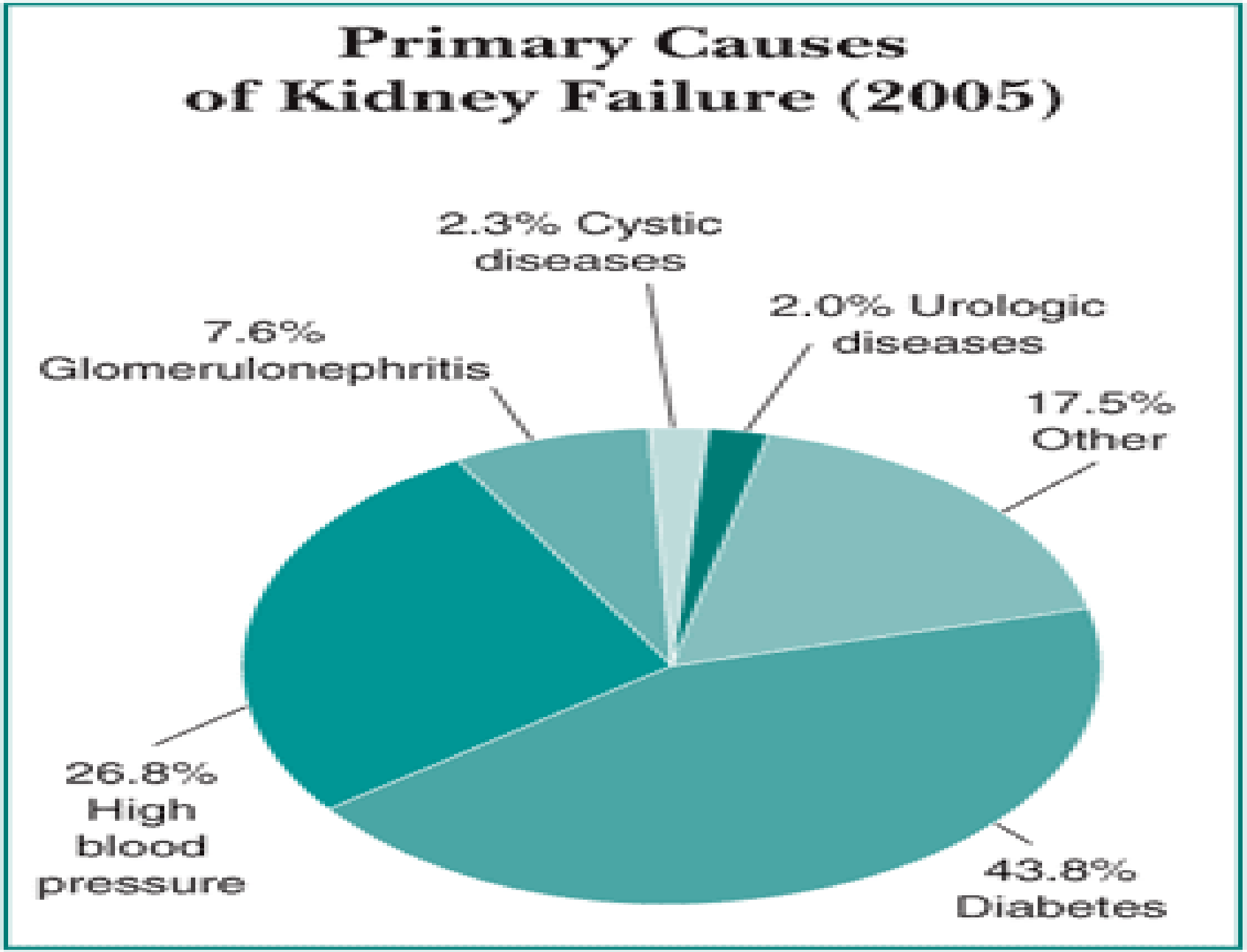
CKD, Management

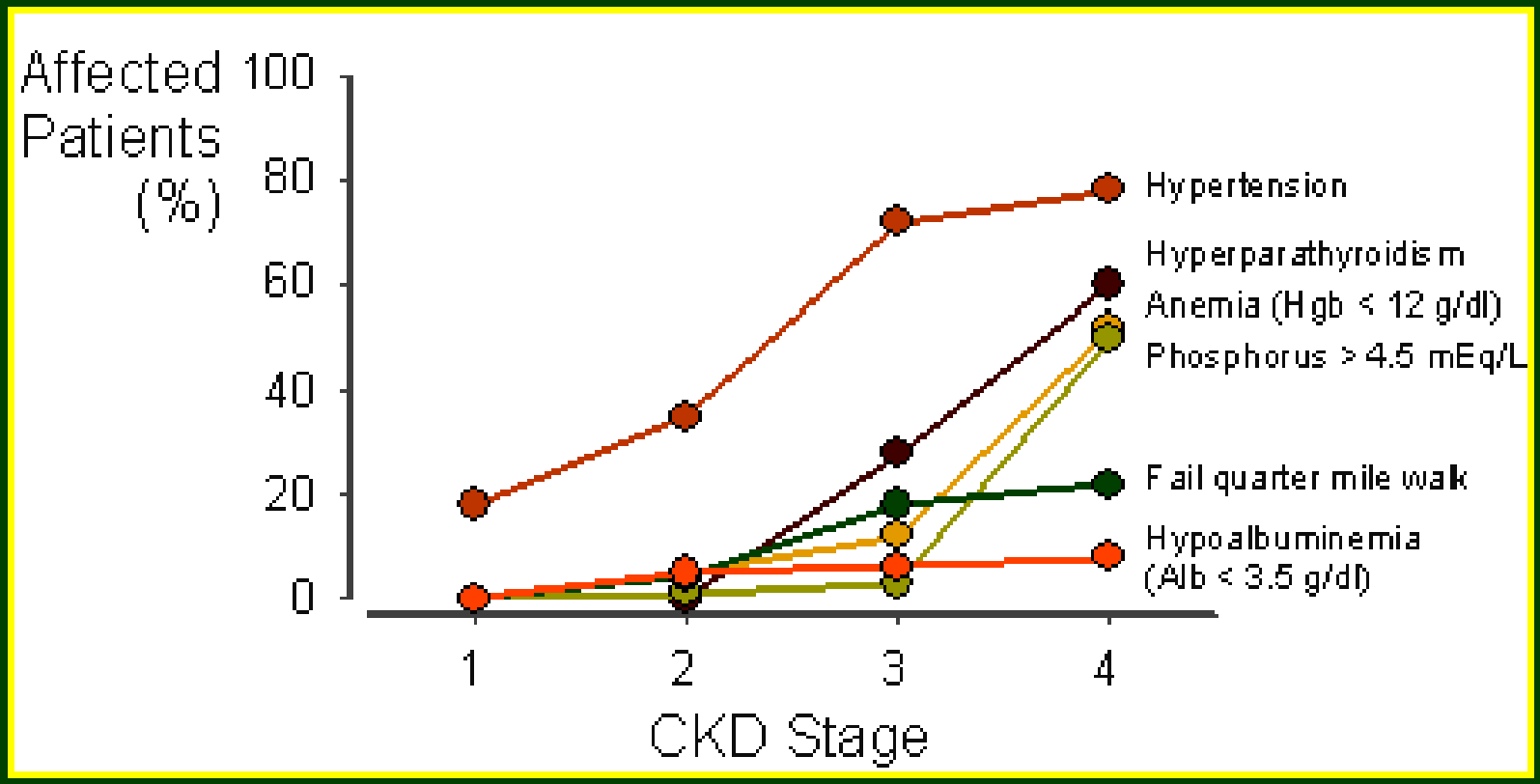

Primary Causes of Kidney Failure (2005)
2.3% Cystic diseases
2.0% Urologic diseases
7.6% Glomerulonephritis
17.5% Other
26.8% High blood pressure
43.8% Diabetes

Progression of chronic kidney disease

- CKD tends to progress inexorably to ESKD, although the rate of progression may depend upon the underlying nephropathy.
- Patients with chronic glomerular diseases tend to deteriorate more quickly than those with chronic tubulointerstitial nephropathies.
- Hypertension and heavy proteinuria are bad prognostic indicators.
- A nonspecific renal scarring process common to renal disorders of different aetiologies may be responsible for progression.

