Chronic Kidney Disease

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EVALUATION OF PATIENTS WITH CKD

The most important initial diagnostic step in the evaluation of a patient presenting with elevated serum creatinine is to ***distinguish*** *newly diagnosed* ***CKD from acute or subacute renal failure***

SUGGESTS CHRONICITY

1. hyperphosphatemia,
2. hypocalcemia,
3. elevated PTH and bone alkaline Phosphatase
4. Normochromic, normocytic anemia
5. bilaterally reduced kidney size <8.5 cm

Diagnosis

- Bilateral Small size Kidneys
- Lab data
- Previous history (3 months ago)
- Nocturia

- Risk of worsening of kidney function is closely linked to the amount of albuminuria

  CKD staging system according to Scr and albumin excretion

  marker for the presence of microvascular disease in general

  too small to detect by urinary dipstick

Step-by-step diagnostic approach

History

Examination

- serum creatinine
- GFR
- Urinalysis
- renal ultrasound
- urine microalbumin : diabetes and CKD if there was no evidence of proteinuria on urine dipstick

proteinuria of >1000 mg/day is associated with a more rapid progressio ESRD

Recommended Equations for Estimation of Glomerular Filtration Rate (GFR) Using *Serum Creatinine Concentration (PCr), Age, Sex, Race,* and *Body Weight*

1) Equation from the Modification of Diet in Renal Disease study* (MDRD)

$$GFR = 186.3 \times (\text{serum creatinine}^{-1.154}) \times (\text{age}^{-0.203}) \times 1.212 \text{ (if African American)} \times 0.742 \text{ (if female)}$$

2) Cockcroft-Gault equation

$$= \frac{(140 - \text{age [years]}) \times (\text{body weight [kg]})}{(72) \times (\text{serum creatinine [mg/dL]})}$$

For males

$= 0.85 \times \text{male value}$

For females

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

GFR categories (ml/min/1.73 m^2) description and range				Persistent albuminuria categories description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

* Stages 1 & 2: no sign and symptom
* Stages 3 & 4: clinical and laboratory complications of CKD
  * *Anemia and associated easy fatigability*;
  * decreased appetite with progressive malnutrition
  * Ca/P
  * mineral-regulating hormones, such as 1,25(OH)2D3 (calcitriol), PTH, FGF-23
  * Na/K, water, acid-base homeostasis
* Stage 5: ESRD (uramic Syndrom)

* *Point: eGFR in many elderly patients is compatible with stage 2 or 3 CKD.*

Additional investigations

- renal biopsy
- Imaging

- **Clinical indicators of kidney damage**

- Microalbuminuria: 30 to 300 mg/g creatinine/day
- Proteinuria: >300 mg proteinuria/day

- Haematuria: >3 red blood cells per high power field on more than 2 occasions

ESTABLISHING THE DIAGNOSIS AND ETIOLOGY OF CKD

Renal biopsy

Contraindications:

- bilaterally small kidneys
- uncontrolled hypertension,
- active urinary tract infection,
- bleeding diathesis (including ongoing anticoagulation),
- and severe obesity

HARRISON'S 18th Edition

Multiple Functions of the Kidneys

1) Excretion of metabolic waste products and foreign chemicals

2) Regulation of water and electrolyte balances

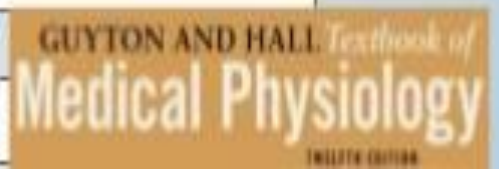
3) Regulation of body fluid osmolality and electrolyte concentrations

