Chronic kidney disease (CKD)

Synonym: chronic renal failure

What is chronic kidney disease?

Chronic kidney disease (CKD) describes abnormal kidney function and/or structure. There is evidence that treatment can prevent or delay the progression of CKD, reduce or prevent the development of complications, and reduce the risk of cardiovascular disease (CVD).

The definition of CKD is based on the presence of kidney damage (ie albuminuria) or decreased kidney function (ie glomerular filtration rate (GFR) <60 ml/minute per 1·73 m²) for three months or more, irrespective of clinical diagnosis.

Accelerated progression of CKD is defined as a sustained decrease in GFR of 25% or more and a change in GFR category within 12 months, or a sustained decrease in GFR of 15 ml/minute/1.73 m^2 per year.[1]

Until recently, the emphasis has been on patients needing dialysis or transplantation. It is now realised that less severe chronic kidney disease is common, and monitoring in primary care will enable the minority of patients who go on to develop a more severe form to be detected at an earlier stage. This is important because the earlier the intervention, the greater the impact.

Epidemiology[2]

The incidence and prevalence of chronic kidney disease varies depending on the population studied, including ethnic group and socio-economic class.

- The large UK primary care five-year study (n = 130,226 adults, based on a single estimated GFR reading) found:
    - The age-standardised prevalence of CKD stages 3-5 was 8.5% (10.6% in women and 5.8% in men).
    - An exponential increase in the prevalence of CKD stages 3-5 with increasing age.
- A UK retrospective longitudinal cohort study of data from more than 400 primary care practices in the General Practice Research Database in 2010 found the prevalence of CKD stages 3-5 was 5.9%. Of these:
    - 5.4% had CKD stage 3; 0.4% had CKD stage 4; and 0.1% had CKD stage 5.
    - 0.5% of people were aged 18-39 years; 6.7% of people were aged 40-59 years; and 92.9% of people were aged 60 years or over.

Chronic kidney disease causes[2]

There are many possible causes and risk factors for chronic kidney disease, including:

- Hypertension.
- Diabetes mellitus.
- Glomerular disease - eg, acute glomerulonephritis.
- Current or previous history of acute kidney injury.
- Potentially nephrotoxic drugs - eg, aminoglycosides, ACE inhibitors, angiotensin-II receptor antagonists, bisphosphonates, calcineurin inhibitors (such as ciclosporin or tacrolimus), diuretics, lithium, mesalazine and NSAIDs.
- Conditions associated with obstructive uropathy - eg, structural renal tract disease, neurogenic bladder, benign prostatic hypertrophy, urinary diversion surgery, recurrent urinary tract calculi.

- Multisystem diseases with potential renal involvement - eg, systemic lupus erythematosus (SLE), vasculitis, myeloma.
- Family history of CKD stage 5, or hereditary kidney disease.
- Cardiovascular disease.
- Obesity with metabolic syndrome (obesity alone is not a risk factor).
- Gout.
- Solitary functioning kidney.
- Low birth weight (2.5 kg or lower).
- Incidental finding of haematuria or proteinuria.

For people with any of these risk factors, offer testing for CKD using eGFR and ACR. Monitor at least annually for people taking potentially nephrotoxic drugs.

Classification of chronic kidney disease[1]

Kidney function should be assessed using a combination of GFR and albumin:creatinine ratio (ACR) categories. Increased ACR and decreased GFR are associated with increased risk of adverse outcomes. Increased ACR and decreased GFR in combination multiply the risk of adverse outcomes.

- **Stage 1: normal** - eGFR >90 ml/minute/1.73 m^2 with other evidence of chronic kidney damage (see below).
- **Stage 2: mild impairment** - eGFR 60-89 ml/minute/1.73 m^2 with other evidence of chronic kidney damage.
- **Stage 3a: moderate impairment** - eGFR 45-59 ml/minute/1.73 m^2.
- **Stage 3b: moderate impairment** - eGFR 30-44 ml/minute/1.73 m^2.
- **Stage 4: severe impairment** - eGFR 15-29 ml/minute/1.73 m^2.
- **Stage 5: established renal failure (ERF)** - eGFR less than 15 ml/minute/1.73 m^2 or on dialysis.