Time Progression from diagnosis of CKD Stage 3 to ESRD

Complications of CKD: Prevalence increases by stage



Comorbidities of CKD

- Hypertension
- Anemia
- Diabetes
- Osteodystrophy
- Metabolic acidosis
- Malnutrition

Consensus Development Conference Panel. *Ann Intern Med.* 1994;121:62-70.
Foley RN, Parfrey PS. In: Brady HR, Wilcox CS, eds. *Therapy in Nephrology and Hypertension.* 1999:505-509.
Remuzzi G, Minetti L. In: Brady HR, Wilcox CS, eds. *Therapy in Nephrology and Hypertension.* 1999:480-487.
Meyer KB, Levey AS. *J Am Soc Nephrol.* 1998;9(suppl):S31-S42.
Delmez JA, Slatopolsky E. In: Brady HR, Wilcox CS, eds. *Therapy in Nephrology and Hypertension.* 1999:497-504.

Table 35. Classification and Management of Comorbid Conditions in Chronic Kidney Disease

Type of Comorbid Condition	Examples	Management Goals
Diseases causing CKD	Diabetes High blood pressure Obstruction of the urinary tract	Improve CKD, Improve functioning and well-being, Integration of care with management of CKD
Diseases unrelated to CKD	Chronic obstructive pulmonary disease, Gastroesophageal reflux disease, Degenerative joint disease, Alzheimer's disease, Malignancies	Improve functioning and well-being, Integration of care with management of CKD
Cardiovascular disease (CVD)	Atherosclerotic CVD Coronary heart disease Cerebrovascular disease Peripheral vascular disease Left ventricular hypertrophy Heart failure	Evaluation and management of traditional and CKD-related CVD risk factors, Possibly improve CKD, Improve functioning and well-being, Integration of care with management of CKD

Management of chronic kidney disease

- **The underlying cause** of CKD should be treated aggressively wherever possible.
- *Renoprotection*
- The multidrug approach to chronic nephropathies has been formalized in an international protocol.

