immunosuppressive drugs have also been used but their efficacy is uncertain.

2- Secondary FSGS: Treat underlying cause, reducing proteinuria by inhibiting the renin–angiotensin system

Progression to CKD is common in patients who do not respond to glucocorticoids and the disease frequently recurs after renal transplantation..

Diseases typically presenting with nephrotic syndrome

3-Membranous nephropathy: is the most common cause of nephrotic syndrome in .
people of European descent.

Causes :

1-Primary : most common and It is caused by antibodies(usually autoantibodies) directed at antigen(s) expressed on the surface of podocytes, including the M-type phospholipase A2 receptor 1, and is characterised by thickening of the glomerular basement membrane on light microscopy .

2- Secondary causes, such as heavy metal poisoning, drugs (NSAIDS , penicillamines , infections, lupus and tumours.

-Prognosis : Approximately one-third of patients with idiopathic membranous nephropathy undergo spontaneous remission, one-third remain in a nephrotic state, and one-third develop progressive CKD.

Management:

1- Tight blood pressure control, in particular with inhibitors of the renin–angiotensin– aldosterone system.

2-Primary type : Immunosuppression treatment may improve both the nephrotic syndrome and the long-term prognosis and regimens include steroids with either cyclophosphamide or rituximab

3- Secondary membranous nephropathy treatment is directed at the underlying cause.

Complications of Nephrotic syndrome

1- Risk for infections

2- Hypercoagulable state

3- Risk of malnutrition

4- Steroids and immunosupressive side effects

5- Accelerated atherosclerosis

Diseases typically presenting with mild nephritic syndrome

Patients with mild glomerulonephritis typically present with non-visible haematuria and modest proteinuria, and their renal disease tends to follow a slowly progressive course.

IgA nephropathy and mesangiocapillary glomerulonephritis (MCGN) typically fall in this category. However, their presentation is highly variable:

IgA nephropathy occasionally presents with rapidly progressive glomerulonephritis while MCGN may present with nephrotic syndrome.

Other diseases that present with haematuria, modest proteinuria and slow progression include Alport syndrome.

IgA nephropathy

This is one of the most common types of glomerulonephritis and can present in many ways. These are often detected during routine screening: for example, at occupational medical . A particular hallmark of IgA nephropathy in young adults is the occurrence of acute self-limiting exacerbations, often with visible haematuria, in association with minor respiratory infections. examinations

---presentation:

1-Haematuria is the earliest sign and non-visible haematuria is almost universal

2- hypertension is also very common

3- Proteinuria can also occur but is usually a later feature.

4-Occasionally, IgA nephropathy progresses rapidly in association with crescent formation on biopsy.

Management :

1- control of blood pressure, with renin–angiotensin system inhibitors preferable in those with proteinuria.

2- There is some evidence for additional benefit from several months of high-dose glucocorticoid treatment in those at high risk of progressive disease

Mesangiocapillary glomerulonephritis

Also known as membranoproliferative glomerulonephritis, is a pattern of injury seen on renal biopsy that is characterised by an increase in mesangial cellularity with thickening of glomerular capillary walls. The typical presentation is with proteinuria and haematuria.

>>>It can be classiffed into two main subtypes:

1- The first is characterised by deposition of immunoglobulins within the glomeruli. This subtype is associated with chronic infections, autoimmune diseases and monoclonal gammopathy.

2- The second is characterised by deposition of complement in the glomeruli and is associated with inherited or acquired abnormalities in the complement pathway. This category comprises ‘dense deposit disease.

Treatment of MCGN associated with immunoglobulin deposits consists of the identification and treatment of the underlying disease, if possible, and the use of immunosuppressive drugs such as mycophenolate mofetil or cyclophosphamide.

Henoch–Schönlein purpura

This condition most commonly occurs in children but can also be observed in adults. It is a systemic vasculitis that often arises in response to an infectious trigger.

