# 4

## Screening and Management: Overview

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The scope of the problem presented by chronic kidney disease (CKD) worldwide has been detailed in the two preceding chapters. To recapitulate what was discussed in Chapter 1, CKD is defined on the basis of a measured or estimated glomerular filtration rate (eGFR) $<60$ mL/min/1.73 m$^2$ and/or evidence of kidney damage for at least 3 months (Table 4-1). CKD is classified according to five glomerular filtration rate GFR stages (Table 4-2) and degree of albuminuria (Table 4-3). Recent evidence has demonstrated that the degree of albuminuria provides prognostic information that is at least as important as GFR staging, such that information about both parameters should be considered for optimal staging and risk stratification.

### SCREENING

Early identification and management of CKD is highly cost-effective and can reduce the risk of kidney failure progression and cardiovascular disease by up to 50% (Johnson, 2004). General practitioners, other primary health care clinicians, and nonrenal specialists play a crucial role in CKD early detection and management. Although the case for widespread population screening has been argued (de Jong and Brenner, 2004), the available evidence suggests that the optimal cost-effective strategy is targeted, opportunistic screening of patients with one or more risk factors for CKD (Howard, 2009; Boulware, 2003; Collins, 2009). All people attending their doctor should be assessed for CKD risk factors as part of routine primary health encounters. If a patient has any one of the key risk factors for CKD, they should undergo a kidney health check as per the algorithm depicted in Figure 4-1. Guideline-based approaches to screening adult patients with CKD are described in Chapters 42 and 43, and in Chapter 39 a Canadian approach is presented that focuses on Canada's efforts to involve family practitioners in this process.

Targeting patients with a family history of CKD may represent an important group for screening, although there have been few studies examining the prevalence and predictive value of a family history of kidney disease in CKD screening programs. Freedman et al. (2005) reported that approximately 23% of incident dialysis patients have close relatives with end-stage kidney disease. Similarly, a cross-sectional study of 196 first- and second-degree relatives of 178 hemodialysis patients observed a significantly higher prevalence of CKD in relatives compared with their counterpart controls (16% versus 7.5%) (Tsai, 2010). In a cohort of 1,742 people participating in targeted, free, community-based CKD screenings (Kidney Education Outreach Program [KEOP]), 24% reported a family history of kidney disease and 60% tested positive for microalbuminuria (Harward, 2009).

Screening programs for detection of CKD in children exist in a number of Asian countries, but data on the cost-effectiveness of such programs are limited (Hogg, 2009). Current American Academy of Pediatrics guidelines do not recommend routine screening of children for CKD and are supported by a recent analysis that reported that screening dipstick urinalysis is not cost-effective (Sekhar, 2010).

Urine testing is also very sensitive for detecting hematuria and can identify all significant bleeding. Because hematuria is often related to menstruation or urinary tract infection, a positive urinary dipstick for blood should be repeated and then

| T A B L E |
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| **4–1** Definition of Chronic Kidney Disease |

1. GFR <60 mL/min/1.73 m$^2$ for ≥3 months with or without evidence of kidney damage[a]; OR
2. Evidence of kidney damage (with or without decreased GFR) for ≥3 months, as evidenced by any of the following:
   - Albuminuria (micro- or macro-)
   - Proteinuria (see Chapter 1, Table 1-6).
   - Persistent hematuria (where other causes, such as urologic conditions, have been excluded)
   - Pathologic abnormalities (e.g., abnormal renal biopsy)
   - Radiologic abnormalities (e.g., scarring or polycystic kidneys seen on renal imaging)

GFR, glomerular filtration rate.
[a]Methods for measuring or calculating GFR are discussed in Chapter 1.

| T A B L E |
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| **4–2** Stages of Chronic Kidney Disease According to Measured or Estimated Glomerular Filtration Rate |

| Kidney Function Stage | GFR (mL/min/1.73 m$^2$) | Description |
|---|---|---|
| 1 | ≥90 | Normal or increased GFR |
| 2 | 60–89 | Normal or slightly decreased GFR |
| 3a | 45–59 | Mild-moderate decrease in GFR |
| 3b | 30–44 | Moderate-severe decrease in GFR |
| 4 | 15–29 | Severe decrease in GFR |
| 5 | <15 or on dialysis | End-stage kidney failure |