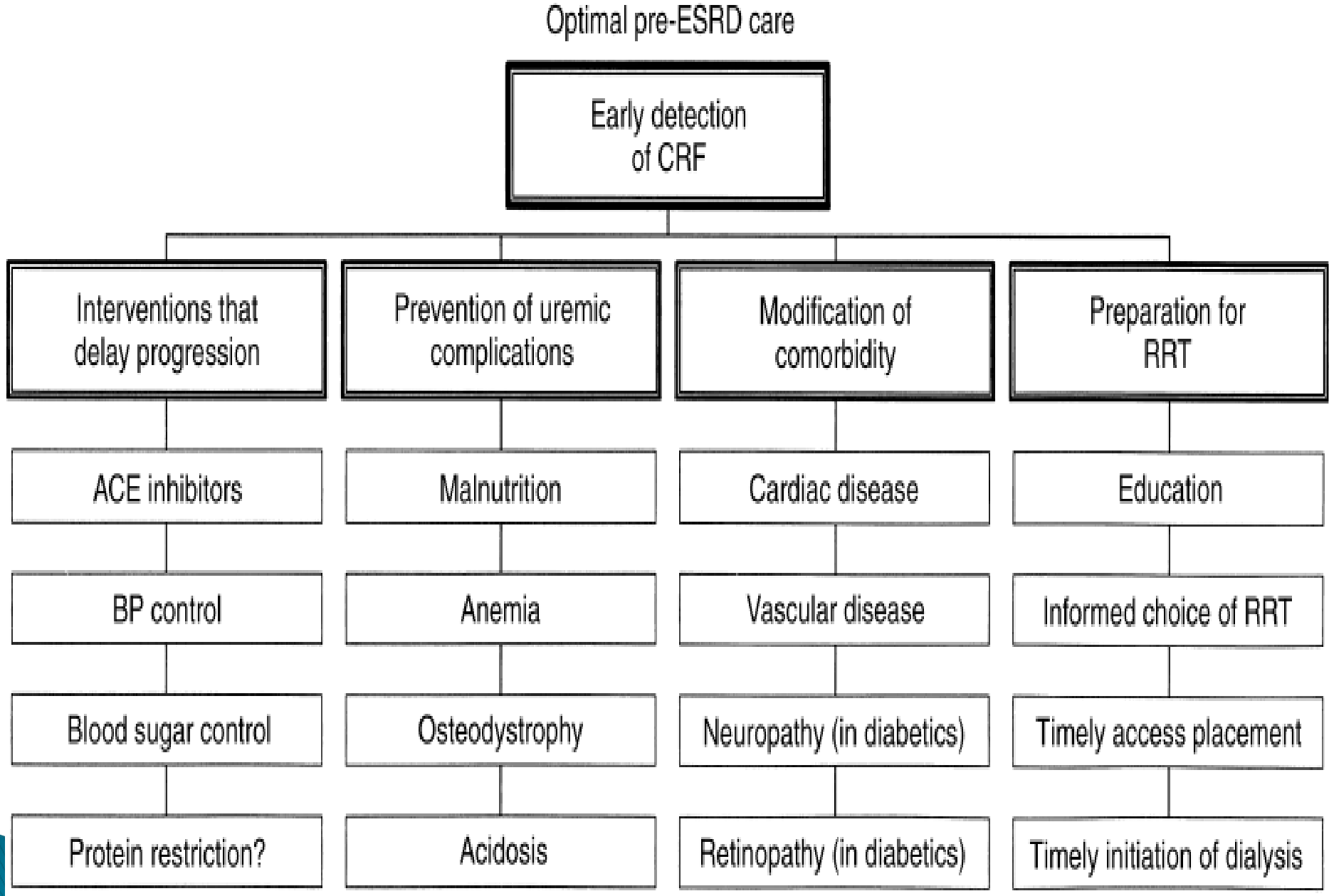
Goals of CKD Management

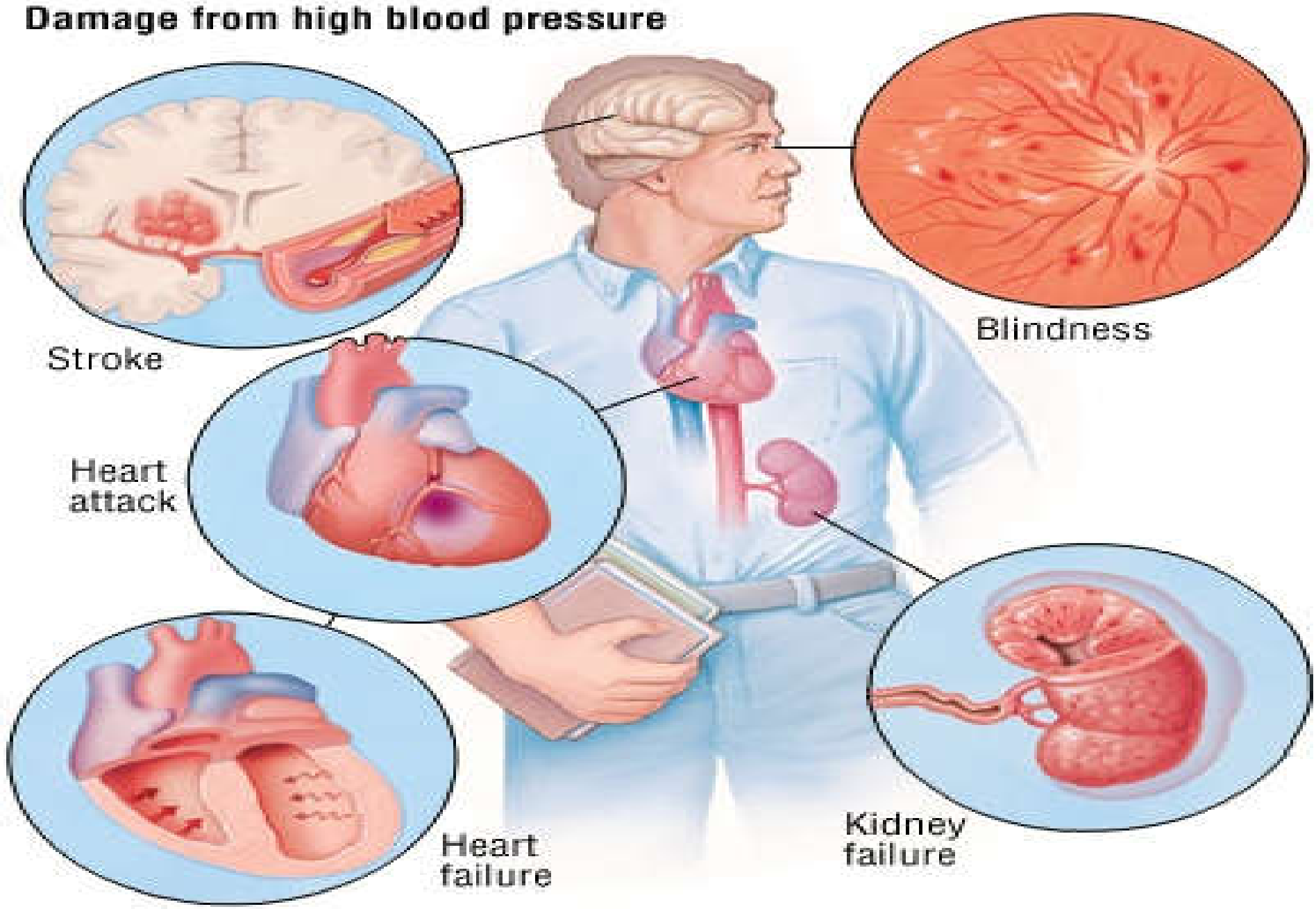
- Achieve/maintain optimal nutritional status
- Prevent protein energy malnutrition
- Slow the rate of disease progression
- Prevention/treatment of complications and other medical conditions
  - **DM**
  - **HTN**
  - **Dyslipidemias and CVD**
  - **Anemia**
  - **Metabolic acidosis**
  - **Secondary hyperparathyroidism**

Goals of Treatment of CKD Stages 3, 4

Physiologic Parameters	Recommended Values
Blood pressure	130/80 mm Hg
Hemoglobin A_{1C}	> 6.5 to < 7.0%
Hemoglobin concentration	11–12 g/dL
Serum phosphorus	Maintain normal limits
Serum PTH	35 – 110 pg/mL

Abbreviations: CKD, chronickidney disease; PTH, parathyroid hormone.


Optimal pre-ESRD care
Early detection of CRF
Interventions that delay progression
Prevention of uremic complications
Modification of comorbidity
Preparation for RRT
ACE inhibitors
BP control
Blood sugar control
Protein restriction?
Malnutrition
Anemia
Osteodystrophy
Acidosis
Cardiac disease
Vascular disease
Neuropathy (in diabetics)
Retinopathy (in diabetics)
Education
Informed choice of RRT
Timely access placement
Timely initiation of dialysis


Damage from high blood pressure
Stroke
Blindness
Heart attack
Heart failure
Kidney failure

SUPPORT FOR CHRONIC KIDNEY DISEASE MANAGEMENT

Renoprotection

- Goals of treatment: BP <120/80
- Proteinuria <0.3 g/24 h
- **Treatment**
- Patients with chronic kidney disease and proteinuria >1 g/24 h: ACE inhibitor increasing to maximum dose
- Add angiotensin receptor antagonist if goals are not achieveda
- Add diuretic to prevent hyperkalaemia and help to control BP
- Add calcium-channel blocker (verapamil or diltiazem) if goals not achieved
- **Additional measures**
- Statins to lower cholesterol to <4.5 mmol/L
- Stop smoking (three-fold higher rate of deterioration in CKD)
- Treat diabetes (HbA1c <7%, 53 mmol/mol)
- Normal protein diet (0.8–1 g/kg bodyweight)

Correction of complications

- **Hyperkalaemia (3.5-5.5 mEq/L)**
- Hyperkalaemia often responds to dietary restriction of potassium intake.
- Drugs which cause potassium retention

Causes of hyperkalaemia

Decreased excretion	Increased release from cells
Acute kidney injury Drugs: Amiloride Triamterene Spironolactone/ ACE inhibitors/ACE blockers NSAIDs Ciclosporin treatment Heparin treatment Aldosterone deficiency Addison's disease Acidosis	(decreased Na+/K+-ATPase activity) Acidosis Diabetic ketoacidosis Rhabdomyolysis/tissue damage Tumour lysis **Increased extraneous load** Potassium chloride Salt substitutes Transfusion of stored blood

Correction of severe hyperkalaemia

- **Immediate**
- *ECG monitor and i.v. access*
- *Protect myocardium* 10 mL of 10% calcium gluconate i.v. over 5 min
- Effect is temporary but dose can be repeated after 15 min
- *Drive K+ **into cells***
- Insulin 10 units + 50 mL of 50% glucose i.v. over 10– 15 min followed by regular checks of blood glucose and plasma K+
- Repeat as necessary:
- and/or correction of severe acidosis (pH <6.9) – infuse $NaHCO_3$ (1.26%)
- and/or salbutamol 0.5 mg in 100 mL of 5% glucose over 15 min (rarely used)
- **Later**
- *Deplete body K+ **(to decrease plasma K+ over** the next 24 hours)*
- Polystyrene sulphonate resins:
- 15 g orally up to three times daily with laxatives 30 g rectally followed 9 h later by an enema
- Haemodialysis or peritoneal dialysis if the above fails.

Acidosis

- Correction of acidosis helps to correct hyperkalaemia in CKD, and may also decrease muscle catabolism.
- Sodium bicarbonate supplements are often effective (4.8 g (57 mmol) of $Na+$ and $HCO3-$ daily
- Interestingly, correction of metabolic acidosis by sodium bicarbonate at a mean dose of 1.8 g/day was also associated with marked reduction in the rate of progression of CKD and development of ESKD in patients with stage 4 and 5 CKD.
- Calcium carbonate, also used as a calcium supplement and phosphate binder, has a beneficial effect on acidosis.

Table 6. Factors That May Predispose to Soft-Tissue Calcification in Stages 4 and 5 CKD

- Hyperphosphatemia
- An increase in serum calcium-phosphorus product
- Secondary hyperparathyroidism
- Local tissue injury
- A rise in local pH of tissue
- Removal of calcification inhibitors by dialysis
- Excessive calcium intake

Table 16. Factors Prevalent in CKD Patients Which May Influence the Type of Osteodystrophy Lesion

- Prolonged aluminum exposure
- Glucocorticoid therapy as in patients with parenchymatous kidney diseases and in kidney transplant recipients
- Previous parathyroidectomy
- Vitamin D treatment
- Diabetes mellitus[a]
- β_2-microglobulinemia amyloidosis
- Metabolic acidosis
- Hypophosphatemia secondary to aggressive dietary phosphate restriction or excessive use of phosphate binders

[a] Diabetes mellitus is a common cause of CKD and is responsible for 30%-40% of patients reaching dialysis.

Calcium and phosphate control and suppression of PTH

- Hypocalcaemia and hyperphosphataemia should be treated aggressively, preferably with regular (e.g. 3-monthly) measurements of serum PTH to assess how effectively hyperparathyroidism is being suppressed.
- *Dietary restriction of phosphate is seldom effective alone,* because so many foods contain it.