It presents with a tetrad of features:

1-a characteristic petechial rash typically affecting buttocks and lower legs

2-abdominal pain due to vasculitis involving the gastrointestinal tract

3-arthralgia

4- renal disease characterised by visible or non-visible haematuria, with or without proteinuria.

Renal biopsy shows mesangial IgA deposition and appearances that are indistinguishable from acute IgA nephropathy .

Treatment is supportive in nature; in most patients, the prognosis is good, with spontaneous resolution, though relapses are common. Some patients, particularly adults and those with severe or persistent proteinuria, progress to develop ESRD.

Diseases typically presenting with rapidly progressive glomerulonephritis

(RPGN) is characterised by rapid loss of renal function over days to weeks, usually in association with hypertension ,oedema and non-visible haematuria .Variable amounts of proteinuria can be detected as well .

Red cell casts and dysmorphic red cells may be observed on urine microscopy.

Renal biopsy typically shows crescentic lesions often associated with necrotising lesions within the glomerulus ,particularly in small-vessel vasculitides.

This pattern of presentation is typical of post-infectious glomerulonephritis, anti-GBM disease and small-vessel vasculitides , SLE and occasionally in IgA and other nephropathies.

Anti-glomerular basement membrane disease

Anti-GBM disease is a rare autoimmune disease in which antibodies develop against the α3 chain of type 4 collagen in the GBM which is restricted to the basement membranes of glomeruli and lungs, and hence the disease may present with rapidly progressive glomerulonephritis, lung haemorrhage, or disease of both organs known as Goodpasture's disease.

Patients with anti-GBM disease should be treated with plasma exchange combined with glucocorticoids and immunosuppressants, but early diagnosis is essential, as renal function is rarely recoverable in those requiring dialysis at presentation.

The combination of glomerulonephritis and pulmonary haemorrhage may also be observed with small-vessel vasculitis (particularly granulomatosis with polyangiitis, previously known as Wegener's granulomatosis) and lupus.

Infection-related glomerulonephritis

1-Post-infectious glomerulonephritis is observed most commonly in children and young adults, and typically presents 10 days after a streptococcal throat infection or longer after a skin infection.

The clinical presentation ranges from mild abnormalities on urinalysis to RPGN with severe AKI. The anti-streptolysin (ASO) test is positive in up to 95% of patients with streptococcal throat infections with low c3 and c4.

Treatment is supportive, with control of blood pressure and fluid overload with salt restriction, diuretics and dialysis if required. Antibiotic therapy is rarely needed, as the renal disease occurs after the infection has subsided.

The medium-term prognosis for children and most adults is good, with recovery of renal function typical even in those requiring dialysis therapy. Some patients may develop CKD 20–30 years after the original presentation.

2- An immune complex-mediated disease may also be observed during an infection, typically a staphylococcal infection such as endocarditis, skin infection or pneumonia, but also with subacute endocarditis due to Streptococcus viridans.. In addition to supportive measures, antibiotic therapy is required, as infection is usually concurrent with renal disease

Inherited glomerular diseases

1-Alport syndrome:

Most cases arise from a mutation or deletion of the COL4A5 gene on the X chromosome, which encodes the alpha 5 subunit of type IV collagen, resulting in inheritance as an X-linked recessive disorder .

Mutations in COL4A3 or COL4A4 genes are less common and cause autosomal disease, which may be recessive or dominant and affect males and females equally.

Affected patients progress from haematuria to ESRD in late adolescence or their twenties. Female carriers of COL4A5 mutations usually have haematuria but less commonly develop significant renal disease.

2- Thin glomerular basement membrane disease:

-In thin glomerular basement membrane disease there is non-visible haematuria without associated hypertension, proteinuria or a reduction in GFR. Autosomal dominant inheritance.

-The glomeruli appear normal by light microscopy but, on electron microscopy, the GBM is abnormally thin. The condition may be familial and some patients are carriers of Alport mutations.

Monitoring of these patients is advisable, as proteinuria may develop in some and there appears to be an increased rate of progressive CKD in the long term.