NB: patients with a GFR of >60 ml/minute/1.73 m^2 **without** evidence of chronic kidney damage should **NOT** be considered to have CKD and do not necessarily need further investigation.

The other evidence of chronic kidney damage may be one of the following:

- Persistent microalbuminuria.
- Persistent proteinuria.
- Persistent haematuria (after exclusion of other causes - eg, urological disease).
- Structural abnormalities of the kidneys, demonstrated on ultrasound scanning or other radiological tests - eg, polycystic kidney disease, reflux nephropathy.
- Biopsy-proven chronic glomerulonephritis.

Chronic kidney disease symptoms (presentation)

Chronic kidney disease is usually asymptomatic and often unrecognised because there are no specific symptoms, and it is often not diagnosed, or is diagnosed at an advanced stage.

Symptoms

- It may be discovered by chance following a routine blood or urine test.
- Specific symptoms usually develop only in severe CKD, and include anorexia, nausea, vomiting, fatigue, weakness, pruritus, lethargy, peripheral oedema, dyspnoea, insomnia, muscle cramps, pulmonary oedema, nocturia, polyuria and headache.
- Sexual dysfunction is common.
- Hiccups, pericarditis, coma and seizures are only seen in very severe CKD.

Signs

- The physical examination is often not very helpful but may reveal findings characteristic of the underlying cause (eg, SLE, severe arteriosclerosis, hypertension) or complications of CKD (eg, anaemia, bleeding diathesis, pericarditis).

- Signs of CKD include increased skin pigmentation or excoriation, pallor, hypertension, postural hypotension, peripheral oedema, left ventricular hypertrophy, peripheral arterial disease, pleural effusions, peripheral neuropathy and restless legs syndrome.

Chronic kidney disease screening

Patients who are at increased risk of developing chronic kidney disease should be offered screening tests to detect CKD, which should include assessment of the eGFR as well as urine ACR. The National Institute for Health and Care Excellence (NICE) recommends:[1]

- Monitor glomerular filtration rate (GFR) at least annually if taking medicines that can adversely affect kidney function, such as calcineurin inhibitors (for example, ciclosporin or tacrolimus), lithium or NSAIDs (long-term chronic use of NSAIDs).
- Test for CKD using GFR and urinary albumin:creatinine ratio (ACR) to adults with any of the risk factors listed under the 'CKD Causes' section above.
- Monitor adults, children and young people for the development or progression of CKD for at least three years after acute kidney injury (longer for people with acute kidney injury stage 3) even if eGFR has returned to baseline.

Differential diagnosis

Acute kidney injury (AKI)

- Making the distinction between AKI and CKD can be very difficult. A history of chronic symptoms of fatigue, weight loss, anorexia, nocturia and pruritus all suggest CKD.
- The history and examination will provide clues, but renal ultrasound will provide the most important information. Renal abnormalities on ultrasound, such as small kidneys in chronic glomerulonephritis or large cystic kidneys in adult polycystic kidney disease, will almost always be present in patients with CKD.

Acute-on-chronic kidney disease

Acute-on-chronic kidney disease may have features indicating CKD but also features suggesting a cause of an acute deterioration of renal function - eg, infection.

Investigations[1] [2]

Investigations are focused on assessment of renal function and therefore stage of chronic kidney disease, identification of the underlying cause and assessment of complications of CKD.

- Assessment of renal function:
    - Serum urea is a poor marker of renal function, because it varies significantly with hydration and diet, is not produced constantly and is reabsorbed by the kidney.
    - Serum creatinine also has significant limitations. The level can remain within the normal range despite the loss of over 50% of renal function.
    - A gold-standard measurement is an isotopic GFR, but this is expensive and not widely available.
    - For most purposes in primary care, the best assessment or screening tool is the eGFR - see the separate Assessing renal function article.

- Biochemistry:
    - Plasma glucose: to detect undiagnosed diabetes or assess control of diabetes.
    - Serum sodium: usually normal, but may be low.
    - Serum potassium: raised.
    - Serum bicarbonate: low.
    - Serum albumin: hypoalbuminaemia in patients who are nephrotic and/or malnourished (low levels at the start of dialysis are associated with a poor prognosis).
    - Serum calcium: may be normal, low or high.
    - Serum phosphate: usually high.
    - Serum alkaline phosphatase: raised when bone disease develops.
    - Serum parathyroid hormone: rises progressively with declining renal function.
    - Serum cholesterol and triglycerides: dyslipidaemia is common.
- Haematology:
    - Normochromic normocytic anaemia; haemoglobin falls with progressive CKD.
    - White cells and platelets are usually normal.