4) Regulation of arterial pressure

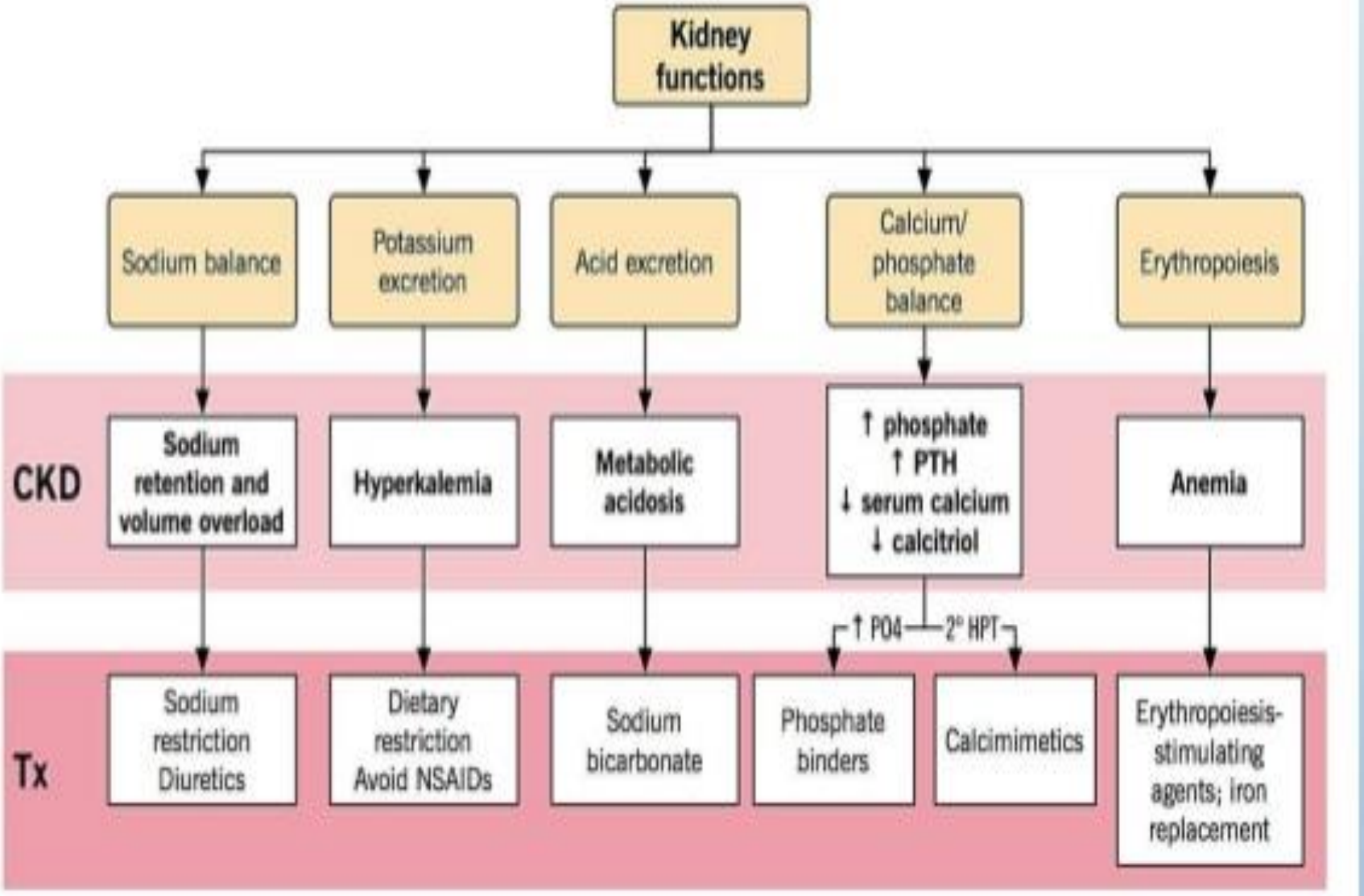
5) Regulation of acid-base balance

6) Secretion, metabolism, and excretion of hormones

7) Gluconeogenesis



Complications of CKD



CLINICAL & LABORATORY MANIFESTATIONS OF CKD AND UREMIA

Water and electrolytes

Sodium and Water Homeostasis

- Total-body content of sodium and water: modestly increased, may not be apparent clinically
- Disruption in urinary excretion
  - Retention
    - HTN
      - Accelerate nephron loss
- Hyponatremia: not commonly
  - Often responds to water restriction

- Overt ECFV expansion:
  - peripheral edema, sometimes hypertension poorly responsive to therapy
  - Salt restriction.
  - loop diuretics, including furosemide, bumetanide, or torsemide
  - loop diuretics (higher doses) with metolazone (DCT)
  - No thiazide

- Inability of kidney in preservation of salt and water

  Prone to hypovolemia

pulmonary oedema

- Fluid overload, especially those with concomitant congestive heart failure
- Treatment loop diuretics :prevent episodes of pulmonary oedema and manage peripheral oedema
- In some instances, a combination diuretic regimen (e.g., a loop and a thiazide diuretic) more effective diuresis in patients
- Failure to maintain fluid balance in those with advanced stages 4 and 5 CKD is an indication to start renal replacement therapy

Potassium Homeostasis

- Augmented potassium excretion in the GI tract
- *Hyperkalemia:*
  - increased dietary potassium intake, protein catabolism, hemolysis, hemorrhage, transfusion of stored red blood cells, and metabolic acidosis.
  - Medications: RAS inhibitors and spironolactone and amiloride, eplerenone, triamterene
  - hyporeninemic hypoaldosteronism (DM), renal diseases that preferentially affect the distal nephron
    - obstructive uropathy
    - sickle cell nephropathy.

