deficient as CKD progresses. EPO and iron deficiency are common causes of anemia in CKD. Administration of synthetic EPO results in correction of anemia, improved quality of life and anemia-related symptoms, and decreased dependence on blood transfusions. Caution must be exercised, because higher doses of EPO that result in elevations of the serum hemoglobin to more than 12 g/dL may be associated with a higher risk for adverse cardiovascular events. Bleeding disorders, primarily from defects in platelet adherence and aggregation, are common. Bleeding in uremic patients usually can be controlled with cryoprecipitate, 1-deamino-(8-D-arginine)-vasopressin (DDAVP), conjugated estrogens, and dialysis.

Defects occur in both humoral and cellular immune systems in patients with CKD. Although the leukocyte count is typically normal and appropriately responsive in advanced CKD, patients are generally immunosuppressed and susceptible to infections. This may be the result of functional abnormalities of polymorphonuclear leukocytes, lymphocytes, and other cellular host defenses. Additionally, patients with CKD may have a variable immune response to vaccination.

Endocrine and Metabolic

Thyroid function testing may be less reliable in patients with uremia. Common laboratory findings include an increased triiodothyronine (T_3) resin uptake, a low T_3 level resulting from the impaired conversion of thyroxin to T_3 peripherally, and normal thyroxin levels. Thyroid-stimulating hormone levels are usually normal.

A deranged pituitary-gonadal axis can result in sexual dysfunction manifested by impotence, decreased libido, amenorrhea, sterility, and uterine bleeding. Patients have decreased plasma levels of testosterone, estrogen, and progesterone, with normal or increased levels of follicle-stimulating hormone, luteinizing hormones, and prolactin. Pregnancy is uncommon in female patients who have a GFR of less than 30 mL/minute.

Lipid abnormalities are also common in CKD. They are most consistent with type IV hyperlipoproteinemia, with a marked increase in plasma triglycerides and less of an increase in total cholesterol. The activity of lipoprotein lipase is decreased in uremia, resulting in reduced conversion of very-low-density lipoprotein to low-density lipoprotein and thus hypertriglyceridemia. The treatment of choice is the hydroxymethylglutaryl–coenzyme A reductase (HMG-CoA) inhibitor class of drugs because of their pluripotent effects on inflammation and atherosclerosis.

Electrolytes

Hyperkalemia occurs in patients with CKD as a result of decreased renal clearance of potassium, intracellular-to-extracellular shifts of potassium in the setting of metabolic acidosis related to kidney failure, and also the concomitant use of medications such as RAAS blockers. The primary method of treatment is dietary reduction of potassium but may also include use of loop diuretics or potassium-binding medications. Hypokalemia is much less common in CKD but may occur in the setting of very poor nutritional intake or use of high-dose potassium-wasting diuretic medications.

Skin

Uremic hue, a yellowish skin color, is likely the result of retained liposoluble pigments, such as lipochromes and carotenoids. Uremic hue usually responds to dialysis, control of hyperparathyroidism, improved calcium and phosphate balance, and, occasionally, ultraviolet radiation. Calciphylaxis, or calcific uremic arteriolopathy, results in painful skin calcification and is often seen in patients with uncontrolled hyperparathyroidism. Use of warfarin is a risk factor for this condition. Nail findings include the half-and-half nail, characterized by red, pink, or brownish discoloration of the distal nail bed, pale nails, and splinter hemorrhages. Other common signs and symptoms are pruritus and ecchymoses due to disorders of bleeding.

DIAGNOSIS

Comprehensive care for the patient with kidney disease includes screening, diagnosis, and treatment of CKD to manage complications and prevent further progression (E-Fig 32-4). Screening for CKD is recommended for patients with high-risk comorbid conditions, including diabetes mellitus and hypertension, and also for those with a family history of kidney disease. The diagnosis of CKD requires evidence of kidney damage that has persisted for at least 3 months. Imaging abnormalities are important, but more commonly CKD is detected by the presence of albuminuria or by reductions in the clearance of toxins by the kidney (i.e., elevated serum creatinine or blood urea nitrogen). Albuminuria may be detected in a spot collection of urine and is best reported as an albumin-to-creatinine ratio (ACR). In general, an ACR greater than 30 mg/g confirmed on several samples and without evidence of urinary infection raises concern for a diagnosis of CKD and warrants additional investigation.

Clearance of toxins by the kidney is most often assessed by the estimated glomerular filtration rate (eGFR). Initial assessment should be performed using a serum creatinine–based estimating equation such as the Modification of Diet in Renal Disease (MDRD) study equation or the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Each of these has limitations and cautions regarding application of its results, and a detailed overview can be found in the KDIGO 2012 Clinical Practice Guidelines. The serum biomarker cystatin C may be considered and integrated into another estimating equation for patients who have an eGFR between 45 and 59 mL/min/1.73 m^2 and may not have albuminuria or kidney imaging abnormalities to confirm evidence of CKD.

Once a diagnosis of CKD is established, management goals include (1) prevention of progression of CKD, (2) identification and treatment of symptoms and complications of CKD, and (3) preparation of patients for RRT if appropriate.

TREATMENT

Prevention of Progression

In addition to treatment of the specific underlying cause of kidney disease, it is important to consider methods to slow the progression of CKD once it is diagnosed. These methods include optimal control of hypertension, diabetes, and other