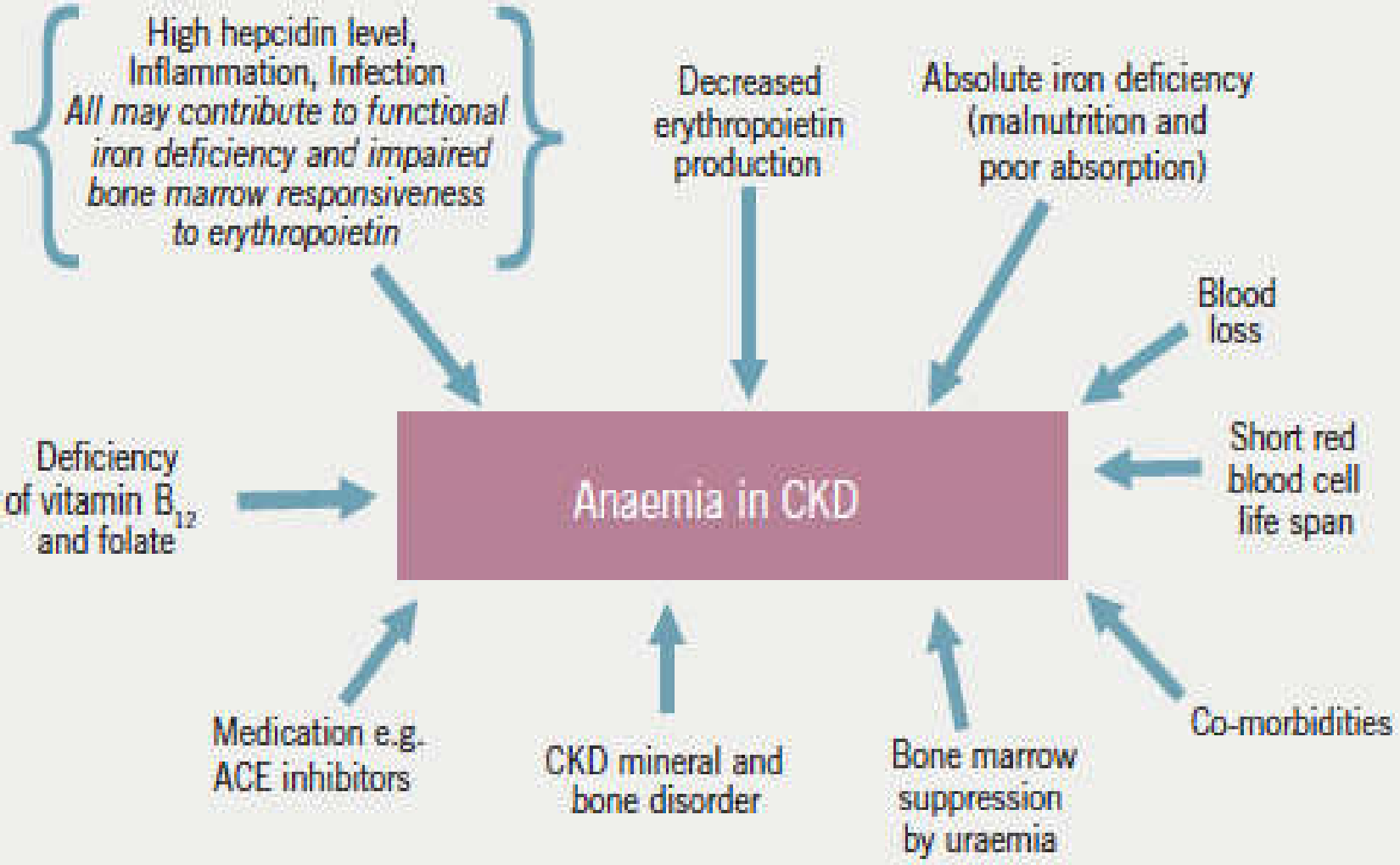
- Oral calcium carbonate or acetate reduces absorption of dietary phosphate but is contraindicated where there is hypercalcaemia or hypercalciuria.
- Aluminium-containing gut phosphate binders are very effective but absorption of aluminium poses the risk of aluminium bone disease and development of cognitive impairment.
- They are now rarely used in the developed countries but are still used in the developing countries because they are extremely cheap.

Treatment

- *Gut phosphate binders.*
- *The polymer sevelamer* reduces the calcium load and attenuates vascular calcification and also lowers cholesterol levels by 10%. However, it has not been shown to reduce mortality.
- Lanthanum carbonate is a non-calcium, non-aluminium phosphate binder that is effective and has a good safety profile.
- *Nicotinamide, an alternative to phosphate binders,*
- blocks the intestinal sodium/inorganic phosphate (Na/Pi) co-transporter. It reduces phosphate levels and PTH levels alongside improvement in the lipid profile in dialysis patients.

- *Calcitriol (1,25-dihydroxycholecalciferol) or a vitamin D analogue, such as alfacalcidol, used in early CKD has*
- no deleterious effect upon renal function provided hypercalcaemia is avoided.
- Vitamin D therapy has the disadvantage that it increases not only calcium but also phosphate absorption and may therefore exacerbate hyperphosphataemia and ectopic calcification including calciphylaxis (calcification of small vessels).

- *Calcimimetic agents (e.g. cinacalcet, a calcium sensing* receptor agonist,) have also been tried in established secondary hyperparathyroidism with successful suppression of PTH levels an lowering of calcium × phosphate product.
- The long-term safety and efficacy of these agents has recently been confirmed and several observational studies have demonstrated that use of cinacalcet is associated with survival advantage



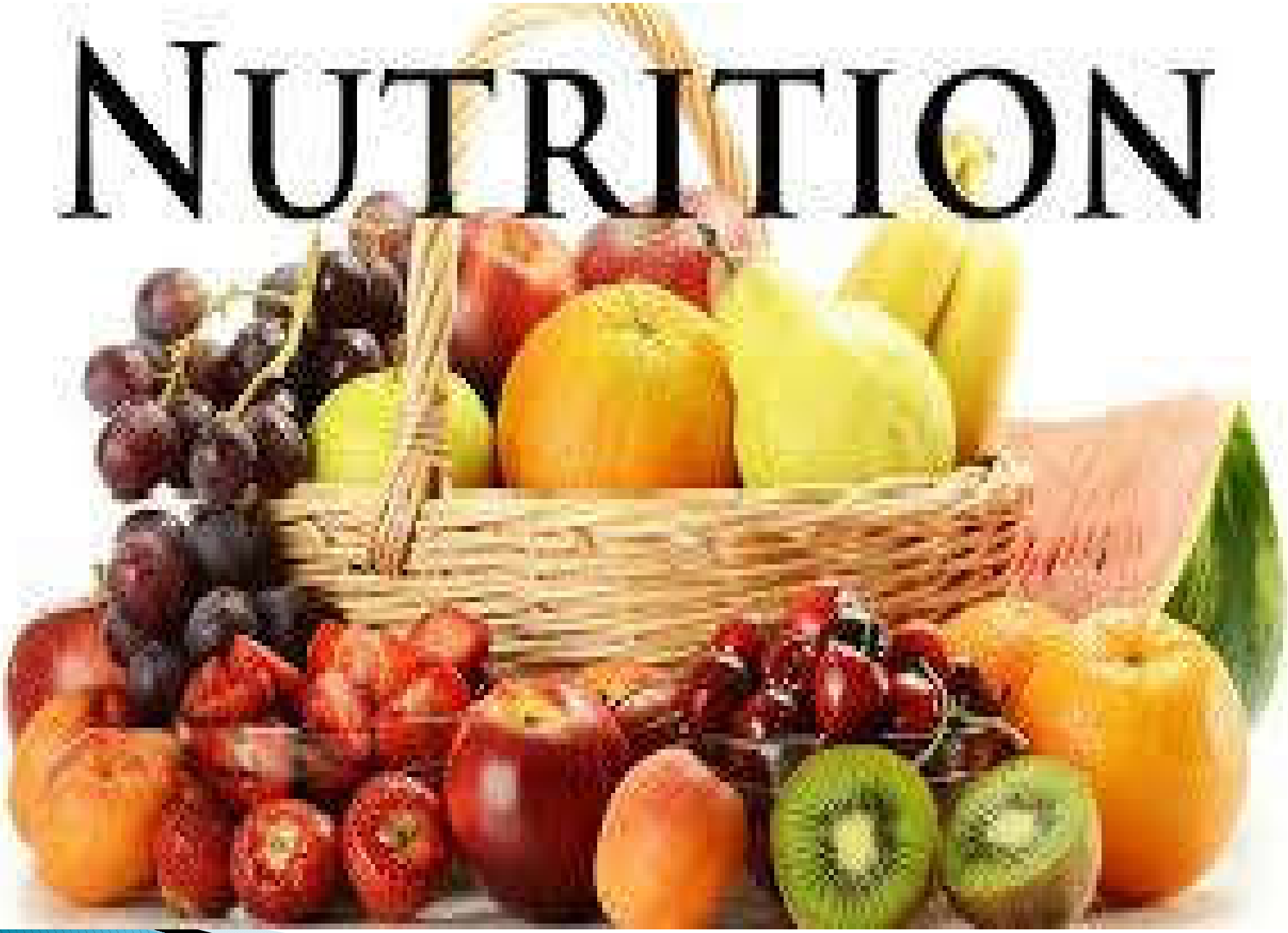
Adapted from Agarwal AK. *J A Med Dir Assoc* 2006;7:S7–S12