Cystic diseases of the kidney

Autosomal dominant polycystic kidney disease (PKD) is a common condition, with a prevalence of approximately 1:1000. Mutations in the PKD1 gene account for 80% of cases and those in PKD2 for about 15% (coding for polycystin 1 and 2) .

- Prognosis : The surrounding normal kidney tissue is compressed and progressively damaged. The median age of ESRD is approximately 52 years with a PKD1 mutation and 70 years with a PKD2 mutation.

Presentation :

- Affected people are usually asymptomatic until later life but hypertension occurs from the age of 20 onwards.

- About 30% of patients with PKD also have hepatic cysts , but disturbance of liver function is rare. Sometimes (almost always in women) the cysts cause massive and symptomatic hepatomegaly, usually concurrent with renal enlargement but occasionally with only minor renal involvement.

-Berry aneurysms of cerebral vessels are an associated feature in about 5% of patients with PKD. This feature appears to be largely restricted to certain families (and presumably specific mutations).

-Mitral and aortic regurgitation is frequent but rarely severe

-Colonic diverticula and abdominal wall hernias may occur.

Investigations : The diagnosis is usually based on family history, clinical findings and ultrasound examination. Cysts may also be identified by other imaging modalities, such as MRI

Ultrasound demonstrates cysts in approximately 95% of affected patients over the age of 20 and is the screening method of choice. The following criteria exist for an ultrasound diagnosis of PKD in patients with a family history but unknown genotype:

1-15–39 years of age: at least three unilateral or bilateral kidney cysts

2- 40–59 years of age: at least two cysts in each kidney

3-60 years or older: at least four cysts in each kidney. have PKD genes respectevely . .

Management :

1-Blood pressure control is important because cardiovascular morbidity and mortality are so common in renal disease.

2- Patients with PKD are usually good candidates for dialysis and transplantation. Sometimes kidneys are so large that one or both have to be removed to make space for a renal transplant. Otherwise, they are usually left in situ unless they are a source of pain or infection

Renal vascular disease

1- Renal artery stenosis : is the most common cause of secondary hypertension. Most cases of renal artery stenosis are caused by atherosclerosis. Rare causes include vasculitis, thromboembolism and aneurysms.

Renal artery stenosis is more likely if:

1-hypertension is severe, of recent onset or difficult to control

2- kidneys are asymmetrical in size

3-Flash pulmonary oedema occurs repeatedly

4-There is peripheral vascular disease of the lower limbs

5-There is renal impairment and renal function has deteriorated on angiotensin-.

converting enzyme inhibitors or angiotensin II receptor blockers artery.

Investigations:

1- CT angiography or MR angiography should be performed to confirm the diagnosis

2- Biochemical testing may reveal impaired renal function and an elevated plasma renin activity, sometimes with hypokalaemia due to hyperaldosteronism.

3-Ultrasound may also reveal a discrepancy in size between the two kidneys

Treatment

1- Medical therapy first line -statins and low-dose aspirin in those with atherosclerotic disease

2- Interventions to correct the vessel narrowing should be considered in:

1-Young patients (age below 40) suspected of having renal artery stenosis

2-Those whose blood pressure cannot easily be controlled with antihypertensive agents OR malignant HTN

3-Those who have a history of ‘flash’ pulmonary oedema

4-Deteriorating renal function

Reno-vascular disease

2- Acute renal infarction :

An uncommon condition which is typically present with acute loin pain , usually in association with non-visible haematuria, but pain may be absent in some cases. Severe hypertension is common .

-If occlusion of the main renal arteries is bilateral or if there is occlusion in a single functioning kidney, the presentation is with AKI and the patient is typically anuric.

Investigations : Blood levels of lactate dehydrogenase (LDH) and CRP are commonly raised. CT scan is important to visualize the occlusion .

Management is largely supportive, and includes anticoagulation if a source of thromboembolism is identified.

It is sometimes possible to perform stenting of an acutely blocked main renal artery to try to restore renal blood flow; in most cases, however, presentation is too late to salvage renal function..

