Chronic Kidney Disease: Detection and Evaluation

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Chronic kidney disease affects an estimated 27 million adults in the United States, and is associated with significantly increased risk of cardiovascular disease and stroke. Patients should be assessed annually to determine whether they are at increased risk of developing chronic kidney disease based on clinical and sociodemographic factors. Diabetes mellitus, hypertension, and older age are the primary risk factors that warrant screening. Other risk factors include cardiovascular disease, family history of chronic kidney disease, and ethnic and racial minority status. Serum creatinine levels can be used to estimate the glomerular filtration rate, and spot urine testing can detect proteinuria. After the diagnosis of chronic kidney disease is made, staging based on estimated glomerular filtration rate determines prognosis, evaluation, and management. Further evaluation should focus on the specific type of kidney disease and on identifying complications related to the disease stage. Patients should be assessed for risk factors leading to the further loss of kidney function and cardiovascular disease. Patients with estimated glomerular filtration rates less than 30 mL per minute per 1.73 m^2, significant proteinuria, or rapid loss of kidney function should be referred to a nephrologist for further evaluation and management. (*Am Fam Physician.* 2011;84(10):1138-1148. Copyright © 2011 American Academy of Family Physicians.)

Chronic kidney disease (CKD) affects an estimated 27 million adults in the United States and is associated with increased mortality, morbidity, and health care costs.[1,2] CKD is also associated with significantly increased risks of cardiovascular disease[3] and stroke.[4] The incidence and prevalence of CKD among U.S. adults have increased dramatically since 1991.[5] More than 500,000 Americans were treated for end-stage renal disease in 2007.[6] The increases are partly explained by the increasing prevalence of diabetes mellitus and hypertension, the leading risk factors for CKD. Awareness of CKD among patients has modestly increased in recent years, but remains low. According to the 2003-2004 National Health and Nutrition Examination Survey, less than 5 percent of patients with stage 1 or 2 CKD and less than 10 percent with stage 3 reported having been diagnosed with CKD; only 45 percent of patients with stage 4 were aware of their condition.[7] Although clinical laboratories report estimated glomerular filtration rate (GFR) directly to physicians, CKD recognition remains low.[8] In 2002, the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative published practice guidelines to help primary care physicians identify patients with early CKD and improve health outcomes.[9]

CKD is defined by the presence of structural or functional abnormalities of the kidney with or without an accompanying reduction in GFR. Persons with CKD may have one or more of the following: pathologic abnormalities, markers of kidney damage (i.e., imaging abnormalities and abnormalities in serum or urine, including proteinuria and abnormal urinary sediment), or GFR less than 60 mL per minute per 1.73 m^2 for at least three months. If the duration of the abnormality is unknown, the possibility of acute kidney injury should be considered and appropriate evaluation performed for reversible causes. Most persons who have received kidney transplants are considered to have CKD.

Detection of CKD

INDICATIONS FOR SCREENING

Annual CKD screening is recommended by the American Diabetes Association,[10] by the National Kidney Foundation for patients at risk,[9,11] by the Joint National Committee on Hypertension[12] for patients with diabetes and hypertension, and by the American Heart Association for patients with cardiovascular disease.[13] The U.S. Preventive Services Task Force has not examined the evidence or made recommendations for screening. Cardiovascular disease, a family history of CKD, and ethnic or racial minority status do not significantly increase the risk of CKD in adults older than 60 who have diabetes and hypertension.[14] Risk factors are listed in *Table 1*.[9]

SCREENING TESTS

CKD is typically detected by measuring serum creatinine levels to calculate the GFR and by measuring the urinary albumin/creatinine ratio to detect proteinuria.[15] Although the most common causes of CKD are diabetes and hypertension (*Table 2*[9,16]), the disease can be caused by many other conditions. Urinalysis can detect signs of glomerulonephritis, tubulointerstitial disease, vasculitis, hereditary nephritis, and lupus nephritis; however, it is not routinely recommended in otherwise healthy patients.