GFR, glomerular filtration rate.

| T A B L E |
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| **4–3** Stages of Chronic Kidney Disease According to Albuminuria |

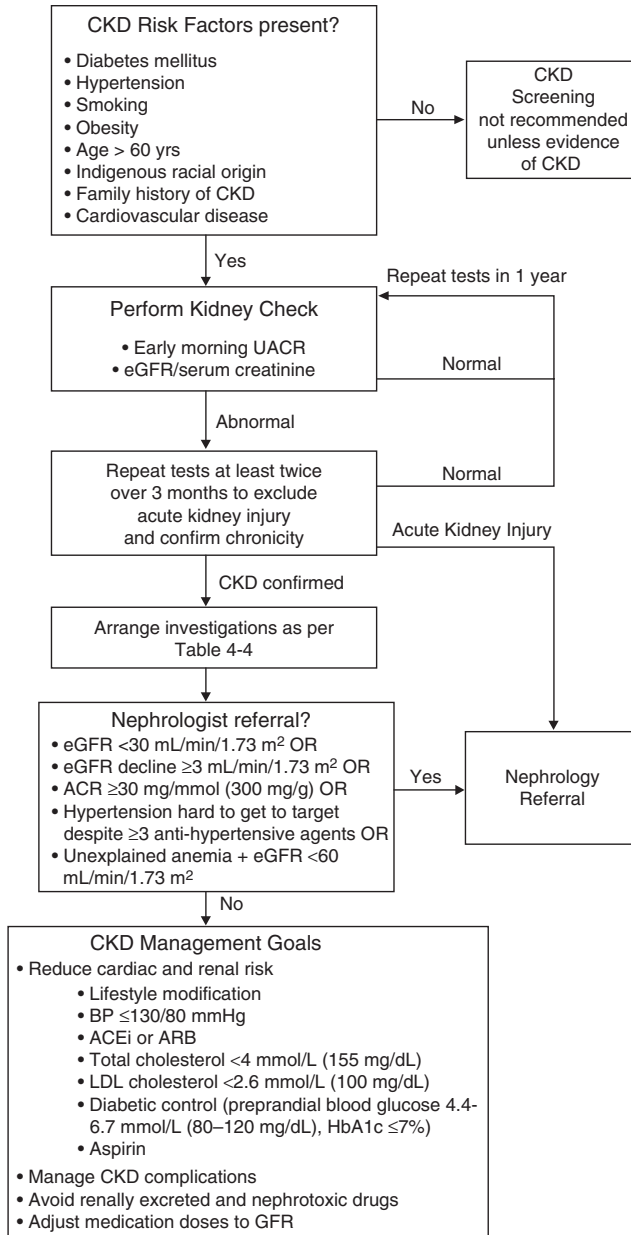| Albuminuria Stage | Urine Albumin: Creatinine Ratio (mg/mmol) | 24-h Urine Albumin (mg/day) |
|---|---|---|
| Normoalbuminuria | <3 (<30 mg/g) | <30 |
| Microalbuminuria | 3–30 (30–300 mg/g) | 30–300 |
| Macroalbuminuria | >30 (>300 mg/g) | >300 |

CKD Risk Factors present?

- Diabetes mellitus
- Hypertension
- Smoking
- Obesity
- Age > 60 yrs
- Indigenous racial origin
- Family history of CKD
- Cardiovascular disease

No → CKD Screening not recommended unless evidence of CKD

Yes ↓

Perform Kidney Check

- Early morning UACR
- eGFR/serum creatinine

Repeat tests in 1 year

Normal

Abnormal ↓

Repeat tests at least twice over 3 months to exclude acute kidney injury and confirm chronicity

Normal

Acute Kidney Injury

CKD confirmed ↓

Arrange investigations as per Table 4-4

↓

Nephrologist referral?