Investigations

15.29 Suggested investigations in chronic kidney disease

Initial tests	Interpretation
Urea and creatinine	To assess stability/progression: compare to previous results
Urinalysis and quantification of proteinuria	Haematuria and proteinuria may indicate glomerular disease and need for biopsy (p. 391). Proteinuria indicates risk of progressive CKD requiring preventive ACE inhibitor or ARB therapy
Electrolytes	To identify hyperkalaemia and acidosis
Calcium, phosphate, parathyroid hormone and 25(OH)D	Assessment of renal osteodystrophy
Albumin	Low albumin: consider malnutrition, inflammation, nephrotic syndrome
Full blood count (±Fe, ferritin, folate, B_{12})	If anaemic, exclude common non-renal explanations, then manage as renal anaemia
Lipids, glucose ±HbA_{1c}	Cardiovascular risk high in CKD: treat risk factors aggressively
Renal ultrasound	Only if there are obstructive urinary symptoms, persistent haematuria, family history of polycystic kidney disease or progressive CKD. Small kidneys suggest chronicity. Asymmetric renal size suggests renovascular or developmental disease
Hepatitis and HIV serology	If dialysis or transplant is planned. Hepatitis B vaccination recommended if seronegative
Other tests	Consider relevant tests from Box 15.25, especially if the cause of CKD is unknown

(ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; 25(OH)D = 25-hydroxyvitamin D)

Other investigations

1- ANA , anti dsDNA ,ANCAS ,C3,C4 (? Vasculitis , SLE)

2- Urine and serum protein electropheresis (? Myeloma)

3- Blood film (fragmented rbcs, low platelets

in TTP / HUS)

4- antibodies to GBM in patients with Goodpasture's disease, Antibodies directed against M-type phospholipase A2 receptor (anti-PLA2R) are positive in about 70%–80% of cases of primary membranous nephropathy.

5- CT scan (? Masses/ stones)

6- Renal doppler US/ angiography is renal vascular disease suspected (Angio can be diagnostic and theraputic in some cases)