- Most patients asymptomatic

- The hallmark for the severity of hyperkalaemia is identification of cardiac disturbances on an ECG with peaked T waves, prolongation of the conduction system, sine wave, or asystole.
- intravenous calcium; medicines to shift potassium into the cells, such as insulin and dextrose; beta-agonists and the focused removal of potassium from the body with loop diuretics, if kidney function is intact; sodium polystyrene sulfonate (e.g., Kayexalate™) for GI loss of potassium; and, in severe cases, haemodialysis.

Hypokalemia:

* is not common
* reduced dietary potassium intake, especially in association with:
  * excessive diuretic therapy
  * concurrent GI losses

Metabolic Acidosis

- Daily proton production: 50-100 meq
- common in advanced CKD
  - less ammonia production as urinary buffer.
  - Hyperkalemia further depresses ammonia production
- *Hyperkalemia and hyperchloremic metabolic acidosis*
  - *In more advanced disease:*
    - high anion gap (Limited urinary excretion of acid)
- In most patients
  - Metabolic acidosis is mild
  - pH is rarely <7.35
  - *corrected with oral sodium bicarbonate supplementation*

- Compensatory mechanisms:
  - Increased amoniagenesis in intact nephrons
  - Bone buffering system
- when the serum bicarbonate concentration falls below 20–23:
  - may be associated with the development of protein catabolism
  - Alkali supplementation may attenuate the catabolic state and possibly slow CKD progression

DISORDERS OF CALCIUM AND PHOSPHATE METABOLISM

Bone Manifestations of CKD

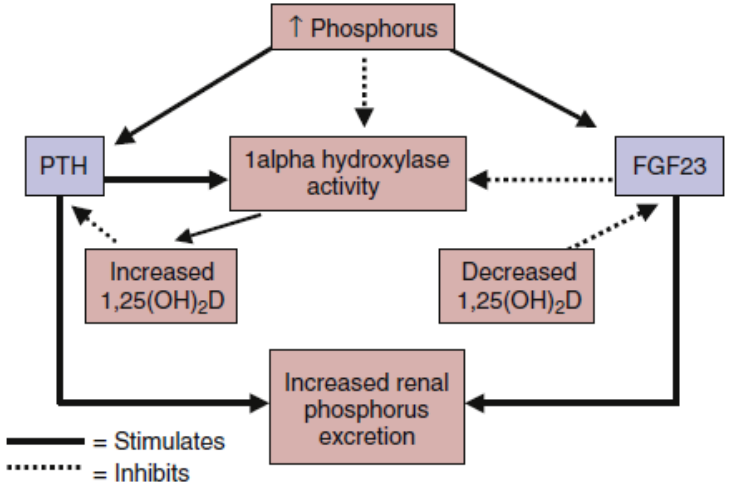
- high bone turnover with increased iPTH levels
  - osteitis fibrosa cystica
  - classic lesion of secondary hyperparathyroidism
  - bone pain and fragility, brown tumors, compression syndromes, and erythropoietin resistance
  - uremic toxin (muscle weakness, fibrosis of cardiac muscle, and nonspecific constitutional symptoms)

- low bone turnover with low or normal PTH levels:

1. 1. adynamic bone disease
   - Risk factor: diabetics and the elderly
   - reduced bone volume and mineralization may result from: excessive suppression of PTH production, chronic inflammation, or both.
   - Suppression of PTH: use of vitamin D preparations or from excessive calcium exposure in the form of calcium-containing phosphate binders
   - Complications: increased incidence of fracture and bone pain and an association with increased vascular and cardiac calcification (tumoral calcinosis")
2. Osteomalacia: AL overload, vit D deficiency