- Serology:
    - Autoantibodies, particularly antinuclear antibodies, classical antineutrophil cytoplasmic antibodies (c-ANCA), protoplasmic-staining antineutrophil cytoplasmic antibodies (p-ANCA), antiglomerular basement membrane (anti-GBM) antibodies (very suggestive of underlying Goodpasture's syndrome) and serum complement.
    - Hepatitis serology: ensure not infected and vaccinate against hepatitis B.
    - HIV serology: performed before dialysis or transplantation.

- Urine:
    - Urinalysis: dipstick proteinuria may suggest glomerular or tubulointerstitial disease. Urine sediment with red blood cells and red blood cell casts suggests proliferative glomerulonephritis. Reagent strips should not be used to identify proteinuria in children and young people.
    - Pyuria and/or white cell casts suggest interstitial nephritis (especially if eosinophils are present in the urine) or urinary tract infection (UTI).
    - Proteinuria: the degree of proteinuria correlates with the rate of progression of the underlying kidney disease and is the most reliable prognostic factor in CKD. For the initial detection of proteinuria, use urine ACR rather than protein:creatinine ratio (PCR) because of the greater sensitivity for low levels of proteinuria. Check an ACR between 3 mg/mmol and 70 mg/mmol in a subsequent early morning sample to confirm the result. A repeat sample is not needed if the initial ACR is 70 mg/mmol or more. Regard a confirmed ACR of 3 mg/mmol or more as clinically important proteinuria.
    - Patients in whom initial urinalysis reveals microscopic haematuria should have a urine culture performed to exclude a UTI. If a UTI is excluded, two further tests should be performed to confirm the presence of persistent microscopic haematuria. Do not use urine microscopy to confirm a positive result.
    - Patients over 40 years of age with persistent non-visible/microscopic haematuria in the absence of significant proteinuria or a reduced GFR should be referred to a urology department for further investigation.
    - Serum and urine protein electrophoresis: to screen for a monoclonal protein possibly representing multiple myeloma.
- ECG and echocardiography: to detect left ventricular hypertrophy and ischaemia, and to assess cardiac function.

- Imaging of the renal tract:
    - Plain abdominal X-ray: may show radio-opaque stones or nephrocalcinosis.
    - Intravenous (IV) pyelogram: not often used because of potential for contrast nephropathy.
    - Renal ultrasound:
        - Small echogenic kidneys are seen in advanced CKD.
        - Kidneys are usually initially large and then become normal in size in advanced diabetic nephropathy.
        - Structural abnormalities may be seen - eg, polycystic kidneys.
        - It is also used to screen for hydronephrosis caused by urinary tract obstruction, or involvement of the retroperitoneum with fibrosis, tumour or diffuse adenopathy.
    - Offer a renal ultrasound scan to all people with CKD who: [1]
        - Have accelerated progression of CKD.
        - Have visible or persistent invisible haematuria.
        - Have symptoms of urinary tract obstruction.
        - Have a family history of polycystic kidney disease and are aged over 20 years.
        - Have a GFR of less than 30 ml/minute/1.73 m^2.
        - Are considered by a nephrologist to require a renal biopsy.
    - Retrograde pyelogram: may be indicated if there is clinical suspicion of obstruction despite a negative ultrasound study finding.

    - Renal radionuclide scan:
        - Useful to screen for renal artery stenosis when performed with captopril administration but is unreliable for GFR of less than 30 ml/minute.
        - Also quantifies differential renal contribution to total GFR.
    - CT scan: to define renal masses and cysts, seen on ultrasound, better; this is the most sensitive test for identifying renal stones.
    - MRI:
        - For patients who require a CT scan but who cannot receive IV contrast.
        - Like CT scan and renal venography, it is reliable in the diagnosis of renal vein thrombosis.
        - Magnetic resonance angiography is also useful for diagnosis of renal artery stenosis, although renal arteriography remains the investigation of choice.
    - Micturating cystourethrogram: for diagnosis of vesicoureteric reflux.
- Renal biopsy.