- **Anaemia treatmet**
- The anaemia of erythropoietin (EPO) deficiency can be treated with synthetic (recombinant) human EPO (epoetin-α or -β, or the longer-acting darbepoetin-α or polyethylene glycol-bound epoetin-β).
- Blood pressure, haemoglobin concentration and reticulocyte count are measured every 2 weeks and the dose adjusted to maintain a target haemoglobin of 110–120 g/L.

- *Failure to respond to 300 U/kg weekly, or a fall in haemoglobin*
- after a satisfactory response, may be due to iron deficiency, bleeding, malignancy, infection, inflammation or formation of anti-EPO neutralizing antibodies.
- The demand for iron by the bone marrow is enormous when erythropoietin is commenced.
- Patients on EPO therapy are regularly monitored for iron status

- **Correction of anaemia with EPO**
- improves quality of life, exercise tolerance and sexual and cognitive function in dialysis patients,
- and leads to regression of left ventricular hypertrophy.
- Avoidance of blood transfusion also reduces the chance of sensitization to HLA antigens, which may otherwise be a barrier to successful renal transplantation.
- The *disadvantages of erythropoietin therapy are that it is*
- expensive and causes a rise in blood pressure in up to 30% of patients, particularly in the first 6 months.
- A rare complication is encephalopathy with fits, transient cortical blindness and hypertension.