- eGFR <30 mL/min/1.73 m$^2$ OR
- eGFR decline ≥3 mL/min/1.73 m$^2$ OR
- ACR ≥30 mg/mmol (300 mg/g) OR
- Hypertension hard to get to target despite ≥3 anti-hypertensive agents OR
- Unexplained anemia + eGFR <60 mL/min/1.73 m$^2$

Yes → Nephrology Referral

No ↓

CKD Management Goals

- Reduce cardiac and renal risk
  - Lifestyle modification
  - BP ≤130/80 mmHg
  - ACEi or ARB
  - Total cholesterol <4 mmol/L (155 mg/dL)
  - LDL cholesterol <2.6 mmol/L (100 mg/dL)
  - Diabetic control (preprandial blood glucose 4.4–6.7 mmol/L (80–120 mg/dL), HbA1c ≤7%)
  - Aspirin
- Manage CKD complications
- Avoid renally excreted and nephrotoxic drugs
- Adjust medication doses to GFR

**FIGURE 4-1.** Algorithm for screening and management of chronic kidney disease in adult patients.

confirmed with urine microscopy and culture. Urine phase contrast microscopy often can help differentiate between glomerular and nonglomerular hematuria. The approach to management of persistent microscopic hematuria is detailed in Chapter 24.

## ONCE CHRONIC KIDNEY DISEASE HAS BEEN DIAGNOSED, WHAT ADDITIONAL INVESTIGATIONS SHOULD BE ORDERED?

When CKD is initially diagnosed, it is important to be sure that acute kidney disease is not missed by assuming that the first abnormal eGFR represents a long-standing condition. An early repeat of the test is appropriate if there is any suspicion of an acute condition. Furthermore, it is also important to exclude treatable pathology, such as urinary tract obstruction, vasculitis, nephrotic syndrome, and rapidly progressive glomerulonephritis. Particular attention should be paid to symptoms (e.g., urinary symptoms, rash, arthritis, or other features of a connective tissue disorder), known medical problems, previous urinary tract infections, cardiovascular risk factors, use of potentially nephrotoxic drugs (e.g., nonsteroidal anti-inflammatory drugs, intravenous drugs, previous compound analgesic use, Chinese herbal therapies), and family history of kidney disorders (e.g., polycystic kidneys). Physical examination should concentrate particularly on the skin, joints, cardiovascular system, and abdomen (palpable kidneys or bladder, audible renal bruits). Digital rectal examination of the prostate should be considered in older men. Recommended laboratory investigations are listed in Table 4-4.

## MANAGEMENT OF PATIENTS WITH CHRONIC KIDNEY DISEASE

The review and management of patients with CKD in the primary care setting depends on the CKD stage and individual circumstances (Table 4-5, Fig. 4-1) and is described throughout this handbook.

| TABLE 4-4 | Diagnostic Evaluation in Patients with Confirmed Chronic Kidney Disease |
| --- | --- |

1. Generally indicated
   - Full blood count
   - Serial serum urea/electrolytes/creatinine/eGFR/albumin
   - Fasting lipids and glucose
   - Urine microscopy and culture
   - Renal ultrasound scan
2. Sometimes indicated
   - $HbA_{1c}$ (if diabetic)
   - Serum calcium, phosphate, PTH and iron studies (if eGFR $<$60 mL/min/1.73m$^2$)
   - Serum and urine electrophoresis ($>$40 years old)
   - Antinuclear antibodies, extractable nuclear antigens, complement studies (if rash, arthritis, or features of connective tissue disease)
   - Antiglomerular basement membrane antibody (if pulmonary symptoms or acutely deteriorating kidney function)
   - Antineutrophil cytoplasmic antibodies, cryoglobulins (if constitutional symptoms, rash or respiratory symptoms, or acutely deteriorating kidney function)
   - Hepatitis B, hepatitis C, human immunodeficiency virus serology (if risk factors)
   - Renal biopsy (especially if persistent UACR $>$60 mg/mmol or proteinuria $>$1,000 mg/day)

eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone; UACR, urine albumin-to-creatinine ratio.