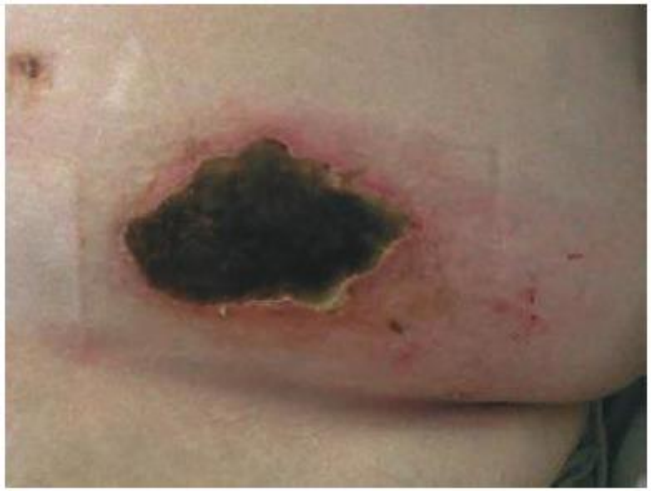
renal osteodystrophy

- elevation in PTH as a result of phosphorus retention and hypocalcaemia from 1,25 vitamin D deficiency as the GFR declines
- Severe hyperparathyroidism and hyperphosphataemia :risk factors for death, cardiovascular disease, and vascular calcification
- Patients with stage 3 to 5 CKD should be routinely monitored
- 25-dihydroxyvitamin D should be monitored and treated if the level is <30 nanograms/L.


↑ Phosphorus
PTH
1alpha hydroxylase activity
FGF23
Increased 1,25(OH)2D
Decreased 1,25(OH)2D
Increased renal phosphorus excretion
= Stimulates
= Inhibits

- strong association between hyperphosphatemia and increased cardiovascular mortality rate
- Vascular and heart valve calcification
  - age
  - hyperphosphatemia
  - low PTH levels
- Hyperphosphatemia: vascular cells to an osteoblast-like profile, leading to vascular:
  - Calcification
  - Ossification

- Calciphylaxis:
  - livedoreticularis and advances to patches of ischemic necrosis, especially on the legs, thighs, abdomen, and breasts
  - vascular occlusion in association with extensive vascular and soft tissue calcification
- Matrix GLA protein: preventing vascular calcification
- Warfarin: decrease regeneration of matrix GLA protein



NEUROMUSCULAR ABNORMALITIES

- Neuropathy
  1. CNS:
     - memory and concentration and sleep disturbance
     - asterixis, myoclonus, seizures, and coma
  2. PNS:
     - sensory nerves > motor
     - lower extremities > upper
     - distal parts of the extremities > proximal
  3. Autonomic
- Myopathy
- Subtle clinical manifestations of uremic neuromuscular disease usually become evident at stage 3 CKD

- “restless leg syndrome”: ill-defined sensations of sometimes debilitating discomfort in the legs and feet relieved by frequent leg movement.
- If dialysis is not instituted soon after onset of sensory abnormalities, motor involvement follows, including muscle weakness
- Many of the these complicaions will resolve with dialysis,

GASTROINTESTINAL AND NUTRITIONAL ABNORMALITIES

* Uremic fetor:
  * a urine-like odor on the breath
  * Breakdown of urea to ammonia in saliva
  * often associated with an unpleasant metallic taste (dysgeusia). Gastritis, peptic disease, and mucosal ulcerations at any level of the GI tract
* prone to constipation: worsened by of calcium and iron supplements.
* Retention of uremic toxins: anorexia, nausea, vomiting (malnutrition)

protein malnutrition

Previously,patients with advanced CKD were placed on low-protein diets,

but this recommendation has limitations
due to its worsening of malnutrition.

recommended for patients with CKD to have 0.6 g/kg protein
intake daily and those with nephrotic syndrome 0.8 g/kg protein intake
daily, to account for protein losses
in the urine.

If patients are not able to maintain nutrition, then initiation of renal
replacement therapy may
be warranted.[97]

ENDOCRINE-METABOLIC DISTURBANCES

- Glucose metabolism:

1. Slower declinein blood glucose after a glucose load.
2. FBS: normal or only slightly elevated
3. slight to moderate elevation in insulin levels both in the fasting and postprandial states.