NUTRITION

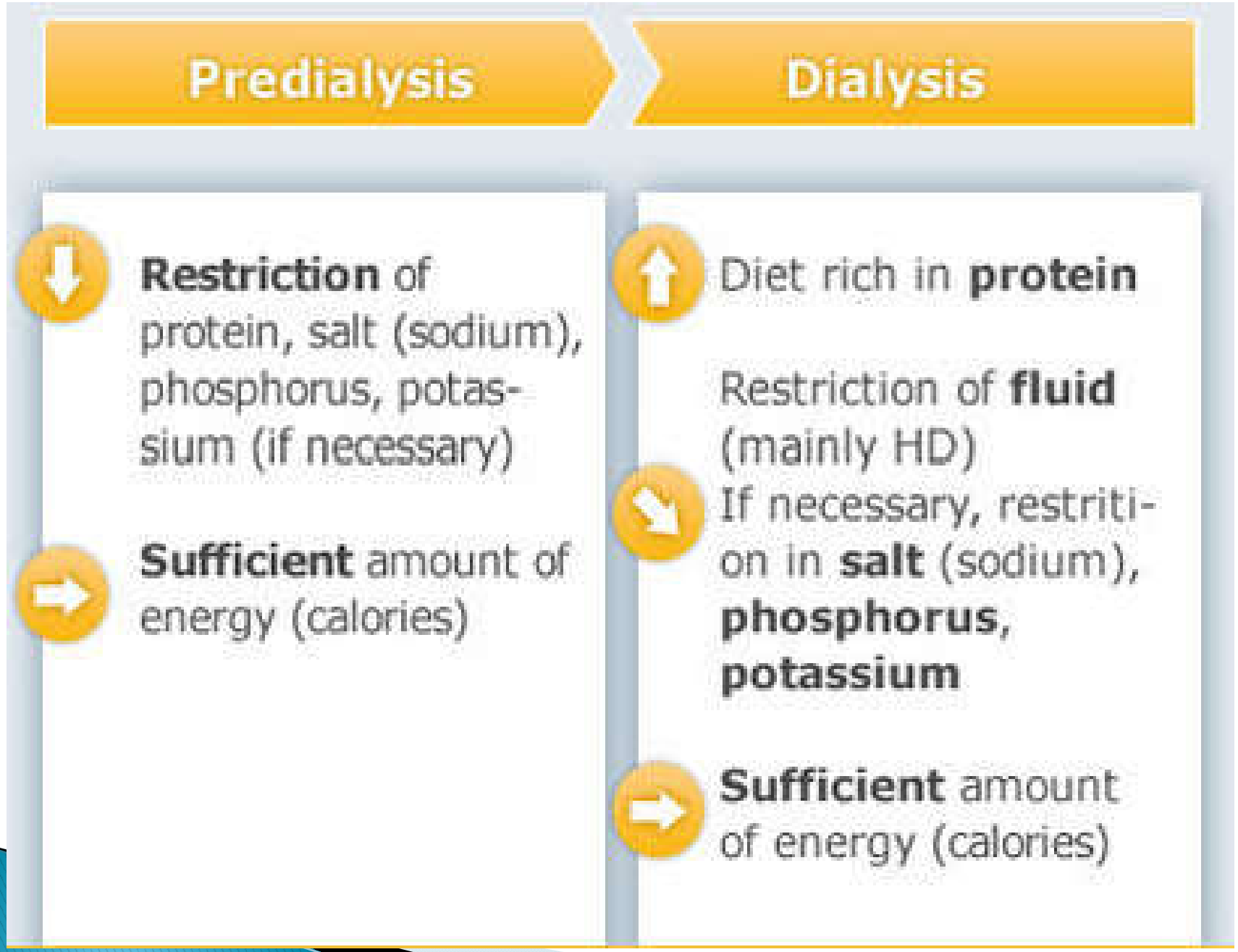


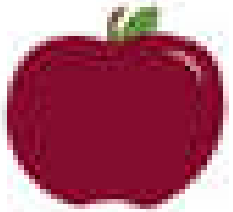
Chronic Kidney Disease

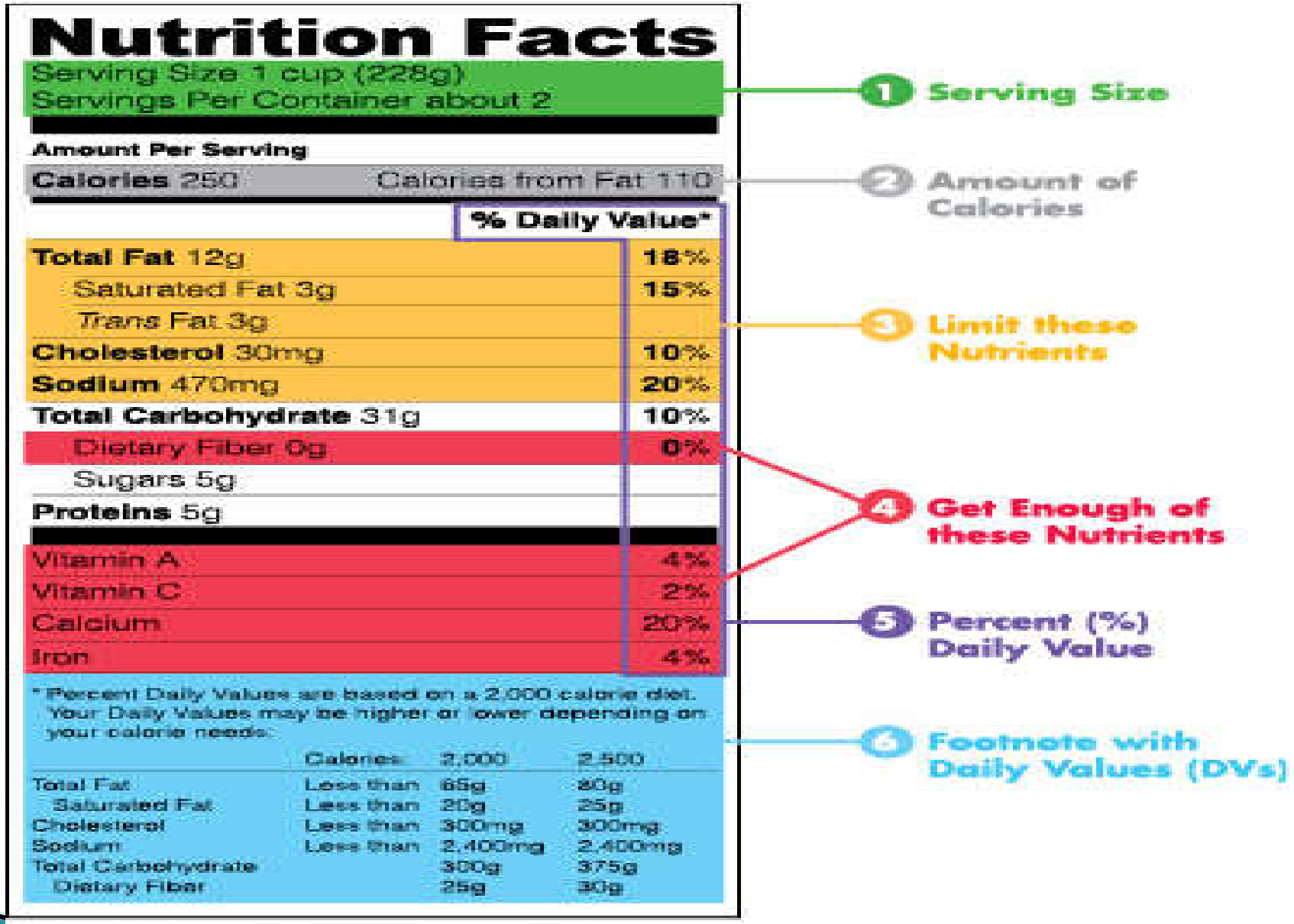
Nutritional Management

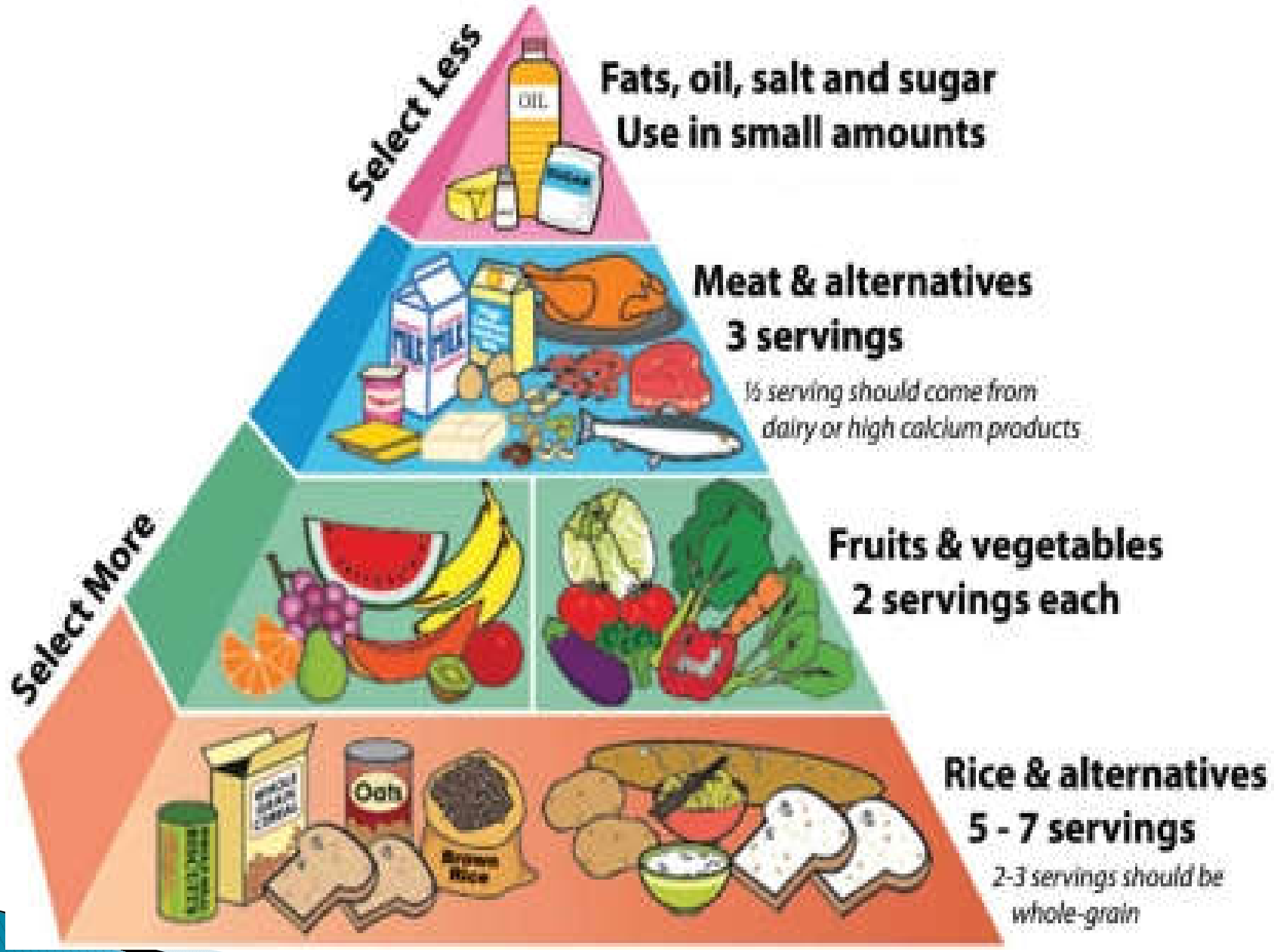
Ensure adequate intake

- Delay introduction until cat feels well
  - Learned food aversion
- Canned diets
  - Energy from fat cf carbohydrate
  - Increased fluid intake