ESTIMATING GFR

The GFR is the best measure of kidney function. Normal GFR varies by age, sex, and body size. GFR is approximately 120 to 130 mL per minute per 1.73 m² in young adults, and decreases by an average of 1 mL per minute per 1.73 m² per year after 30 years of age.[9] A GFR less than 60 mL per minute per 1.73 m² represents a loss of at least one-half of normal kidney function; below this level, there is an increased prevalence of CKD complications.

Creatinine clearance is used to estimate the GFR. Because creatinine is filtered and secreted by the proximal tubules, the creatinine clearance exceeds the GFR. Generation of creatinine is determined by muscle mass and diet, whereas tubular secretion could be decreased by the use of medications such as trimethoprim and cimetidine (Tagamet).

The serum creatinine level is an insensitive marker of GFR early in the course of

Table 1. Risk Factors for CKD

Autoimmune disease	Lower urinary tract obstruction
Diabetes mellitus	Minority status (e.g., blacks, American Indians, Asians, Pacific Islanders)
Exposure to certain chemicals and environmental conditions (e.g., lead, cadmium, arsenic, mercury, uranium)	Neoplasia
	Nephrolithiasis
Exposure to certain drugs (Table 6[25])	Older age
Family history of CKD	Recovery from acute kidney injury
Hypertension	Reduction in kidney mass
Low birth weight	Systemic infections
Low income or education	Urinary tract infections

CKD = chronic kidney disease.

Adapted with permission from National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis.* 2002;39(2 suppl 1):S77.

CKD. A 33 percent decrease in GFR may raise the creatinine level from 0.8 to only 1.2 mg per dL (70.72 to 106.08 µmol per L). If the prior creatinine level is not known, this decrease in GFR may go unrecognized. When estimated GFR is suspected to be inaccurate—for example, in patients with severe malnutrition or paraplegia—a 24-hour urine collection should be performed to evaluate creatinine clearance.

Three equations are typically used to estimate GFR: the Cockcroft-Gault equation,[17] the Modification of Diet in Renal Disease (MDRD) equation,[18] and the more accurate Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)[19] formula (Table 3).[17-19] The Cockcroft-Gault equation systematically overestimates GFR. The MDRD is reasonably accurate in patients with CKD, but it underestimates GFR when it is greater than 60 mL per minute per 1.73 m^2, and it may misidentify persons with normal kidney function as having CKD. The MDRD can also be affected by fluctuations

Table 2. Etiology and Prevalence of Kidney Disease

Disease type	Etiology and examples	Prevalence among patients with end-stage renal disease in 2010 (%)
Diabetic kidney disease	Type 2 diabetes mellitus	32.5
	Type 1 diabetes mellitus	5.7
Nondiabetic kidney disease		
Vascular diseases	Hypertension, ischemic renal disease	24.8
Glomerular diseases	Primary: lupus nephritis, vasculitis, membranous nephropathy, minimal change disease, focal segmental glomerulosclerosis, immunoglobulin A nephropathy	18
	Secondary: infections (e.g., hepatitis B and C, human immunodeficiency virus–associated bacterial endocarditis), amyloidosis, heroin use, malignancy (e.g., leukemia, Hodgkin lymphoma, carcinoma)	
Cystic diseases	Polycystic kidney disease	7
Tubulointerstitial disease	Urinary tract infections, nephrolithiasis, obstruction, sarcoidosis, multiple myeloma, drug toxicity (e.g., proton pump inhibitors, lithium, nonsteroidal anti-inflammatory drugs)	3.8

Information from references 9 and 16.

Table 3. Equations for Estimating Glomerular Filtration Rate

Equation	Variables	Available at
Chronic Kidney Disease Epidemiology Collaboration	Age, sex, race, serum creatinine level	National Kidney Foundation Web site: http://www.kidney.org/professionals/kdoqi/gfr_calculator.cfm
		Nephron Information Center Web site: http://www.nephron.com/MDRD_GFR.cgi
Cockcroft-Gault	Age, weight, sex, serum creatinine level	Nephron Information Center Web site: http://nephron.com/cgi-bin/CGSI.cgi
Modification of Diet in Renal Disease	Age; sex; race; and serum urea, nitrogen, albumin, and creatinine levels	National Kidney Disease Education Program Web site: http://www.nkdep.nih.gov/professionals/gfr_calculators/idms_con.htm
		Nephron Information Center Web site: http://nephron.com/cgi-bin/MDRDSIdefault.cgi