| TABLE 4-5 | Chronic Kidney Disease Management Plan | |
|---|---|---|
| **CKD Stage** | **Review** | **Clinical Action Plan** |
| 1–2 (eGFR >60) | Every 3–6 months<br>■ Blood pressure<br>■ Weight<br>■ UACR (quarterly)<br>■ Urea, creatinine, electrolytes<br>■ eGFR<br>■ Fasting glucose<br>■ Fasting lipids | ■ Initial investigations to exclude treatable CKD (Table 4-4)<br>■ Reduce cardiovascular risk<br>■ Reduce CKD progression |
| 3a and 3b (eGFR 30–59) | Every 1–3 months<br>■ Blood pressure<br>■ Weight<br>■ UACR (quarterly)<br>■ Urea, creatinine, electrolytes<br>■ eGFR<br>■ Fasting glucose<br>■ Fasting lipids<br>■ Full blood count<br>■ Iron stores (3–6 months)<br>■ Calcium and phosphate<br>■ Parathyroid hormone (quarterly) | As above plus<br>■ Early detection and management of CKD complications<br>■ Avoidance of renally excreted and nephrotoxic medications<br>■ Adjustment of medications to levels appropriate for kidney function<br>■ Appropriate specialist referral when indicated (Fig. 4-1) |
| 4–5 (eGFR <30) | Every month<br>■ Blood pressure<br>■ Weight<br>■ UACR (quarterly)<br>■ Urea, creatinine, electrolytes<br>■ eGFR<br>■ Fasting glucose<br>■ Fasting lipids<br>■ Full blood count<br>■ Iron stores (quarterly)<br>■ Calcium and phosphate<br>■ Parathyroid hormone (quarterly) | As above plus<br>■ Referral to nephrologists for physical and psychosocial preparation for dialysis, transplantation, or conservative medical management<br>■ Discuss advanced health-care directive |

CKD, chronic kidney disease; UACR, urine albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate.

### Smoking and Drug Abuse

Smoking is associated with more severe proteinuria and kidney failure progression in patients with CKD. The clinical evidence for this association is stronger for diabetic patients. Stopping smoking has been associated with retardation of CKD progression. Use of cocaine and injection drugs (see Chapter 5) is responsible for a substantial amount of CKD and acute kidney injury as well.

### Obesity

Caloric restriction leading to weight loss has been shown to result in amelioration of CKD in overweight/obese individuals (Chapter 6), as evidenced by diminished proteinuria and improved kidney function. Bariatric surgery may also ameliorate CKD.

### Sodium and Potassium

Restriction of dietary sodium to 100 mmol/day (2.3 g sodium or 6 g salt per day) or less has been shown to reduce blood pressure and albuminuria in patients with CKD (Jones-Burton, 2006) and is recommended. However, there are no long-term studies evaluating the impact of dietary sodium restriction on CKD progression or cardiovascular end points. A high potassium intake is associated with health benefits, as are foods high in potassium, notably fruits and vegetables. For this reason, potassium-rich foods should not be restricted in CKD patients unless this becomes necessary based on serum potassium values nearly at or exceeding the upper end of the normal range (Chapters 7 and 8).

### Protein Restriction

A mildly restricted protein diet, consisting of 0.8 g/kg/day, with adequate energy is generally recommended for adults with CKD as discussed in Chapter 9. If prescription of a lower protein diet ($\leq$0.6 g/kg/day) to slow CKD progression is attempted, such a diet must be closely monitored, and the potential modest benefits of such a diet on GFR decline must be weighed carefully against the concomitant risks of worsening clinical and biochemical parameters of nutrition. For children, reduction of dietary protein intake to the lowest safe amounts recommended by the World Health Organisation (0.8–1.1 g/kg/day depending on age) has not been shown to decrease the progression of CKD.

### Phosphate

It is becoming appreciated that even mildly increased levels of serum phosphate are associated with increased cardiovascular risk. However, the effect of dietary phosphate restriction has not been evaluated in patients with CKD; therefore, restriction of phosphate intake generally is not recommended in patients with early (stages 1–3) CKD (Johnson, 2004). Nevertheless, as described in Chapters 10 and 11, a very considerable portion of phosphate in the Western diet comes from phosphate-containing food additives. Avoiding such food additives to the greatest extent possible should be a relatively risk-free method of reducing exposure to dietary phosphate. As CKD advances, most guidelines do recommend restricting phosphate intake and even ingestion of phosphate binders as required to keep serum phosphate within the normal range.