Chronic kidney disease monitoring[1]

The minimum frequency of eGFR creatinine monitoring will depend on:

- The underlying cause of CKD.
- The rate of decline in eGFR or increase in ACR (but CKD progression is often non-linear).
- Other risk factors, including heart failure, diabetes and hypertension.
- Changes to treatment (such as renin-angiotensin-aldosterone system antagonists, NSAIDs and diuretics).
- Intercurrent illness (eg, acute kidney injury).
- Whether the person has chosen conservative management of CKD.

ACR monitoring should be individualised based on a person's individual characteristics, risk of progression and whether a change in ACR is likely to lead to a change in management.

NICE recommends the minimum number of monitoring checks (eGFR creatinine) per year for adults, children and young people with, or at risk of, CKD as follows:

	ACR category A1: normal-mildly increased (less than 3 mg/mmol)	ACR category A2: moderately increased (3-30 mg/mmol)	ACR category A3: severely increased (over 30 mg/mmol)
GFR category G1: normal and high (90 or over)	0 to 1	1	1 or more
GFR category G2: mild reduction (60-89)	0 to 1	1	1 or more
GFR category G3a: mild-moderate reduction (45-59)	1	1	2
GFR category G3b: moderate-severe reduction (30-44)	1 to 2	2	2 or more
GFR category G4: severe reduction (15-29)	2	2	3
GFR category G5: kidney failure (under 15)	4	4 or more	4 or more

Criteria for referral to specialist services[1]

Take into account the individual's wishes and comorbidities when considering referral.

- People with chronic kidney disease in the following groups should normally be referred for specialist assessment:
    - A 5-year risk of needing renal replacement therapy of greater than 5% (measured using the 4-variable kidney failure risk equation.[3]
    - GFR less than 30 ml/minute/1.73 m^2, with or without diabetes (stage 4 or 5).
    - ACR 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated.
    - ACR 30 mg/mmol or more, together with haematuria.
    - Sustained decrease in GFR of 25% or more, and a change in GFR category or sustained decrease in GFR of 15 ml/minute/1.73 m^2 or more within 12 months.
    - Hypertension that remains poorly controlled despite the use of at least four antihypertensive drugs at therapeutic doses.
    - Known or suspected rare or genetic causes of CKD.
    - Suspected renal artery stenosis.
- People with CKD and renal outflow obstruction should normally be referred to urological services, unless urgent medical intervention is required.
- Consider discussing management issues with a specialist in cases where it may not be necessary for the person with CKD to be seen by the specialist.
- Once a referral has been made and a plan jointly agreed, consider routine follow-up at the person's GP surgery rather than in a specialist clinic and specify criteria for future referral or re-referral.

Chronic kidney disease treatment and management[1]

General principles

- Many patients equate kidney disease with renal dialysis. It is important to explain that CKD is a spectrum of disease. Mild CKD is common and rarely progresses to a more severe form later.
- Explain eGFR and that this will need to be monitored on a regular basis to ensure that the condition is not deteriorating.
- If relevant, discuss the link between hypertension and CKD and that maintaining tight blood pressure control can limit the damage to the kidneys.
- Discuss the link between CKD and an increased risk of developing CVD.
- Encourage people with CKD to take exercise, achieve a healthy weight and stop smoking.
- Patients with diabetes mellitus and CKD should achieve good glycaemic control.
- Review all prescribed medication regularly to ensure appropriate doses.
- Avoidance of nephrotoxins - eg, IV radiocontrast agents, NSAIDs, aminoglycosides.
- Immunise against influenza and pneumococcus.

In those newly diagnosed with eGFR less than 60 ml/minute/1.73 m^2

- Review all previous measurements of serum creatinine to estimate GFR and assess the rate of deterioration.
- Review all medication including over-the-counter drugs; particularly consider recent additions (eg, diuretics, NSAIDs, or any drug capable of causing interstitial nephritis, such as penicillins, cephalosporins, mesalazine).
- Urinalysis: haematuria and proteinuria suggest glomerulonephritis, which may progress rapidly.
- Clinical assessment: eg, look for sepsis, heart failure, hypovolaemia, palpable bladder.
- Repeat serum creatinine measurement within five days to exclude rapid progression.