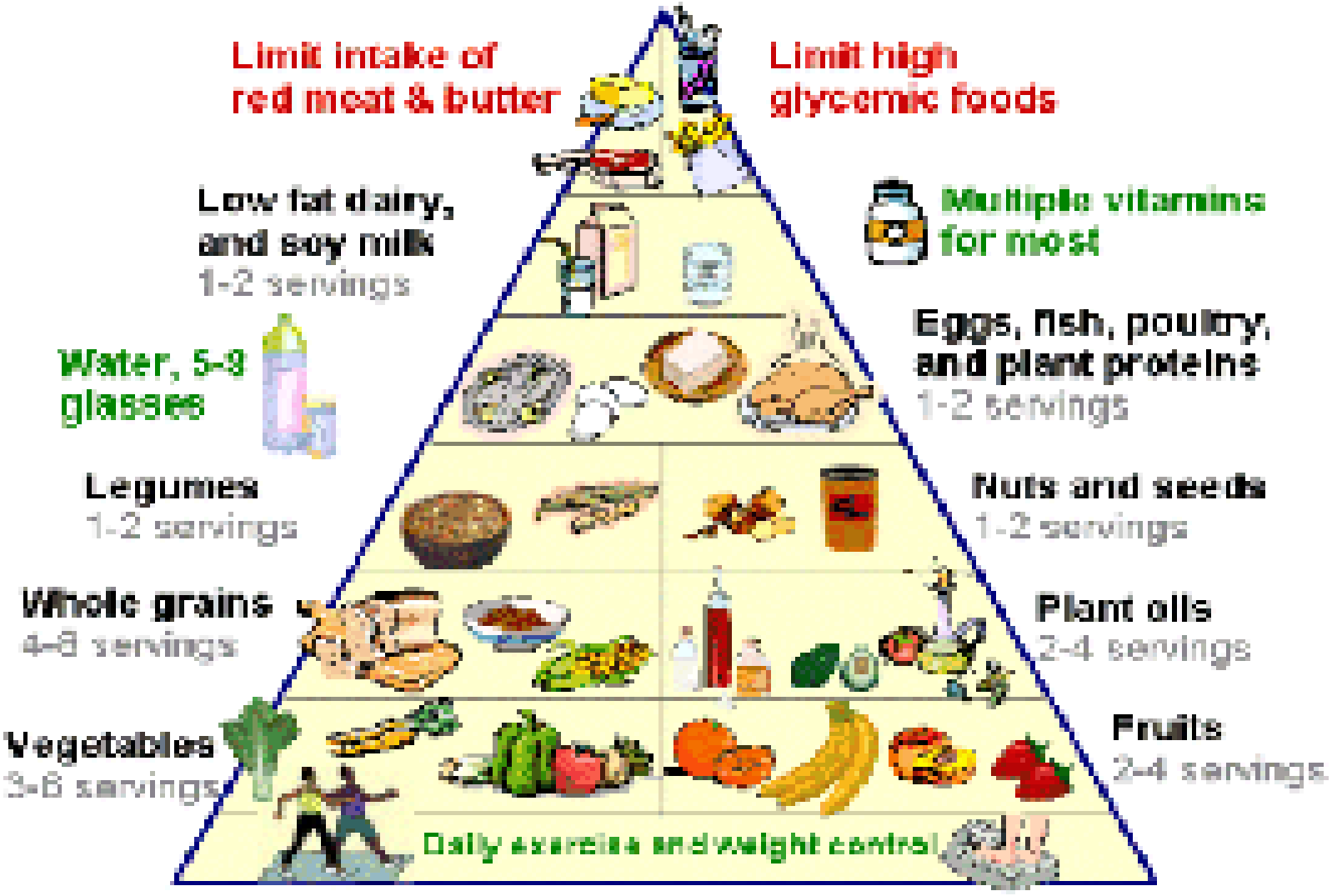

Predialysis
Dialysis
Restriction of protein, salt (sodium), phosphorus, potas-sium (if necessary)
Sufficient amount of energy (calories)
Diet rich in protein
Restriction of fluid (mainly HD)
If necessary, restriti-on in salt (sodium), phosphorus, potassium
Sufficient amount of energy (calories)

	Choose and prepare foods with less salt (sodium). Use less salt at the table.
	Select the right kinds and smaller amounts of protein.
	Choose foods that are healthy for your heart, like lean cuts of meat, skinless chicken, fish, fruits, vegetables, and beans.
	Read the Nutrition Facts Label, especially for sodium, to help you pick the right foods and drinks.


Nutrition Facts
Serving Size 1 cup (228g)
Servings Per Container about 2
Amount Per Serving
Calories 250
Calories from Fat 110
% Daily Value*
Total Fat 12g 18%
Saturated Fat 3g 15%
Trans Fat 3g
Cholesterol 30mg 10%
Sodium 470mg 20%
Total Carbohydrate 31g 10%
Dietary Fiber 0g 0%
Sugars 5g
Proteins 5g
Vitamin A 4%
Vitamin C 2%
Calcium 20%
Iron 4%
* Percent Daily Values are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs:
Calories: 2,000 2,500
Total Fat Less than 65g 80g
Saturated Fat Less than 20g 25g
Cholesterol Less than 300mg 300mg
Sodium Less than 2,400mg 2,400mg
Total Carbohydrate 300g 375g
Dietary Fiber 25g 30g
For educational purposes only. This label does not meet the labeling requirements described in 21 CFR 101.9.
1 Serving Size
2 Amount of Calories
3 Limit these Nutrients
4 Get Enough of these Nutrients
5 Percent (%) Daily Value
6 Footnote with Daily Values (DVs)


Select Less
Fats, oil, salt and sugar
Use in small amounts
Meat & alternatives
3 servings
½ serving should come from
dairy or high calcium products
Select More
Fruits & vegetables
2 servings each
Rice & alternatives
5 - 7 servings
2-3 servings should be
whole-grain

New Food Pyramid



Drug therapy

- This should be minimized in patients with CKD.
- Tetracyclines (with the possible exception of doxycycline) should be avoided in view of their anti-anabolic effect and tendency to worsen uraemia.
- Drugs excreted by the kidneys, such as gentamicin, should be prescribed only in the absence of any alternative and drug levels monitored if feasible.
- Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided.
- Potassium-sparing agents, such as spironolactone and amiloride, pose particular dangers, as do artificial salt substitutes, all of which contain potassium.

Abbreviated MDRD study equation†:

$$\text{GFR (mL per minute per 1.73 m}^2\text{)} = 186 \times (S_{Cr})^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if black})$$

Cockcroft-Gault equation:

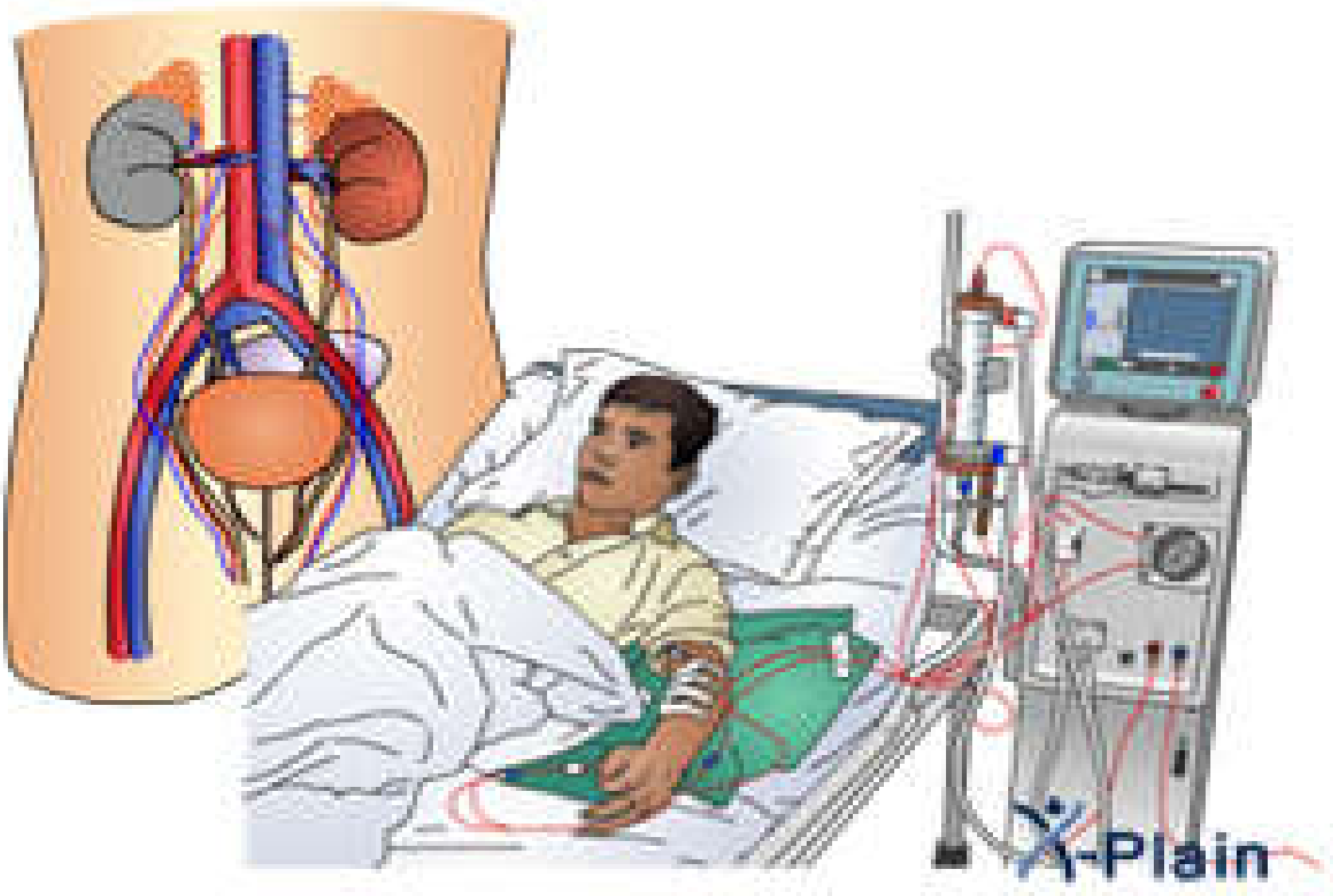
$$C_{Cr}\ \text{(mL per minute)} = \frac{(140 \quad \text{age}) \times \text{weight}}{72 \times S_{Cr}} \times (0.85 \text{ if female})$$

Renal replacement therapy

- Approximately 100 white individuals per million population commence renal replacement therapy in the UK each year.
- The corresponding figure in black Africans and Asians in the UK is three to four times higher, largely owing to diabetic and hypertensive nephropathy.
- The aim of all renal replacement techniques is to mimic the excretory functions of the normal kidney, including excretion of nitrogenous wastes,
- Maintenance of normal electrolyte concentrations, and maintenance of a normal extracellular volume.

Indications for starting renal replacement therapy

Indication	Comments
Anuria or oliguria	Urine volumes < 200 ml/12 hours
Hyperkalaemia	Serum potassium persistently > 6.5 mmol/litre
Severe acidaemia	pH < 7.1
Serum urea > 30 mmol/litre or creatinine > 300 µmol/litre	Values are not absolute, only a guide
Refractory fluid overload	Especially if compromising lung function
Uraemic complications	Encephalopathy, pericarditis, neuropathy or myopathy
Temperature control	Hyper- or hypothermia
Drug overdose	See Figure 7
Sepsis	


X-Plain

Haemodialysis

- **Basic principles**
- In haemodialysis, blood from the patient is pumped through an array of semipermeable membranes (the dialyser, often called an ‘artificial kidney’), which bring the blood into close contact with dialysate, flowing countercurrent to the blood.
- The plasma biochemistry changes towards that of the dialysate owing to diffusion of molecules down their concentration gradients.

- **Dialysis prescription**
- Dialysis must be tailored to an individual patient to obtain optimal results.
- *Initiation of dialysis*
- In clinical practice there is a wide variation in the timing of the starting dialysis therapy in patients with stage 5 CKD.
- There is a general tendency to start dialysis earlier with eGFR close to 15 mL/min rather then below 10 mL/min, despite a recent study showing that early initiation of dialysis was not associated with an improvement in survival or clinical outcomes.

- *Frequency and duration*
- Frequency and duration of dialysis are adjusted to achieve
- adequate removal of uraemic metabolites and to avoid excessive fluid overload between dialysis sessions.
- An adult of average size usually receives 4–5 hours' treatment three times a week.

Table 11. Factors Implicated in the Pathogenesis of Hypertension in Dialysis Patients

1. Sodium and volume excess
2. Increased activity of vasoconstrictors
    - The renin-angiotensin-aldosterone system
    - The sympathetic nervous system
    - Endothelin
    - Ouabain-like substances
3. Decreased activity of vasodilators
    - Nitric oxide
    - Kinins
    - Atrial natriuretic peptide
4. Erythropoietin use
5. Divalent ions and parathyroid hormone
6. Structural changes in the arteries
7. Pre-existent essential hypertension
8. Renovascular disease
9. Miscellaneous: anemia, AV fistula, vasopressin, serotonin, calcitonin gene-related peptide

Peritoneal dialysis

- Peritoneal dialysis utilizes the peritoneal membrane as a semipermeable membrane, avoiding the need for extracorporeal circulation of blood.
- This is a very simple, low technology treatment compared to haemodialysis.
- The principles are simple.
- A tube is placed into the peritoneal cavity through the anterior abdominal wall.
- Dialysate is run into the peritoneal cavity, usually under gravity.
- Urea, creatinine, phosphate and other uraemic toxins pass into the dialysate down their concentration gradients.

- *Continuous ambulatory peritoneal dialysis (CAPD).*
- Dialysate is present within the peritoneal cavity continuously, except when dialysate is being exchanged.
- Dialysate exchanges are performed three to five times a day, using a sterile no-touch technique to connect 1.5–3 L bags of dialysate to the peritoneal catheter;
- each exchange takes 20–40 min. This is the technique most often used for maintenance peritoneal dialysis in patients with ESKD.

- **Complications of all long-term dialysis**
- Cardiovascular disease and sepsis are the leading causes of death in long-term dialysis patients.
- Causes of fatal sepsis include peritonitis complicating peritoneal dialysis and *Staph. aureus infection (including endocarditis)* complicating the use of indwelling access devices for haemodialysis.
- *Dialysis amyloidosis*
- This is the accumulation of amyloid protein as a result of failure of clearance of β2-microglobulin. This protein is the light chain of the class I HLA antigens and is normally freely filtered at the glomerulus but is not removed by cellulose-based haemodialysis membranes.
- The protein form amyloid deposits, which may cause median nerve compression in the carpal tunnel or a dialysis arthropathy.

Transplantation

- Successful renal transplantation offers the potential for almost complete rehabilitation in ESKD. This mode of renal replacement therapy has significant survival advantage compared to dialysis patients on transplant waiting lists.
- It allows freedom from dietary and fluid restriction; anaemia and infertility are corrected; and the need for parathyroidectomy is reduced.
- It is the treatment of choice for most patients with ESKD.

- The technique involves the anastomosis of an explanted human kidney, usually either from a cadaveric donor or from a living close relative, on to the iliac vessels of the recipient
- The donor ureter is placed into the recipient's bladder. Unless the donor is genetically identical (i.e. an identical twin), immunosuppressive treatment is needed, for as long as the transplant remains in place, to prevent rejection.

- in patient selection and assessment of donor–recipient compatibility, improvements in surgical techniques and the development of more efficient immunosuppressive regimens have increased patient and graft survival.
- Some 80% of grafts now survive for 5–10 years in the best centres, and 50% for 10–30 years.
- However, the half-life of renal allografts is still 13–16 years.
- The three most common causes of late graft loss are death with functioning graft, recurrence of renal disease and chronic allograft nephropathy


KIDNEY HEALTH INFORMATION SERVICE
1800 454 363