### Uric Acid

As described in Chapter 12, there is limited evidence suggesting that treating asymptomatic hyperuricemia in CKD patients with allopurinol or rasburicase may be beneficial in terms of both blood pressure control and progression of kidney disease. However, safety concerns with allopurinol and the high cost of alternative agents may limit their routine use in day-to-day clinical practice.

### Advanced Glycation End Products

Advanced glycation end products (AGEs) are ubiquitous in foods, but are much higher in fatty meats and in all foods subjected to very high temperatures during preparation (e.g., food that has been grilled or fried). Serum levels of AGEs increase acutely after ingestion of foods containing AGEs, and in the short term there is impaired flow-induced endothelial vasodilatation. In observational studies, high

serum levels of AGEs are associated with increased mortality risk (see Chapter 13). One can reduce exposure to dietary AGEs by eating more boiled or steamed food and more vegetables than meats. However, the effects of dietary AGE avoidance on clinically relevant outcomes have not been systematically evaluated.

### Vitamins and Supplements

The primary vitamin that may need to be supplied to patients with CKD is vitamin D, in the form of either a not-yet-activated prohormone (cholecalciferol or ergocalciferol) or a dihydroxylated, fully activated hormone or analog (calcitriol, doxercalciferol, paricalcitol). CKD patients have low 25-vitamin D levels even during early-stage disease. There may be mild deficiency of several water-soluble B vitamins in CKD patients who are following a protein-restricted diet, which should be preventable with supplementation. Apart from these instances, vitamin supplementation is not required and may cause adverse effects (Chapter 14).

### Acidosis

As discussed in Chapter 15, CKD patients tend to have a mild to moderate degree of acidosis. The acidosis comes from the proteins in the foods we eat, and it can be neutralized by ingestion of sodium (or uncommonly, potassium) bicarbonate or citrate. Some studies have suggested that alkali supplementation may help maintain bone health, and there is even evidence that it may slow progression of CKD. However, the risk-to-benefit ratio of this approach has not been evaluated. Excessive alkalinization combined with a high ingestion of calcium and vitamin D can lead to so-called calcium-alkali syndrome, with hypercalcemia and rapid impairment of renal function.

### Alcohol

No specific recommendations can be made about alcohol consumption in patients with CKD because of conflicting epidemiological evidence.

### Cola Beverages

Soft-drink (especially cola) consumption has been associated with diabetes, hypertension, and kidney stones. There is limited evidence to suggest that drinking two or more colas per day is associated with a significantly increased risk of CKD (Saldana, 2007). Patients with CKD should therefore minimize their intake of cola.

### Fluid Intake

Drinking large amounts of water has commonly been advocated in the popular press to enhance kidney health. However, there is insufficient evidence to recommend augmenting fluid intake in most patients with CKD. Such patients should obviously avoid dehydration and overhydration.

## REDUCING RISK OF PROGRESSION OF CHRONIC KIDNEY DISEASE AND CARDIOVASCULAR DISEASE

Patients with CKD are at greatly increased risk of both cardiovascular disease and end-stage kidney disease. Irrespective of the underlying cause of CKD, the treatments outlined below (and described in detail in Chapters 16–23) will slow the decline in kidney function and decrease cardiovascular risk. Regular monitoring (at least every 3 months) is essential.

### Lifestyle Modification and Exercise

Lifestyle modification can substantially reduce the risks of hypertension, as well as obesity, diabetes mellitus, cardiovascular disease, and kidney failure progression. Patients with CKD should be encouraged to undertake regular physical exercise that is appropriate for their physical ability and medical history. There is limited

evidence that exercise may have beneficial effects on kidney function in patients with CKD (Johnson, 2006).

### Lipid Lowering

Statins are safe and significantly reduce the risk of all-cause and cardiovascular mortality in hypercholesterolemic CKD patients who are not receiving renal replacement therapy (Strippoli, 2008). They also reduce proteinuria, although they have not been shown to affect the decline of renal function as measured by creatinine clearance (Strippoli, 2008). Treatment targets have not been definitively established, although a total serum cholesterol <4 mmol/L (155 mg/dL) and low-density lipoprotein (LDL) cholesterol <2.6 mmol/L (100 mg/dL) seem reasonable. There has been recent controversy about the ability of statins to increase survival in patients without hypercholesterolemia and some apparent differences between statins in terms of their ability to reduce proteinuria, all of which is discussed in detail in Chapter 16.