7- Renal biopsy

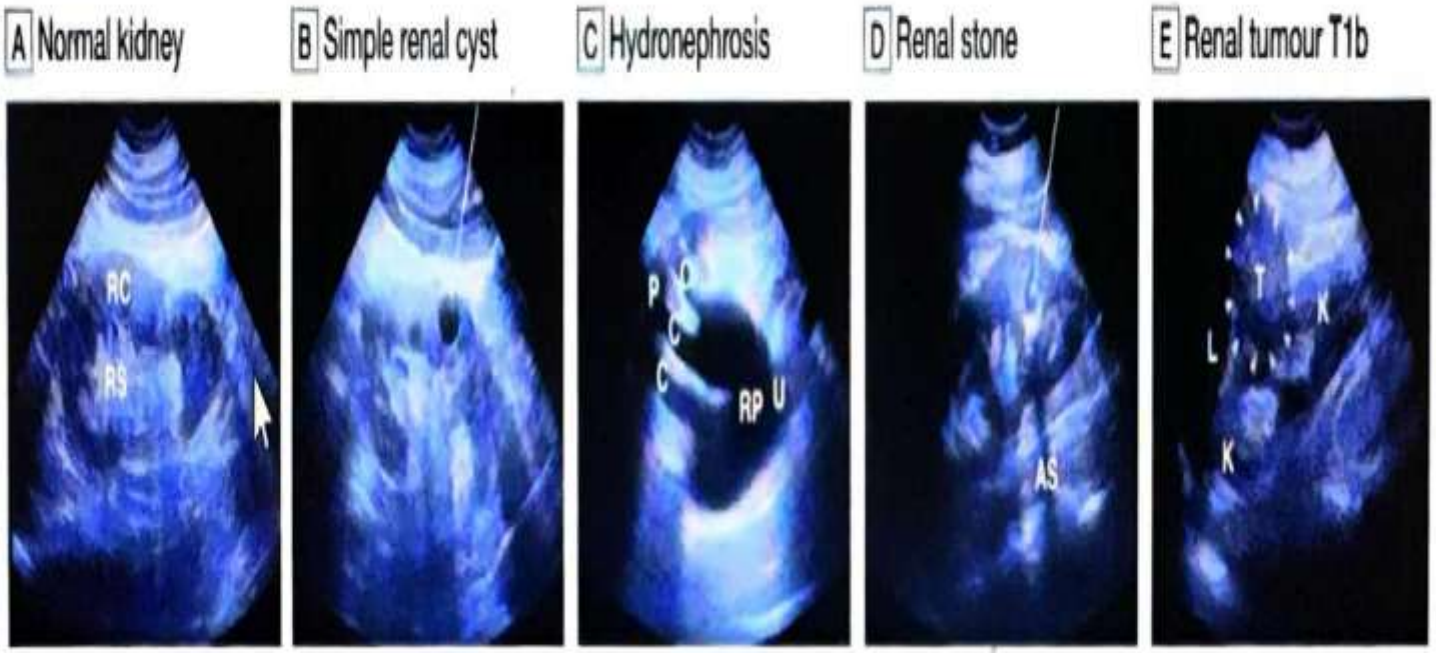


Fig. 18.4 Renal ultrasound. A Normal kidney. The normal cortex is less echo-dense (blacker) than the adjacent liver. B Simple renal cyst: round, echo-free fluid content, no septa, posterior acoustic enhancement. C The renal pelvis and calyces are dilated due to obstruction. The thinness of the parenchyma (P) indicates chronic obstruction. D A typical renal stone with posterior shadowing. E A T1b renal tumour arising from the renal cortex. (AS = posterior acoustic shadow; C = calyx; K = kidney; L = liver; RC = renal cortex; RP = renal pelvis; RS = renal sinus – calyx, renal pelvis, blood vessels, sinus fat; T = tumour; U = ureter) *(A–E) Courtesy of Dr Tobias Klatte, Addenbrooke's Hospital, Cambridge.*

15.5 Renal biopsy

Indications

- Acute kidney injury and chronic kidney disease of uncertain aetiology
- Nephrotic syndrome or glomerular proteinuria (protein:creatinine ratio >100 mg/mol) in adults
- Nephrotic syndrome in children that has atypical features or is not responding to treatment
- Nephritic syndrome
- Renal transplant dysfunction
- Rarely performed for isolated haematuria or isolated low-grade proteinuria in the absence of impaired renal function or evidence of a multisystem disorder

Contraindications

- Disordered coagulation or thrombocytopenia. Aspirin and other antiplatelet agents increase bleeding risk
- Uncontrolled hypertension
- Kidneys <60% predicted size
- Solitary kidney* (except transplants)

Complications

- Pain, usually mild
- Bleeding into urine, usually minor but may produce clot colic and obstruction
- Bleeding around the kidney, occasionally massive and requiring angiography with intervention, or surgery
- Arteriovenous fistula, rarely significant clinically

*Relative contraindication.

Management

The aims of management in CKD are to:

1-Monitor renal function (every 6 months , more frequent in stage 4 and 5)

2-Prevent or slow further renal damage(control BP , ACE inhibitors , treat underlying cause) . A target blood pressure of less than 140/90 mmHg is recommended for patients with CKD and no albuminuria (ACR <3mg/mmol. A lower target of 130/80 mmHg is recommended for those with diabetes or an ACR of more than 70 mg/mmol.

3-Treat risk factors for cardiovascular disease.