Information from references 17 through 19.

in creatinine production and fluid balance; it gives falsely elevated estimated GFRs in malnourished and overhydrated patients and falsely decreased GFRs due to increased serum creatinine levels in patients taking trimethoprim and cimetidine.[20] The CKD-EPI formula provides better GFR estimation in patients with reduced and normal kidney function.[19] In a recent study, the CKD-EPI was found to be the most accurate formula in estimating GFR.[21]

Markers of Kidney Damage

PROTEINURIA

Proteinuria refers to increased excretion of any urinary protein, including albumin and other serum proteins (tubular proteins). A normal urinary protein/creatinine ratio is less than 200 mg per g; proteinuria is a predictor of total mortality and CKD progression, and can help determine the type of CKD. A normal urinary albumin/creatinine ratio is less than 30 mg per g. Patients with albumin/creatinine ratios of 30 to 300 mg per g are classified as having microalbuminuria, and those with ratios greater than 300 mg per g are classified as having macroalbuminuria.[10,11]

Urine dipstick testing is insensitive for the measurement of small amounts of albumin and is not recommended for CKD screening in patients at risk. This test is positive when a large amount (greater than 500 to 1,000 mg per day) of protein is excreted. Patients with positive urine dipstick results should repeat the test in the absence of urinary tract infection, ketosis, and hypovolemia. If the second result is positive, the urinary protein/creatinine ratio should be obtained within three months. Persistent proteinuria can be diagnosed by two positive protein/creatinine ratios one to two weeks apart.[9] Diabetes, the leading cause of nephrotic syndrome in the United States, is diagnosed when the protein/creatinine ratio is greater than 3,000 mg (3.0 g) per g.

ALBUMINURIA

Albumin is a sensitive marker of CKD caused by diabetes, hypertension, and glomerular diseases. Microalbuminuria was the most common abnormality associated with the diagnosis of stages 1 and 2 CKD in the National Health and Nutrition Examination Survey.[5] Microalbuminuria is an inherent part of the diabetes disease process but also can be present with nonrenal conditions (e.g., obesity, inflammation, cancer).[22] Microalbuminuria may indicate increased vascular permeability rather than kidney injury.[23]

Patients with diabetes and microalbuminuria who progress to macroalbuminuria are more likely to progress to end-stage renal disease. Diabetic kidney disease can be diagnosed based on the urinary albumin/creatinine ratio, duration of diabetes, and presence of diabetic retinopathy *(Table 4)*.[11] When albuminuria reaches the range of macroalbuminuria, albumin becomes the dominant urinary protein, and the advantage of measuring albuminuria over

Table 4. Diagnosis of Diabetic Kidney Disease

Screening initiation

At the time of diagnosis of type 2 diabetes mellitus

Five years after diagnosis of type 1 diabetes mellitus

Screening frequency

Annually

Diagnostic criteria

Macroalbuminuria

Microalbuminuria in patients who have had type 1 diabetes for more than 10 years

Microalbuminuria in the presence of diabetic retinopathy

Clinical findings that should prompt consideration of other causes

Absence of albuminuria in patients with stage 3 to 5 chronic kidney disease

Absence of diabetic retinopathy

Active urinary sediment (cells or casts)

Low GFR at the time of diagnosis

More than 30 percent reduction in GFR within two to three months after initiation of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker

Rapidly decreasing GFR (more than 4 mL per minute per 1.73 m^2 per year)

Rapidly increasing proteinuria or nephrotic syndrome

Refractory hypertension

Signs or symptoms of other systemic disease

GFR = glomerular filtration rate.

Information from reference 11.

Assessment of the Patient with Albuminuria

Obtain spot urinary albumin/creatinine ratio

↓

Albuminuria present? —No→ Rescreen in 1 year

↓ Yes

Are conditions that affect urinary albumin excretion present (e.g., urinary tract infection, exercise, fever, congestive heart failure, ketosis)?