- Progressive reduction in insulin requirement
- Oral antidiabetics

* In women:

1. estrogen levels are low
2. Menstrual abnormalities
3. Infertility
4. inability to carry pregnancies to term
5. GFR ~40 mL/min:
   * high rate of spontaneous abortion
   * only ~20% of pregnancies leading to live births,

* In men:

1. reduced plasma testosterone
2. sexual dysfunction
3. oligospermia

* Adolescent children: delayed sexual maturation

DERMATOLOGIC ABNORMALITIES

* Pigmentation: deposition of retained pigmented metabolites, or urochromes in CKD or ESRD
* Pruritus: often tenacious even after dialysis
  * R/o scabies, and treat hyperphosphatemia
  * Local moisturizers
  * mild topical glucocorticoids
  * oral antihistamines
  * ultraviolet radiation

* Nephrogenic fibrosing dermopathy:
  1. progressive subcutaneous induration, especially on the arms and legs.
  2. similar to scleromyxedema
  3. very rarely in patients with CKD
* Current recommendations:
  * CKD stage 3 (GFR 30–59 mL/min): minimized exposure to Gad
  * CKD stages 4–5 (GFR <30 mL/min): avoid the use of gadolinium agents
* rapid removal of gadolinium by hemodialysis (CKD or ESRD) shortly after the procedure

* Hypothermia
* Lipid metabolism:
  * High TG
  * Low HDL

    Due to impaired insulin and LPL function
* Hyperuricemia:

  indication of treatment in asymptomatic cases
  * >13 except in CHF
  * >1100mg/24 urine
  * Tumor lysis syndrome:

  Hydration, allopurinol and rasburicase

Primary prevention

HbA1 c <7%

blood pressure target of <140/90 mmHg

tobacco cessation

BMI <27 to prevent the development of CKD

Screening

all individuals with diabetes and hypertension aged <50 years

all of those aged >50 years

family history of kidney disease

Secondary prevention

- blood pressure of <140/90 mmHg with ACE inhibitors or angiotensin receptor-blocking agents
- lower blood pressure goal in those with proteinuria of >500 mg per 24 hours
- Protein restriction should not be recommended until late stage 4 or 5 disease
- Aspirin use has also been beneficial for cardioprotection in those with CKD

Case history

54-year-old man

10-year history of diabetes and hypertension

fatigue and weight gain of 4.5 kg over the past 3 months

denies any changes in his diet or glycaemic control

intermittent nausea and anorexia

his legs are more swollen at the end of the day but improve with elevation a

Physical examination obese with blood pressure of 158/92 mmHg

findings are cotton wool patches andmicro-aneurysms bilaterally on fundosc

examination and pitting, bilateral lower-extremity oedema.

Topic Outline

IV TREATMENT

A. SLOWING THE PROGRESSION OF CKD

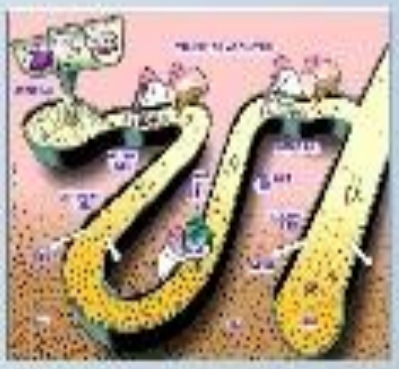
1. Reducing Intraglomerular Hypertension and Proteinuria

B. SLOWING PROGRESSION OF DIABETIC RENAL DISEASE

1. Control of Blood Glucose
2. Control of Blood Pressure and Proteinuria
3. Protein Restriction

C. MANAGING OTHER COMPLICATIONS OF CHRONIC KIDNEY DISEASE

1. Medication Dose Adjustment
2. Preparation for Renal Replacement Therapy
3. Patient Education



Any acceleration in the rate of decline should prompt a search for superimposed acute or subacute processes that may be reversible

1. ECFV depletion,
2. uncontrolled hypertension,
3. urinary tract infection,
4. new obstructive uropathy,
5. exposure to nephrotoxic agents
6. and reactivation or flare of the original
7. disease, such as lupus or vasculitis

CKD progression

- Steps to identify progressive CKD
  - obtain a minimum of three eGFR over not less than 90 days
  - in new cases of reduced eGFR, repeat within 2 weeks to exclude acute deterioration of GFR

- CKD progression is either a decline in eGFR:

  of > 5 ml/min/1.73 m2 within 1 year

  or > 10 ml/min/1.73 m2 within 5 years

SLOWING PROGRESSION OF DIABETIC RENAL DISEASE

Control of Blood Glucose

- preprandial glucose be kept in the **5.0–7.2 mmol/L**, (**90–130 mg/dL**)
- hemoglobin A 1C should be **< 7%**
- use and dose of oral hypoglycemic needs to be reevaluated
  - Chlorpropramide
  - Metformin
  - Thiazolidinediones

SLOWING PROGRESSION OF DIABETIC RENAL DISEASE

Control of Blood Pressure and Proteinuria

- albuminuria
  - a strong predictor of cardiovascular events
  - and nephropathy
- Microalbumin testing
  - At least ANNUALLY