- Check criteria for referral (above). If referral is not indicated, ensure entry into a chronic disease management register and programme.

CVD prevention [4]

- See also the separate Prevention of cardiovascular disease article.
- Patients with CKD should have an annual formal assessment of their cardiovascular risk factors including lipid profile, BMI, exercise, and alcohol and smoking habits, as well as a review of interventions to reduce cardiovascular risk.
- Statins:
    - Statins lower death and major cardiovascular events by 20% in people with CKD not requiring dialysis.
    - Offer atorvastatin 20 mg for the primary or secondary prevention of CVD to people with CKD. Increase the dose if a greater than 40% reduction in non-HDL cholesterol is not achieved and eGFR is 30 ml/minute/1.73 m^2 or more. Agree the use of higher doses with a renal specialist if eGFR is less than 30 ml/minute/1.73 m^2.
- Folic acid and B vitamin supplements should be offered to all renal patients considered nutritionally at risk from deficiency of folic acid or vitamin B. B12 levels and serum and red cell folate should be above the lower limit of the reference range in all CKD patients. Red cell folate levels should be checked if MCV remains high despite normal or high serum folate. Serum folate levels and B12 should be checked six-monthly in CKD 4/5 and three-monthly in dialysis patients, or more frequently if patients remain anaemic or deficient.

- Oral antiplatelets and anticoagulants:
    - Offer antiplatelet drugs to people with CKD for the secondary prevention of CVD, but be aware of the increased risk of bleeding.
    - Consider apixaban in preference to warfarin in people with a confirmed eGFR of 30-50 ml/minute/1.73 m^2 and non-valvular atrial fibrillation who have one or more of the following risk factors: prior stroke or transient ischaemic attack, age 75 years or older, hypertension, diabetes mellitus, symptomatic heart failure.

Blood pressure control

- In adults with CKD and an ACR under 70 mg/mmol, aim for a clinic systolic blood pressure below 140 mm Hg (target range 120 to 139 mm Hg) and a clinic diastolic blood pressure below 90 mm Hg.
- In adults with CKD and an ACR of 70 mg/mmol or more, aim for a clinic systolic blood pressure below 130 mm Hg (target range 120 to 129 mm Hg) and a clinic diastolic blood pressure below 80 mm Hg.
- In children and young people with CKD and an ACR of 70 mg/mol or more, aim for a clinic systolic blood pressure below the 50th percentile for height.
- An angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) should be used for people with CKD and:
    - Diabetes and an ACR of 3 mg/mmol or more.
    - Hypertension and an ACR of 30 mg/mmol or more.
    - An ACR of 70 mg/mmol or more (irrespective of hypertension or CVD).
    - **NB**: a combination of renin-angiotensin system antagonists should not be offered to people with CKD.
- NICE hypertension recommendations (see the separate Management of hypertension article) should be used for people with CKD, hypertension and an ACR of less than 30 mg/mmol if they do not have diabetes.

- In people with CKD, measure serum potassium concentrations and estimate the GFR before starting renin-angiotensin system antagonists. Repeat these measurements between one and two weeks after starting renin-angiotensin system antagonists and after each dose increase.
- Do not routinely offer a renin-angiotensin system antagonist to people with CKD if their pre-treatment serum potassium concentration is greater than 5.0 mmol/L. Stop renin-angiotensin system antagonists if the serum potassium concentration increases to 6.0 mmol/L or more and other drugs known to promote hyperkalaemia have been discontinued.
- Hypertension in dialysis patients: dialysis patients should be on a restricted sodium (<5 g/day) diet. Hypertension on dialysis should initially be managed by ultrafiltration.

Sodium glucose co-transporter 2 inhibitors (SGLT2 inhibitors)

Not all SGLT2 inhibitors are currently licensed for CKD without diabetes.

SGLT2 inhibitors for patients with diabetes and CKD

NICE has updated its guidance on CKD to reflect the fact that new guidance for type 2 diabetes has superseded it. NICE recommends that for adults with type 2 diabetes and CKD who are taking the highest tolerated dose of ACE inhibitor or ARB, an SGLT2 inhibitor should be:

- Offered to patients with an ACR over 30 mg/mmol.
- Considered for patients with ACR 3-30 mg/mmol.