### Glycemic Control

There is strong evidence that intensive glycemic control reduces cardiovascular disease and CKD progression risk in both type 1 and 2 diabetes mellitus (Chapter 17). This benefit needs to be balanced against the risk of complications (severe hypoglycemia, weight gain, and perhaps also increased mortality) that may be associated with lowering of glucose to near-normal levels. The currently recommended targets for diabetic patients with CKD are a preprandial blood glucose level of 4.4–6.7 mmol/L (80–120 mg/dL) and a random $HbA_{1c}$ of <7%.

### Blood Pressure Control

Reducing blood pressure to target levels is the most important treatment step in managing cardiovascular and renal risks in CKD. The blood pressure target recommended by most CKD as well as diabetic guidelines is ≤130/80 mm Hg, but there is limited evidence for additional benefit of using this target as opposed to the slightly higher target, ≤140/90 mm Hg, recommended by most guideline bodies for hypertension treatment in general, and the lower blood pressure target needs to be applied judiciously to elderly patients, where excessively low blood pressure may put them at increased risk. The optimum blood pressure target is a matter of current investigation and debate.

As described in Chapter 18, multiple (often three to four) antihypertensive medications are frequently required in CKD patients to reach blood pressure targets. Angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs) are the preferred initial blood pressure–lowering strategy, because these agents have been shown to be renoprotective independent of blood pressure lowering. The exact role for so-called dual blockade using combined ACEi + ARB therapy, or combined treatment with an ACEi or ARB plus an aldosterone antagonist, is not clear, and at least one recent study (Mann, 2008) has suggested unfavorable risk:benefit with dual (ACEi + ARB) blockade.

It is prudent to measure serum creatinine and eGFR 1 week and 4 weeks after initiating ACEi or ARB therapy. An acute rise in plasma creatinine concentration of <30% that stabilizes within the first month is expected and is associated with a beneficial long-term response compared with patients who experience no change in serum creatinine or eGFR (Johnson, 2004). If the initial rise in creatinine level exceeds 30% above the baseline value, ACEi/ARBs should be discontinued. ACEi/ARBs should also be withdrawn if the serum potassium concentration exceeds 6 mmol/L despite dose reduction, dietary potassium restriction, and concomitant diuretic therapy. The treatment response to ACEi or ARBs can also be monitored by quantitating albuminuria. For each 50% reduction in urinary albumin excretion,

the risks of end-stage kidney disease, cardiovascular events, and heart failure are reduced by 45%, 18%, and 27%, respectively (Palmer, 2007). Diuretics and dietary sodium restriction can also synergistically enhance the blood pressure- and albuminuria-lowering effects of ACEi and ARBs.

In resistant hypertension or with stepwise decline in renal function with other signs of atherosclerosis, renovascular hypertension needs to be considered. Recent evidence suggests that medical management may be the best way to manage such patients (Chapter 19). Resistant hypertension often responds to attention to sodium restriction as well as to addition of drugs blocking aldosterone action or sodium channels in the distal nephron (Chapter 20).

### PERIPHERAL VASCULAR DISEASE AND STROKE RISK

CKD patients are at increased risk of both stroke and peripheral vascular disease (Chapter 21), and some of the trials studying optimal blood pressure targets find that if lower blood pressure targets do show any additional benefit, it is in terms of enhanced protection against stroke. Aspirin has been shown to reduce cardiovascular risk in patients with CKD (Kaisar, 2008), although this potential benefit must be weighed against the significant risk of gastrointestinal bleeding. Recent trends have been to use aspirin with increased caution in terms of primary prevention because of bleeding risk.

### CARDIOPROTECTION

CKD patients are at markedly increased risk of cardiovascular death, and left ventricular hypertrophy, coronary artery disease, and congestive heart failure all are quite common. As discussed in Chapters 22 and 23, the usual cardioprotective strategies used in patients with normal renal function apply, with an important caveat being slightly increased bleeding risk with anticoagulant treatment. Mineral bone disorder (Chapter 10) may affect cardiac disease in this patient group, and adequate provision of vitamin D and prevention of hyperphosphatemia and hyperparathyroidism may be important measures to limit both cardiac dysfunction and vascular calcification, although prospectively controlled trials focusing on the cardiovascular benefits of maintaining optimal calcium-related homeostasis have yet to be carried out.