4- Prepare for RRT, if appropriate

5- Limit complications of renal failure

A-Maintenance of fluid and electrolyte balance mainly potassium levels and the need for diuretics ,

B-Acid–base balance and need for sodium bicarb tabs to maintain bicarb levels of 22

C- Renal bone disease(hyperphosphataemia and inadequate activation of vitamin D)

(Hyperphosphataemia should be treated by dietary restriction of foods with high phosphate content (milk, cheese, eggs and protein-rich foods) and by the use of phosphate-binding drugs that inhibit phosphate reabsorption in the gut. The aim is to maintain serum phosphate values below 1.5 mmol/L (4.6 mg/dL) if possible . Active vitamin D metabolites (either 1-α-hydroxyvitamin D or 1,25-dihydroxyvitamin D) should be administered in patients who are hypocalcaemic or have serum PTH levels more than twice the upper limit of normal

D- Anemia: Due to

1-Deffiency of erythropoietin

2-Toxic effects of uraemia on marrow precursor cells

3-Reduced intake, absorption and utilisation of dietary iron

4-Reduced red cell survival

5-Blood loss due to capillary fragility and poor platelet function

Should be treated with iron and erythropiotin / Hb target haemoglobin is usually between 100 and 120 g/L

Reduction of proteinuria

-Patients with proteinuria are at higher risk of progression of renal disease. ACE inhibitors and ARBs reduce proteinuria and retard the progression of CKD.In addition, ACE inhibitors have been shown to reduce the risk of cardiovascular events and all-cause mortality in CKD.

-Initiation of treatment with ACE inhibitors and ARBs may be accompanied by an immediate reduction in GFR; patients should therefore have their renal function checked within 7–10 days of initiating or increasing the dose of an ACE inhibitor or ARB. Treatment can be continued so long as the reduction in GFR is not greater than 25% and is not progressive.

-Patients on ACE inhibitors/ARBs should therefore be warned to stop taking the medication if they become unwell, such as with fever, vomiting or diarrhoea, restarting once they are better. This also applies to other common medications used in patients with CKD, such as diuretics, metformin and NSAIDs

-ACE inhibitors and ARBs increase serum potassium and should not be commenced in patients with baseline potassium >5.5 mmol/L. In patients with serum potassium >6.0 mmol/L, the dose of ACE inhibitors or ARBs should be reduced or discontinued entirely, but only after all other measures to reduce potassium have been considered.

Foods high in potassium

Fruit: bananas, avocados, figs, rhubarb

Vegetables: tomatoes, spinach, parsnips, courgettes, sprouts, potatoes (including baked, fries, wedges; boiling vegetables reduces potassium content)

Sweets/snacks: crisps, chocolate, toffee, nuts (including peanut butter)

Drinks: beer, cider, wine (spirits contain less potassium), hot chocolate, fruit juice, milk, yoghurt

Some salt substitutes, such as Lo-Salt: sodium chloride is substituted with potassium chloride

Treat risk factors for cardiovascular disease

-Patients with CKD have a higher prevalence of traditional risk factors for atherosclerosis, such as hypertension, hyperlipidaemia and diabetes. Left ventricular hypertrophy is commonly found in patients with CKD, secondary to hypertension or anaemia.

-Both left ventricular hypertrophy and cardiac calcification may increase the risk of arrhythmias and sudden cardiac death.

-To reduce vascular risk, patients with CKD should be encouraged to adopt a healthy lifestyle, including regular exercise, and weight loss and smoking cessation where appropriate. Lipid-lowering drugs reduce cardiovascular events in patients with CKD, although their effcacy may be lower once patients require dialysis.

Preparing for RRT

-Since there is no evidence that early initiation of RRT improves outcome, the overall aim is to commence RRT when symptoms of CKD begin to impact on quality of life but before serious complications have occurred. While there is wide variation between patients, this typically occurs when the eGFR approaches 10 mL/min/1.73 m2.