Only SGLT2 inhibitors with a licence which includes the relevant eGFR threshold should be used.

Dapagliflozin for treating CKD [5]

NICE has issued guidance for dapagliflozin for the treatment of CKD in patients both with and without diabetes. It recommends it as an option for treating CKD in adults who:

- Are already on optimised standard care, including the highest tolerated licensed dose of ACE inhibitors or ARB (unless these are contra-indicated).
- Have an eGFR of 25-75 ml/minute/1.73 m2 at the start of treatment.
- Have type 2 diabetes or an ACR of 22.6 mg/mmol or more.

Nutrition and physical exercise

- All patients with stage 4-5 CKD should have the following parameters measured as a minimum in order to identify undernutrition:
    - Actual body weight (ABW) <85% of ideal body weight (IBW).
    - Reduction in oedema-free body weight (of 5% or more in three months or 10% or more in six months).
    - BMI <20 kg/m^2.
- Recommended daily energy intake: a prescribed energy intake of 30-40 kcal/kg IBW/day is recommended for all patients, depending upon age and physical activity.[6]
- Oral nutritional supplements should be used if oral intake is below the levels indicated above and food intake cannot be improved.
- Enteral feeding via nasogastric (NG) tube or percutaneous endoscopic gastrostomy (PEG) may be required if nutrient intake is suboptimal despite oral supplements. Intradialytic parenteral nutrition (IDPN) or intraperitoneal amino acids may be considered for selected cases if tube feeding is declined or clinically inappropriate.
- Minimum daily dietary protein intake: a prescribed protein intake of 0.8 g/kg IBW/day for patients with stage 4-5 CKD not on dialysis; 1.1-1.4 g/kg IBW/day for patients treated with haemodialysis.[6]
- Patients should receive dietary advice to restrict their sodium intake to <2.4 g/day (100 mmol/day or <6 g/day of salt).

- Patients who develop hyperkalaemia or hyperphosphataemia should receive dietary advice to assist dietary restriction of potassium and phosphate.
- Deficiencies of fat-soluble vitamins, trace elements and carnitine are prevalent in patients with CKD but current evidence does not support preventative or therapeutic supplementation. However, supplementation of oral vitamin D (either colecalciferol or ergocalciferol) may be beneficial.

See also the separate Malnutrition article.

Mineral and bone disorders[7]

- It is recommended that therapeutic decisions should be based on trends, rather than a single laboratory value.
- Do not routinely measure calcium, phosphate, parathyroid hormone (PTH) and vitamin D levels in people with a GFR of 30 ml/minute/1.73 m^2 or more.
- Measure serum calcium, phosphate and PTH concentrations in people with a GFR of less than 30 ml/minute/1.73 m^2. Determine the subsequent frequency of testing by the measured values and the clinical circumstances. Where doubt exists, seek specialist opinion.
- Offer bisphosphonates if indicated for the prevention and treatment of osteoporosis in people with a GFR of 30 ml/minute/1.73 m^2 or more.
- Vitamin D supplements in the management of CKD mineral and bone disorders:
    - Do not routinely offer vitamin D supplementation to manage or prevent CKD mineral and bone disorders.
    - Offer colecalciferol or ergocalciferol to treat vitamin D deficiency in people with CKD and vitamin D deficiency.
    - If vitamin D deficiency has been corrected and symptoms of CKD-mineral and bone disorders persist, offer alfacalcidol (1-alpha-hydroxycolecalciferol) or calcitriol (1-25-dihydroxycolecalciferol) to people with a GFR of less than 30 ml/minute/1.73 m^2.

- Monitor serum calcium and phosphate concentrations in people receiving alfacalcidol or calcitriol supplements.
- Dialysis patients: serum calcium, adjusted for albumin concentration, should be maintained within the normal reference range, measured before a 'short-gap' dialysis session in haemodialysis patients. Ideally, adjusted serum calcium should be maintained between 2.2 and 2.5 mmol/L, with avoidance of hypercalcaemic episodes.