Yes ↓   ↓ No

Treat or wait until resolved, then obtain repeat urinary albumin/creatinine ratio   Go to **A**

↓

Albuminuria present? —No→ Rescreen in 1 year

↓ Yes

A Obtain first-void spot urinary albumin/creatinine ratio twice within 3 to 6 months

↓

Are 2 of 3 tests positive? —No→ Rescreen in 1 year

↓ Yes

30 to 300 mg per g   > 300 mg per g

↓   ↓

Microalbuminuria   Macroalbuminuria

↓   ↓

                           Obtain urinary protein/creatinine ratio

                           ↓

                           Is protein/creatinine ratio > 500 to 1,000 mg per g?

                    No ↓   ↓ Yes

Diagnostic evaluation; begin treatment with ACE inhibitor or ARB; retest in 6 months   Diagnostic evaluation; begin treatment with ACE inhibitor or ARB; consider nephrology consultation

↓

Albuminuria present? —No→ Rescreen in 1 year

↓ Yes

Continue treatment; consider nephrology consultation for patients with refractory proteinuria (albumin/creatinine ratio > 300 mg per g or protein/creatinine ratio > 500 to 1,000 mg per g)
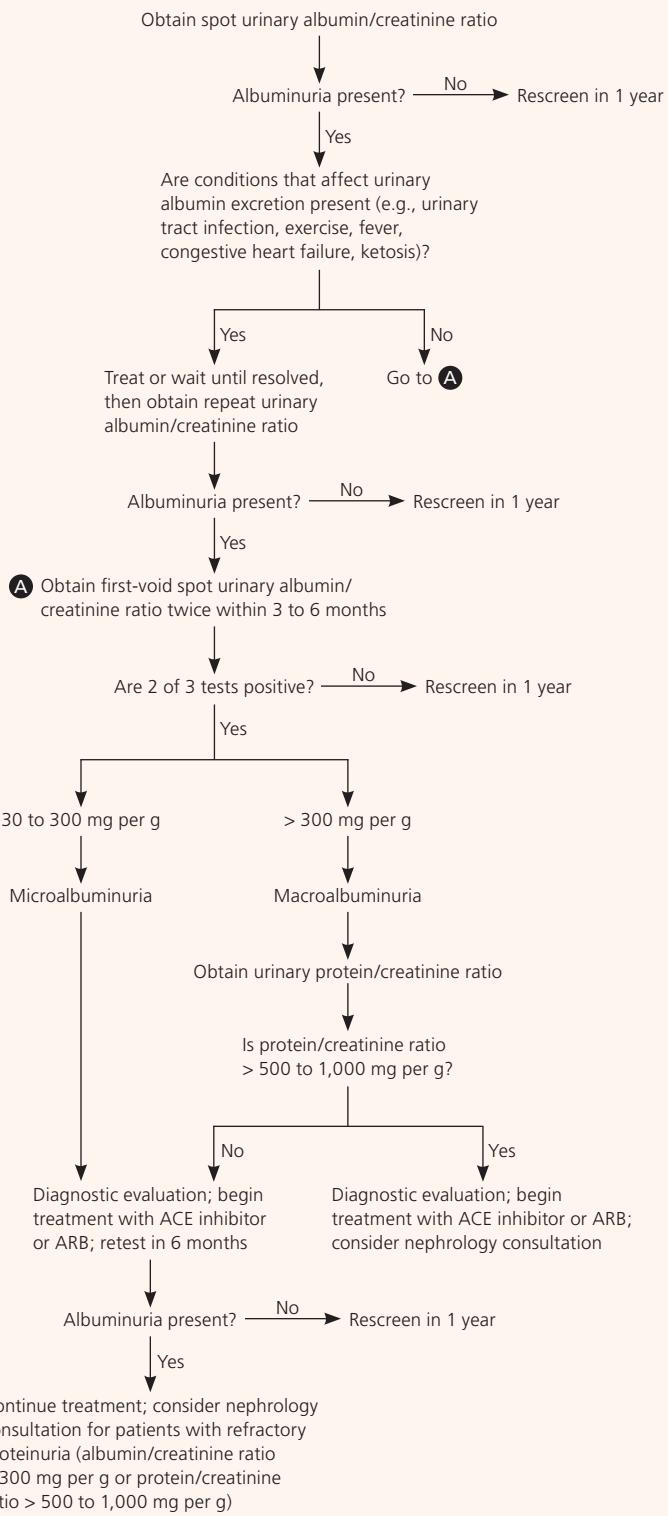
Figure 1. Algorithm for the evaluation of albuminuria. (ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker.)