### NEPHROTIC RANGE PROTEINURIA

An important subset of CKD patients will have a high degree of proteinuria, most commonly owing to advanced diabetic nephropathy, but others will have this either as a result of idiopathic disease affecting the renal filtration barrier in the glomerulus, such as membranous nephropathy or focal glomerulosclerosis, or as a manifestation of a systemic disease that affects multiple organs in the body, not only the kidneys. These problems are discussed in detail in Chapter 25, and management of hepatitis-associated kidney disease is described in Chapter 27.

### ANEMIA

As CKD progresses, anemia worsens, and it was originally thought that prevention of even mild anemia might prevent the development of left ventricular hypertrophy that has been observed to occur as GFR falls. However, randomized trials using erythropoietin-stimulating agents have shown that correction of mild anemia, Hb >100 g/L (10 g/dL), to near normal levels does not have a beneficial effect on cardiac outcomes; correction of mild anemia may increase quality of life measures slightly, but this may occur at the expense of an increased risk of strokes and overall mortality. Thus, current trends are to be cautious in terms of anemia correction,

although keeping Hb >100 g/L (>10 g/dL) using iron and/or erythropoiesis-stimulating agents remains the standard of care. The controversy and recommended treatment strategies are discussed in Chapter 26.

## AVOIDING CONTRAST-INDUCED COMPLICATIONS

An important precipitating or aggravating cause for CKD is the use of iodinated contrast for diagnostic studies. In patients with advanced CKD, use of magnetic resonance imaging contrast agents containing gadolinium has been associated with a fibrosing dermopathy, which can be debilitating and difficult to treat. Prevention recommendations are described in Chapter 28.

## MEDICATION REVIEW AND DRUG DOSING IN CHRONIC KIDNEY DISEASE

Dosage reduction or cessation of renally excreted medications is generally required once the GFR falls below 60 mL/min/1.73 $m^2$. Optimal use of drugs is complicated by the fact that many CKD patients are also elderly. In the elderly, both renal and hepatic excretion of drugs may be diminished, and body composition is different from that of young patients. These issues, along with drug tables listing dosage recommendations, are presented in Chapter 29.

## CHRONIC KIDNEY DISEASE IN SPECIAL POPULATIONS

### Children
The causes of CKD in children are different from those in adults. The measurement and estimation of GFR as well as optimal levels of blood pressure have their own special difficulties, and management of CKD in the very young is highly specialized (see Chapter 30).

### Pregnant Patients
Pregnancy generally does not affect the course of renal disease in women who have normal or near-normal renal function at conception, provided blood pressure is well controlled. Such individuals should not be discouraged from conceiving purely on the basis of their renal disease. CKD progression is accelerated by pregnancy in patients with poorly controlled hypertension or especially in women with pregravid plasma creatinine concentrations >200 mcmol/L (2.25 mg/dL), equivalent to an eGFR <25 mL/min/1.73 $m^2$ in a 30-year-old woman. This is discussed in more detail in Chapter 31.

### Elderly
Do all elderly patients defined to have CKD really have CKD? One of the current controversies with respect to using GFR to diagnose CKD is how to take account of age-related decline in renal function in the elderly. After the age of 30 years, GFR progressively declines at an average rate of 8 mL/min/1.73 $m^2$ per decade. It is estimated that about 25% to 30% of adults older than the age of 70 years will have an eGFR below 60 mL/min/1.73 $m^2$. There is ongoing debate as to whether this age-related GFR decline is normal or pathological. However, an eGFR <45 mL/min/1.73 $m^2$ predicts significantly increased risks of cardiovascular disease and CKD progression in all age groups and should therefore generally be considered pathological (i.e., CKD) rather than physiological or age-appropriate. An eGFR between 45 and 60 mL/min/1.73 $m^2$ (stage 3a CKD, Table 4-2) is predictive of significantly increased risks of adverse clinical outcomes in younger patients (<70 years), although the benefits of identifying older people with an eGFR >45 mL/min/1.73 $m^2$ have yet to be definitively proven. Based on this evidence, the Australasian Creatinine Consensus Working Group (Mathew, 2007) concluded that "in those patients 70 years and