Hyperphosphataemia

Hyperphosphataemia occurs because of insufficient filtering of phosphate from the blood by poorly functioning kidneys. High serum phosphate levels can directly and indirectly increase PTH secretion, leading to the development of secondary hyperparathyroidism. Left untreated, secondary hyperparathyroidism increases morbidity and mortality and may lead to renal bone disease with bone and muscular pain, increased incidence of fracture, bone and joint abnormalities and vascular and soft tissue calcification.

NICE has provided the following guidance for hyperphosphataemia in people with CKD stage 4 or 5:[1]

Dietary management

- A specialist renal dietician should carry out a dietary assessment and give individualised information and advice on dietary phosphate management. Advice on dietary phosphate management should be tailored to the individual patient.
- Give information about controlling intake of phosphate-rich foods (in particular, foods with a high phosphate content per gram of protein, as well as food and drinks with high levels of phosphate additives) to control serum phosphate, while avoiding malnutrition by maintaining a protein intake at or above the minimum recommended level.
- For people on dialysis, take into account possible dialysate protein losses.
- If a nutritional supplement is needed to maintain protein intake in children and young people with hyperphosphataemia, offer a supplement with a lower phosphate content.

Phosphate binders

Before starting phosphate binders for people with CKD stage 4 or 5, optimise diet and, if relevant, dialysis.

- If a combination of phosphate binders is used, titrate the dosage to achieve control of serum phosphate while taking into account the effect of any calcium-based binders used on serum calcium levels.
- Advise that it is necessary to take phosphate binders with food to control serum phosphate.
- At every routine clinical review, assess serum phosphate control, taking into account diet, whether they are taking the phosphate binders as prescribed, and any other relevant factors, such as vitamin D levels, serum parathyroid hormone levels, alkaline phosphatase, serum calcium, medications that might affect serum phosphate, or dialysis.

Phosphate binders - adults

- Offer adults with CKD stage 4 or 5 and hyperphosphataemia calcium acetate to control serum phosphate levels.
- Offer sevelamer carbonate if calcium acetate is not indicated (eg, hypercalcaemia or low serum parathyroid hormone levels) or not tolerated.
- If calcium acetate and sevelamer carbonate cannot be used, consider sucroferric oxyhydroxide, for adults on dialysis if a calcium-based phosphate binder is not needed, or calcium carbonate, if a calcium-based phosphate binder is needed.
- Only consider lanthanum carbonate if other phosphate binders cannot be used.
- If adults with CKD stage 4 or 5 remain hyperphosphataemic after taking the maximum dose recommended or tolerated of a calcium-based phosphate binder, check they are taking it as prescribed, and consider combining a calcium-based phosphate binder with a non-calcium-based phosphate binder.
- For all adults who are taking more than one phosphate binder, titrate the dosage to achieve the best possible control of serum phosphate while keeping serum calcium levels below the upper normal limit.

Phosphate binders - children and young people

- Offer a calcium-based phosphate binder to control serum phosphate levels.
- If serum calcium increases towards or above the age-adjusted upper normal limit, investigate possible causes other than the phosphate binder, and consider reducing the dose of the calcium-based phosphate binder and adding sevelamer carbonate or switching to sevelamer carbonate alone.
- For all children and young people who are taking more than one phosphate binder, titrate the dosage to achieve the best possible control of serum phosphate while keeping serum calcium levels below the upper normal limit.

Renal replacement therapy

Renal replacement therapy includes haemodialysis, peritoneal dialysis, chronic ambulatory peritoneal dialysis and renal transplantation. See the separate Renal replacement therapy and transplantation article.

Chronic kidney disease complications

- Anaemia: left ventricular hypertrophy, fatigue, impaired cognitive functioning.
- Coagulopathy.
- Hypertension: left ventricular hypertrophy, heart failure, stroke, CVD.
- Calcium phosphate loading: cardiovascular and cerebrovascular disease, arthropathy, soft tissue calcification.
- Renal osteodystrophy: disorders of calcium, phosphorus and altered bone morphology, most commonly osteitis fibrosa cystica.[8]
- Bone changes of secondary hyperparathyroidism: bone pain and fractures.
- Neurological: uraemic encephalopathy, neuropathy including peripheral neuropathy.
- Dialysis amyloid: bone pain, arthropathy, carpal tunnel syndrome.