Adapted with permission from Molitch ME, DeFronzo RA, Franz MJ, et al.; American Diabetes Association. Nephropathy in diabetes. Diabetes Care. *2004;27(suppl 1):S81, with additional information from references 9 and 15.*

proteinuria is generally lost.[9] Two out of three abnormal readings are required to confirm persistent albuminuria *(Figure 1).*[9,15,24]

OTHER MARKERS

Other markers of kidney damage include hematuria, cellular casts, serum markers, and imaging abnormalities. Clinical judgment based on the assessment of CKD risk factors should be used to determine if measurement of other markers of kidney damage is indicated.

CKD Staging

Staging is an important step for determining the prognosis, evaluation, and management of CKD. Staging is based on the level of estimated GFR, irrespective of diagnosis *(Table 5).*[9] Markers of kidney damage are required for stages 1 and 2. Using the current classification system, nearly 50 percent of U.S. adults older than 70 years have stage 3 CKD, and most have no evidence of albuminuria.[5] Older patients with stage 3 CKD without proteinuria and stable creatinine levels on repeat testing at three to six months are unlikely to progress to end-stage renal disease and do not have increased mortality risk. Physicians may choose to defer further evaluation in such patients, avoid the use of nephrotoxic medications *(Table 6*[25]*)*, and adjust the dosages of those that are excreted by the kidneys[20] *(Table 7*[9,26]*).*

CKD staging does not include risk-modifying parameters such as degree of albuminuria, age, sex, and cardiovascular risk factors. Revised guidelines, currently under development, will address those issues.

Evaluation of CKD

A thorough initial investigation includes determining the etiology and type of CKD and evaluating for comorbidities. The patient and family histories, physical examination, and blood pressure and weight measurements are the most valuable parts of the CKD evaluation *(Table 8).*[9,27,28] Laboratory tests should include measurement of serum electrolytes and glucose, and a fasting lipid panel. Urinalysis should

Table 5. Stages of CKD and Recommended Action Plan

Stage	Description	Estimated GFR (mL per minute per 1.73 m^2)	Action plan
1	Kidney damage* with normal or increased GFR	≥ 90	Diagnose and treat CKD, treat comorbid conditions, slow progression of CKD, reduce cardiovascular risk
2	Kidney damage* with mildly decreased GFR	60 to 89	Estimate progression
3	Moderately decreased GFR	30 to 59	Evaluate and treat complications
4	Severely decreased GFR	15 to 29	Prepare for kidney transplant
5	Kidney failure	< 15 (or dialysis)	Kidney transplant if uremia present

CKD = chronic kidney disease; GFR = glomerular filtration rate.

*—Presence of markers of kidney damage is required for the diagnosis of stage 1 or 2 CKD.

Adapted with permission from National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. *2002;39(2 suppl 1):S4.*

be performed to evaluate urinary sediment and the urinary albumin/creatinine or protein/creatinine ratio[9] *(Table 9*[9,11,29]*)*. Additional testing may be required to identify rare causes of CKD. Renal ultrasonography is recommended to evaluate kidney size and assess for possible structural abnormalities.[9]

Cardiovascular disease risk assessment—especially smoking status and lipid levels—is important because death is more likely than progression to dialysis in any stage of CKD.[9] Electrocardiography is recommended to identify left ventricular hypertrophy.