MANAGING OTHER COMPLICATIONS OF CHRONIC KIDNEY DISEASE

1. Medication Dose Adjustment

- ***loading dose*** – no dose adjustment
- ***>70% excretion*** is by a nonrenal route – no adjustment
- ***NSAIDs*** should be avoided
- Nephrotoxic medical imaging ***radiocontrast agents and gadolinium*** should be avoided

stages 1-2 without uraemia		
	1st	angiotensin-converting enzyme (ACE) inhibitor or angiotensin-II receptor antagonist
	plus	statin
	adjunct	additional antihypertensive therapy
	2nd	non-dihydropyridine calcium-channel blocker
	plus	statin
	adjunct	additional antihypertensive therapy
stages 3-4 without uraemia		
	1st	angiotensin-converting enzyme (ACE) inhibitor or angiotensin-II receptor antagonist
	plus	statin ± ezetimibe
	adjunct	additional antihypertensive therapy
	adjunct	education about renal replacement therapy
	2nd	non-dihydropyridine calcium-channel blocker
	plus	statin ± ezetimibe
	adjunct	additional antihypertens
	adjunct	education about renal re therapy
■ with anaemia	adjunct	erythropoietin-stimulatir
	adjunct	iron
■ with secondary hyperparathyroidism	plus	dietary modification ± phosphate-binding drug
	adjunct	ergocalciferol
	adjunct	active vitamin D analogue

with metabolic acidosis	adjunct	oral sodium bicarbonate

stage 5 or with uraemia

	1st	dialysis
with secondary hyperparathyroidism	plus	dietary modification ± phosphate-binding drug
	adjunct	calcimimetic ± active vitamin D analogue
	adjunct	ergocalciferol
	2nd	kidney transplant

HEMODIALYSIS

ABSOLUTE INDICATIONS:

- Uremic pericarditis or pleuritis
- Uremic encephalopathy

Common indications:

1. Declining nutritional status
2. Persistent or difficult to treat volume overload
3. Fatigue and malaise
4. Mild cognitive impairment
5. Refractory acidosis, hyperkalemia, and hyperphosphatemia

Recommended dietary intake for chronic kidney and end-stage renal disease patients*

	Chronic kidney disease•	Maintenance hemodialysis
Protein	0.8 to 1.0 g/kg/dayΔ of high biological value protein	>1.2 to 1.3 g/kg/day
Energy	≥35 kcal/kg/day; if the body weight is greater than 120 percent of normal or the patient is greater than 60 years of age a lower amount may be prescribed	
Fat, percent of total energy intake	30 to 40	30 to 40
Polyunsaturated-to-saturated ratio (fatty acid ratio)	1.0:1.0	1.0:1.0
Carbohydrate	Balance of nonprotein calories	
Total fiber, g/day	20 to 25	20 to 25
Minerals, range of intake		
Sodium, mg/day	<2000	<2000
Potassium, meq/day	40 to 70	40 to 70
Phosphorus, mg/day	600 to 800◇	600 to 800◇
Calcium, mg/day	1400 to 1600	1400 to 1600
Magnesium, mg/day	200 to 300	200 to 300
Iron, mg/day	≥10 to 18§	≥10 to 18§
Zinc, mg/day	15	15
Water, mL/day	Up to 3000 as tolerated	Usually 750 to 1500

Monitoring

the rate of progression of CKD serially starting in stage 3a/3b disease
screened for anaemia and bone mineral disorders at least every
6 to 1 2 months :haemoglobin, calcium, phosphorus, and intact parathyroid hormone (PTH).

stage 4 disease, haemoglobin, calcium, phosphorus should be monitored every 3 to 6 months
and intact PTH every 6 to 1 2 months.

stage 5 CKD, anaemia should be evaluated with a
monthly haemoglobin, and bone mineral disease with a calcium and phosp
every 1 to 3 months and
an intact PTH every 3 to 6 months.

Lipids should be checked annually for all patients with CKD

Other recommendations

- Offer a renal ultrasound to all people with CKD who:
  - have progressive 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
  - have stage 4 or 5 CKD
  - are considered by a nephrologist to require a renal biopsy

Referral criteria

- Refer the following people with CKD for discussion or specialist assessment:
  - stage 4 and 5 CKD (with or without diabetes)
  - higher levels of proteinuria
  - proteinuria together with haematuria
  - rapidly declining eGFR
  - poorly controlled hypertension
  - people with rare or genetic causes of CKD
  - suspected renal artery stenosis

THANK YOU