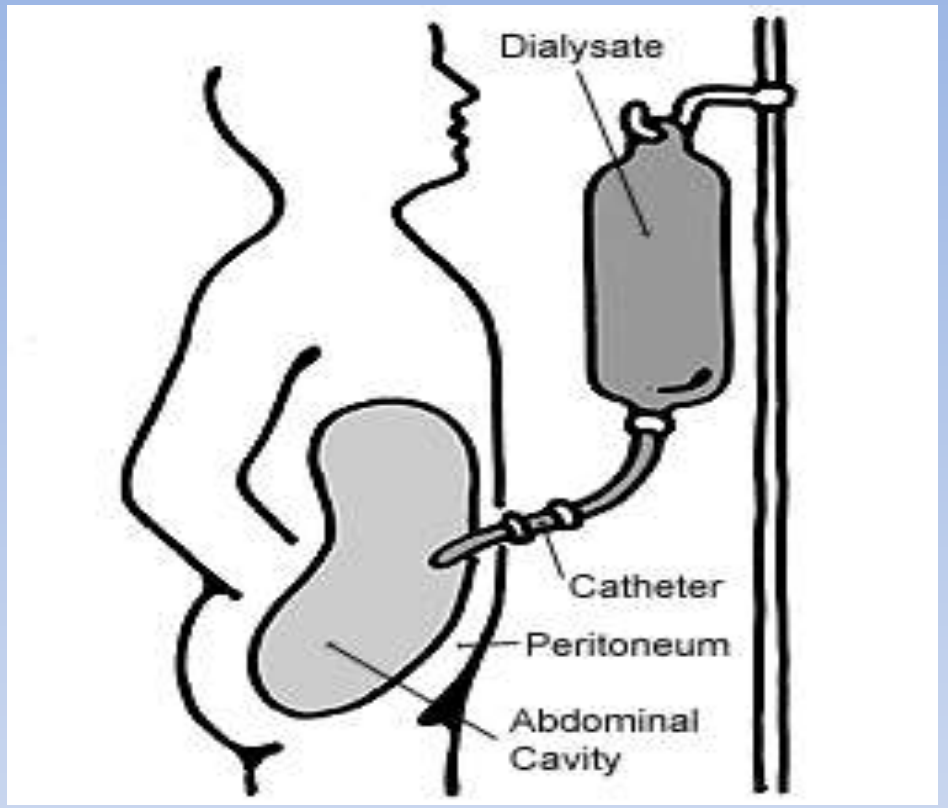
-Preparations for starting RRT should begin at least 12 months before the predicted start date. This involves providing the patient with psychological and social support, assessing home circumstances and discussing the various choices of treatment .

-Depression is common in patients who are on or approaching RRT, and support from the renal multidisciplinary team should be provided both for them and for their relatives, to explain and help them adapt to the changes to lifestyle that may be necessary once RRT starts; this may help to reduce their anxieties about these changes.

-Physical preparations include establishment of timely access for haemodialysis or peritoneal dialysis and vaccination against hepatitis B.

-Possible complications of dialysis: hypotension , arrythmias , bleeding , air embolism , sepsis, peritonitis .

- Renal transplantation offers the best chance of long-term survival in ESRD and is the most cost-effective treatment. All patients with ESRD should be considered for transplantation but many are not suitable due to a combination of comorbidity and advanced age (although no absolute age limit applies). Active malignancy, vasculitis and cardiovascular comorbidity are common contraindications to transplantation, with risk of recurrence of the original renal disease (generally glomerulonephritides) being a less common problem.


Dialysate
Catheter
Peritoneum
Abdominal Cavity


AV Fistula
Doctors Hub

Conservative treatment In older patients

Conservative treatment In older patients and those with multiple comorbidities, conservative treatment of stage 5 CKD, aimed at limiting the adverse symptoms of ESRD without commencing RRT, is increasingly viewed as a positive choice

Current evidence suggests that survival of these patients without dialysis can be similar or only slightly shorter than that of patients who undergo RRT, but they avoid the hospitalisation and interventions associated with dialysis. Patients are offered full medical, psychological and social support to optimise and sustain their existing renal function and to treat complications, such as anaemia, for as long as possible, with appropriate palliative care in the terminal phase of their disease.

Many of these patients enjoy a good quality of life for several years. When quality of life on dialysis is poor, it is appropriate to consider discontinuing it, following discussion with the patient and family, and to offer palliative care.

Dr Razan ALODAT

Thank you