Patients with an estimated GFR of less than 60 mL per minute per 1.73 m^2 require further evaluation to assess for complications. Evaluation for anemia is recommended in women with hemoglobin levels less than 12 g per dL (120 g per L) and in men with levels less than 13.5 g per dL (135 g per L), in addition to nutritional assessment and evaluation for bone disease *(Table 10)*.[9,30,31]

Short-term risks of GFR reduction (e.g., volume depletion, urinary tract obstruction, use of nephrotoxic agents) require immediate recognition to prevent irreversible deterioration of renal function. High cumulative exposure to nonsteroidal anti-inflammatory drugs is associated with rapid progression of CKD.[32] Acetaminophen is the analgesic of choice for short-term treatment of mild to moderate pain in patients with stage 3 to 5 CKD.[33] Nonsteroidal anti-inflammatory drugs may be used in patients with stage 3 CKD for short-term therapy with regular renal function monitoring.[33]

Table 6. Drugs Associated with Nephrotoxicity

Drug	Mechanism of kidney injury
Acyclovir (Zovirax)	Acute interstitial nephritis, crystal nephropathy
Aminoglycosides	Tubular cell toxicity
Amphotericin B	Tubular cell toxicity
Chinese herbal preparations containing aristolochic acid	Chronic interstitial nephritis
Contrast media	Renal ischemia
Lithium	Chronic interstitial nephritis
Nonsteroidal anti-inflammatory drugs	Acute and chronic interstitial nephritis, impaired glomerular hemodynamics
Phenytoin (Dilantin)	Acute interstitial nephritis
Sulfonamides	Acute interstitial nephritis, crystal nephropathy
Vancomycin	Acute interstitial nephritis
Zoledronic acid (Zometa)	Tubular cell toxicity

Information from reference 25.

Table 7. Dosage Adjustment of Common Medications in Patients with Chronic Kidney Disease

Medication	Dosage adjustment based on GFR (mL per minute per 1.73 m²)*		
	> 50	10 to 50	< 10
Acyclovir (Zovirax; oral)	100%	100%	200 mg every 12 hours
Allopurinol (Zyloprim)	75%	50%	25%
Amoxicillin	Every 8 hours	Every 8 to 12 hours	Every 24 hours
Amoxicillin/clavulanate (Augmentin)	Every 12 hours	Estimated GFR 10 to 30 mL per minute per 1.73 m²: every 12 hours Estimated GFR < 30 mL per minute per 1.73 m²: do not use 875-mg/125-mg tablets	Every 24 hours
Atenolol (Tenormin)	100%	50%	25%
Cefazolin	Every 8 hours	Every 12 hours	50% every 24 to 48 hours
Cephalexin (Keflex)	Every 8 hours	Every 8 to 12 hours	Every 12 to 24 hours
Ciprofloxacin (Cipro)	100%	50 to 75%	50%
Clarithromycin (Biaxin)	100%	50 to 100%	50%
Famotidine (Pepcid)	50%	25%	10%
Fluconazole (Diflucan)	100%	50%	50%
Gabapentin (Neurontin)	Estimated GFR 30 to 60 mL per minute per 1.73 m²: 200 to 700 mg twice daily Estimated GFR 16 to 29 mL per minute per 1.73 m²: 200 to 700 mg daily Estimated GFR ≤ 15 mL per minute per 1.73 m²: 100 to 300 mg daily		
Glyburide	100%	Avoid	Avoid
Levofloxacin (Levaquin)	100%	Estimated GFR 20 to 49 mL per minute per 1.73 m²: 500- to 750-mg initial dose, then 250 to 750 mg every 24 to 48 hours Estimated GFR 10 to 19 mL per minute per 1.73 m²: 500-mg initial dose, then 250 to 500 mg every 48 hours	—
Metformin (Glucophage)	Avoid if serum creatinine level is greater than 1.5 mg per dL (132.60 μmol per L) in men or greater than 1.4 mg per dL (123.76 μmol per L) in women, and in patients older than 80 years		
Metoclopramide (Reglan)	100%	75%	50%
Ranitidine (Zantac)	75%	50%	25%
Rosuvastatin (Crestor)	—	GFR < 30 mL per minute per 1.73 m²: 5 mg per day initially; 10 mg per day maximum	
Simvastatin (Zocor)	—	GFR < 30 mL per minute per 1.73 m²: 5 mg per day initially	
Thiazide diuretics†	100%	100%	Avoid
Valacyclovir (Valtrex)	100%	Every 12 to 24 hours	500 mg every 24 hours

GFR = glomerular filtration rate.

*—Percentages refer to percentage of usual dosage.