- Fluid overload: pulmonary oedema, hypertension
- Malnutrition: increased morbidity and mortality, infections, poor wound healing.
- Glucose intolerance due to peripheral insulin resistance.

Management of complications

Water and electrolyte balance

- Patients with chronic kidney disease pass normal volumes of urine. Precise restriction of fluid intake is only required for patients with oliguric end-stage kidney disease. The usual recommendation is for a daily intake of daily urinary output plus 500 ml (for insensible losses).
- Patients should avoid binge drinking and be vigilant in replacing extra fluid losses in hot weather and during episodes of diarrhoea or vomiting.
- Severe acute volume overload may require high-dose loop diuretics or dialysis.
- Dietary restriction of sodium and potassium is appropriate but compliance is greatly improved with sensible and flexible dietary advice.
- Loop diuretics (with the addition of a thiazide diuretic if resistant) improve sodium balance and blood pressure.

Hyperkalaemia

- Hyperkalaemia is treated with dialysis if the potassium level rises above 7 mmol/L.
- Otherwise, treatment is directed towards the cause - eg, excess fruit, chocolate or coffee, gastrointestinal haemorrhage, acidosis or tissue necrosis.
- Hyperkalaemia with the GFR still above 10 ml/minute may be due to hyporeninaemic hypoaldosteronism in patients with diabetes, hypoadrenalism or as a result of treatment with ACE inhibitors.

Anaemia

If not already measured, check the haemoglobin level in people with a GFR of less than 45 ml/minute/1.73 m^2 to identify anaemia (haemoglobin less than 110 g/L).[9] Determine the subsequent frequency of testing by the measured value and the clinical circumstances.

If eGFR is above 60 ml/min/1.73 m^2, anaemia is unlikely to be caused by CKD. If eGFR is between 30 and 60 ml/min/1.73 m^2, anaemia may be caused by CKD. If eGFR is below 30 ml/min/1.73 m^2, anaemia is often caused by CKD.

Acidosis

- Chronic acidosis aggravates hyperkalaemia, inhibits protein synthesis and accelerates calcium loss from bone.
- Oral bicarbonate supplements in the management of metabolic acidosis: consider oral sodium bicarbonate supplementation for people with both a GFR less than 30 ml/minute/1.73 m^2, and a serum bicarbonate concentration of less than 20 mmol/L.

Neurological disorders

- Signs of peripheral nervous system and CNS disorders include peripheral neuropathy, restless legs syndrome, sleep disorders, and cognitive impairment.
- Retained toxins are thought to have a role in these disorders, and intensive dialysis is sometimes associated with amelioration.
- No specific therapies have yet been developed for these neurological manifestations.

Difelikefalin for treating pruritus in people having haemodialysis[10]

- The usual treatment for pruritus (itching) in people with CKD having haemodialysis includes creams/emollients, antihistamines and gabapentin.
- NICE has recommended difelikefalin for treating moderate to severe pruritus in adults with CKD having in-centre haemodialysis. Evidence shows that it reduces itching compared to the usual options.

Chronic kidney disease prognosis

Early diagnosis, regular monitoring and early treatment can prevent development and slow disease progression, reduce complications and the risk of CVD, and improve survival and quality of life.

Chronic kidney disease can progress to end-stage kidney disease in a small but significant percentage of people. Moderate-to-severe CKD is also associated with an increased risk of other significant adverse outcomes such as AKI, falls, frailty and mortality. As kidney dysfunction progresses, some co-existing conditions become more common and increase in severity.

People with CKD are at increased risk of progression to end-stage kidney disease (accelerated progression) if they have either of the following:[1]

- A sustained decrease in GFR of 25% or more over 12 months; **or**
- A sustained decrease in GFR of 15 ml/minute/1.73 m^2 or more over 12 months.

Chronic kidney disease prevention

Early diagnosis and good control of potential causes - eg, diabetes, hypertension and urinary tract obstruction - are key to prevention.

Further reading

- Chronic kidney disease in adults; NICE Quality Standard (July 2017)
- Healthy.io test for home testing of urine albumin to creatinine ratio; NICE advice - Medtech innovation briefing, August 2020

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