older with an eGFR from 45 to 59 mL/min/1.73m$^2$, when stable over time and unaccompanied by other evidence of kidney damage, the GFR value may be interpreted as consistent with a typical eGFR for this age and unlikely to be associated with CKD complications." Some other guidelines, such as the current version of those issued by the Kidney Disease Outcomes Quality Initiative (KDOQI), consider that an eGFR <60 mL/min/1.73m$^2$ for at least 3 months is diagnostic of CKD, regardless of age, although this is in the process of being re-evaluated. A more in-depth discussion of CKD in the elderly is given in Chapter 32.

### Other Special Groups

CKD diagnosis and management has specific nuances in different patient groups. With regard to ethnicity, a propensity to diabetes and to accelerated progression is found in patients of Hispanic and African American descent. In Asians, as discussed in Chapter 33, norms for body mass index as well as prediction equations for eGFR may need to be adjusted slightly, and the strategy to optimize diet will be different in those following a non-Western pattern of food intake. Patients with kidney stones have their own particular set of management issues, as do patients with polycystic kidney disease or those suffering from human immunodeficiency virus (HIV) infection (Chapters 34–36).

## DETECTION AND MANAGEMENT OF CHRONIC KIDNEY DISEASE COMPLICATIONS

Many of the known complications of CKD, such as hypertension, secondary hyperparathyroidism, renal osteodystrophy, anemia, sleep apnea, restless legs, cardiovascular disease, and malnutrition, are often already evident by stage 3 (GFR 30–59 mL/min/1.73 m$^2$). Other complications, such as hyperkalemia, acidosis, and hyperphosphatemia, usually become apparent in stage 4 CKD (GFR 15–29 mL/min/1.73 m$^2$). Uremia and pulmonary edema often become manifest in stage 5 CKD (GFR <15 mL/min/1.73 m$^2$). Regular monitoring for all of these complications (at least 3-monthly in stage 3 and monthly in stage 4) is essential.

## WHEN SHOULD CHRONIC KIDNEY DISEASE PATIENTS BE REFERRED TO A NEPHROLOGIST?

The current indications for referral to a nephrologist are listed in Figure 4-1. These indications seek to identify patients who are at significant risk of progressing to end-stage kidney disease and/or who potentially have an underlying specifically treatable renal condition (e.g., primary glomerulonephritis, connective tissue disease, plasma cell dyscrasia). The decision to refer or not must always be individualized. When referring to a nephrologist, it is important to ensure that the patient has had a recent kidney ultrasound, current blood chemistry, and quantitation of albuminuria.

## PRE-EMPTIVE TRANSPLANTATION, DIALYSIS, OR CONSERVATIVE TREATMENT?

In patients in whom CKD is expected to progress, the discussion of how best to replace lost renal function can begin at a relatively early stage of CKD, but consideration of pre-emptive transplantation, including initiation of a pretransplant workup, must begin in earnest once eGFR has decreased to 20 to 25 mL/min/1.73 m$^2$ (Chapter 37). For those contemplating dialysis, all locally available options, including home hemodialysis, peritoneal dialysis, and in-center hemodialysis need to be presented fairly and the advantages and disadvantages of each carefully debated. For those opting for hemodialysis, a reasonable lag time for creation of a well-functioning arteriovenous fistula is required, as discussed in Chapter 38.

## PRACTICE-RELATED ISSUES, GUIDELINES, AND PATIENT MANAGEMENT AND EDUCATION TOOLS

The optimum method of structuring care for CKD patients depends on the health care infrastructure present in a given country. In Chapter 39, a Canadian approach is presented on how to do this under a single-payer system. In Chapter 40, the challenges of delivering CKD care in the U.S. environment is described. In both systems, the increasing use of multidisciplinary teams and a disease management approach appears to offer great potential advantages. A variety of practice guidelines are available that deal both very specifically with care for CKD patients and care of those with heart disease, diabetes, or hypertension. In addition, a number of organizations throughout the world have developed tool kits and Web sites that offer patient- and provider-focused educational material and treatment algorithms. These are detailed in Chapters 41 through 44.

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