†—Thiazides should not be used in patients with estimated GFR < 30 mL per minute per 1.73 m²; however, metolazone (Zaroxolyn) retains effectiveness at GFR < 30 mL per minute per 1.73 m².

Information from references 9 and 26.

Table 8. Initial Diagnostic Evaluation in Patients with Suspected CKD

Examination component	Diagnostic clues	Findings suggestive of CKD risks and etiology
Review of systems	Recent infections	Poststreptococcal glomerulonephritis
	Risk factors for sexually transmitted disease	HIV infection, hepatitis B or C
	Skin rash or arthritis	Autoimmune disease (e.g., systemic lupus erythematosus, cryoglobulinemia)
	Symptoms during urination	Urinary tract infection, obstruction, or stone
Medical history	Diabetes mellitus (5 to 10 years' duration)	Microalbuminuria with evidence of retinopathy and elevated BP
	Diabetes (10 to 15 years' duration)	Albuminuria, retinopathy, hypertension
	Hypertension	Severe BP elevation, often with target organ damage
Family history of kidney disease	Males and females are affected equally in every generation	Autosomal dominant polycystic kidney disease
	Males in every generation are affected	Sex-linked recessive disease (e.g., Alport syndrome)
	Less frequent than every generation	Autosomal recessive polycystic kidney disease
Physical examination	Abdominal findings	Bruit (renal artery stenosis, fibromuscular dysplasia), flank pain, distended bladder
	Cardiovascular findings	Heart failure, ventricular hypertrophy
	Carotid bruit	Carotid artery disease
	Decreased peripheral pulses	Peripheral vascular disease
	General findings	Cushingoid appearance, edema
	Increased BP and weight	Hypertension, obesity
	Musculoskeletal findings	Arthritis, synovitis
	Ophthalmoscopic findings	Hypertensive or diabetic retinal disease
	Skin changes	Rash and skin changes in autoimmune disease or neurofibromatosis
Laboratory tests	Abnormal serum and urine protein electrophoresis	Multiple myeloma, amyloidosis, light-chain deposition disease
	Decreased serum complement levels C3 and C4	Poststreptococcal glomerulonephritis, membranoproliferative glomerulonephritis, lupus nephritis, cryoglobulinemia
	Eosinophiluria	Atheroembolic disease, tubulointerstitial disease
	Positive antiglomerular basement membrane antibody test	Goodpasture syndrome, antiglomerular basement membrane–associated rapidly progressive glomerulonephritis
	Positive antineutrophil cytoplasmic antibody test	Wegener granulomatosis, microscopic polyangiitis, pauci-immune rapidly progressive glomerulonephritis
	Positive antinuclear antibody test	Lupus nephritis
	Positive cryoglobulin test	Cryoglobulinemia
	Positive hepatitis B serology	Membranous nephropathy, membranoproliferative nephritis
	Positive hepatitis C serology	Mixed cryoglobulinemia, membranoproliferative glomerulonephritis, membranous nephropathy
	Positive HIV serology	Focal and segmental glomerulosclerosis
Ultrasonography	Doppler ultrasonography	May be useful in investigation of venous thrombosis, less so in arterial stenosis
	General findings	May show nephrocalcinosis, discrete stones, hydronephrosis, cysts,* or masses
	Increased echogenicity	May indicate cystic disease or medical renal disease
	Large kidneys	Generally indicate tumors, infiltrating diseases, or diseases causing nephrotic syndrome
	Size disparities and scarring	Suggest vascular, urologic, or tubulointerstitial diseases due to stones or infection
	Small hyperechoic kidneys	Generally indicate CKD

BP = blood pressure; CKD = chronic kidney disease; HIV = human immunodeficiency virus.

*—Simple cysts and duplicated collection systems are considered normal variants and are not indicative of kidney damage. Complex cysts or masses require urologic evaluation to rule out malignancy.

Information from references 9, 27, and 28.

Table 9. Urinary Sediment Abnormalities and Associated Kidney Disease

Associated kidney disease	Predominant abnormality on urinalysis						
	ACR or PCR (mg per g creatinine)	RBCs	RBC casts*	WBCs	WBC casts	Tubular cells	Granular casts
Cystic kidney disease	PCR 200 to 1,000	+					
Diabetic kidney disease, earlier stages	ACR 30 to 300						
Diabetic kidney disease, later stages	ACR > 300 or PCR > 500 to 1,000						
Hereditary nephritis or disease of small vessels (microangiopathy)	PCR < 1,000	+				+	+
Hypertensive disease	PCR 200 to 1,000						
Noninflammatory glomerular disease (minimal change disease, focal segmental glomerulosclerosis, associated with neoplasm)	PCR > 1,000						
Proliferative glomerulonephritis (systemic lupus erythematosus, vasculitis, infections) or hereditary nephritis	PCR > 500	+	+	±	±		
Tubulointerstitial nephritis	PCR 200 to 1,000	±		+	+		

ACR = albumin/creatinine ratio; PCR = protein/creatinine ratio; RBCs = red blood cells; WBCs = white blood cells; + = abnormality present; ± = abnormality may or may not be present.

*—Detection of RBC casts requires careful preparation and thorough and repeated examination of sediment from freshly obtained urine specimens. Even under ideal conditions, RBC casts may not always be detected in patients with proliferative glomerulonephritis.

Adapted with permission from Levey AS, Perrone RD, Madaio MP. Laboratory assessment of renal disease: clearance, urinalysis and renal biopsy. In: Brenner BM, Rector FR. The Kidney. Philadelphia, Pa.: W.B. Saunders; 1991:919-968, with additional information from references 9 and 11.

Table 10. Additional Clinical Interventions for Adults with CKD

Clinical finding	CKD stage	Parameters to assess	Frequency of evaluation
Anemia	All	Complete blood count with differential; reticulocyte count; iron, ferritin, and transferrin levels	Once per year (more frequently if abnormal)
Malnutrition	3 to 5	Weight, serum albumin level, dietary history	Every 6 to 12 months in stage 3; every 1 to 3 months in stages 4 and 5
Metabolic bone disease	3 to 5	Alkaline phosphatase level	Once in stage 3; every 12 months in stages 4 and 5
		Calcium and phosphorus levels	Every 6 to 12 months in stage 3; every 3 to 6 months in stage 4; every 1 to 3 months in stage 5
		Consider duel energy x-ray absorptiometry	No routine testing
		25-hydroxyvitamin D level	Once, then as indicated
		Parathyroid hormone level	Once, then as indicated in stage 3; every 6 to 12 months in stage 4; every 3 to 6 months in stage 5
Neuropathy	3 to 5	Paresthesias, mental status, sleep disturbances (e.g., restless legs syndrome); consider sleep study and nerve conduction study	As indicated
Reduced level of functioning and well-being	3 to 5	Health literacy assessment, social support, standardized self-administered instruments (e.g., Dartmouth-Northern New England Primary Care Cooperative Information Project charts, Duke Health Profile, 36-item Medical Outcomes Study [SF-36], Kidney Disease Quality of Life scale)	Once, then as indicated

CKD = chronic kidney disease.

Information from references 9, 30, and 31.

Table 11. Indications for Nephrology Referral

Acute, complex, or severe cardiovascular disease

Anemia of CKD

Bone and mineral disorder of CKD

Difficult to manage adverse effects of medications

Hyperkalemia (potassium level > 5.5 mEq per L [5.50 mmol per L] despite treatment)

Refractory proteinuria (urinary protein/creatinine ratio > 500 to 1,000 mg per g or urinary albumin/creatinine ratio > 300 mg per g)

Resistant hypertension (target blood pressure not achieved with use of at least three antihypertensive drugs)

Stage 4 CKD (estimated GFR < 30 mL per minute per 1.73 m²)

Unexplained decrease in estimated GFR > 30 percent over four months

CKD = chronic kidney disease; GFR = glomerular filtration rate.

Information from references 9 and 15.

Indications for Nephrology Referral

Nephrology consultation is indicated when the estimated GFR is less than 30 mL per minute per 1.73 m², or earlier if necessary (Table 11).[9,15] Partnership between primary care physicians and nephrologists is key to successful CKD management. The National Kidney Foundation's suggested multidisciplinary clinical action plan for CKD is available at http://www.kidney.org/professionals/KDOQI/cap.cfm.

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