Improving Outcomes for Patients with Chronic Kidney Disease: Part 1

Identifying CKD and slowing disease progression: a clinical review.

ABSTRACT: The burden of chronic kidney disease (CKD) is rising both in this country and worldwide. An estimated 10% to 15% of U.S. adults are currently living with CKD. Reducing the CKD burden requires a systematic, interdisciplinary approach to care. The greatest opportunities to reduce the impact of CKD arise early, when most patients are being followed in primary care; yet many clinicians are inadequately educated on this disease. Nurses are well positioned to facilitate the implementation of collaborative care. This two-part article aims to provide nurses with the basic information necessary to assess and manage patients with CKD. Part 1 offers an overview of the disease, describes identification and etiology, and discusses ways to slow disease progression. Part 2, which will appear next month, addresses disease complications and treatment of kidney failure.

Keywords: chronic kidney disease, collaborative care, end-stage renal disease, interdisciplinary care, kidney disease

The burden of chronic kidney disease (CKD) is rising, both in the United States and worldwide.[1,2] Recent estimates indicate that between 10% and 15% of U.S. adults may have CKD.[3,4] More than half a million Americans have kidney failure treated by dialysis or transplantation (also known as end-stage renal disease [ESRD]), with the incidence of ESRD more than three times higher in African Americans than in white Americans.[4] Recently published data from the Global Burden of Disease Study indicate that deaths from CKD worldwide rose 32% between 2005 and 2015.[1]

Reducing the CKD burden requires a systematic, interdisciplinary approach similar to that described by the chronic care model,[5] which has been implemented in managing a range of other chronic diseases, including diabetes and chronic lung disease. Among CKD patients, interdisciplinary care models have been associated with delayed disease progression[6]; improved metabolic status at the time of dialysis initiation[7]; shorter hospital stays[7]; and reductions in unplanned urgent dialysis, cardiovascular events, and infections.[7] The greatest opportunities to reduce the impact of CKD arise early, when most patients are being followed in primary care. Although evidence-based guidelines for managing CKD are available,[8,9] implementation of recommended care is poor.[4] Many clinicians feel inadequately educated on disease basics,

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including diagnostic tests, such as the glomerular filtration rate (GFR) and urine albumin level; the progressive nature of CKD; and the transition to ESRD.[10]

An effective collaborative approach to care for CKD patients will address disease management, provide nutritional counseling, address the emotional and educational needs of patients and families, and promote self-management. Nurses are well positioned to facilitate the health care team's implementation of such care. This two-part article will provide nurses with the basic information necessary to assess and manage patients with CKD. Part 1 offers an overview of kidney physiology, describes disease identification and etiology, and discusses ways to slow disease progression. Part 2, which will appear next month, addresses disease complications and treatment of kidney failure.

REVIEW: KIDNEY PHYSIOLOGY

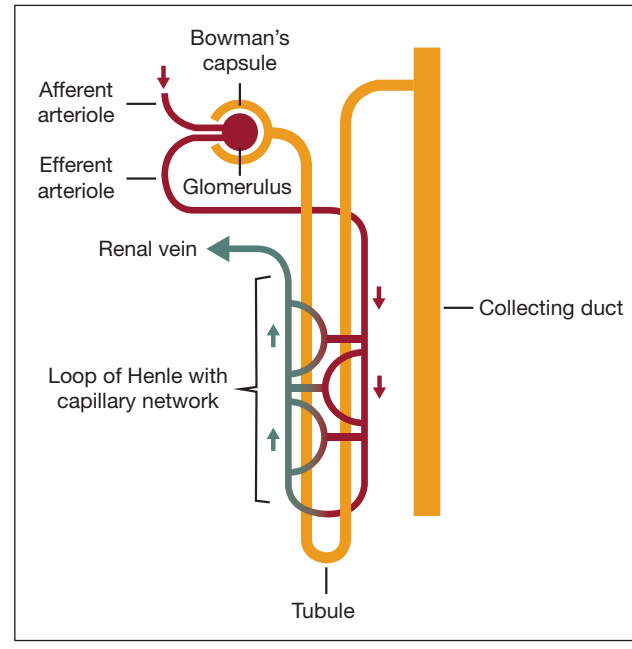
The kidneys function to maintain homeostasis (metabolic balance) in the body. They control blood composition and volume by maintaining stable concentrations of inorganic anions, including sodium, potassium, and calcium. They also maintain the blood's acid–base balance and remove metabolic wastes for excretion through the bladder and urethra.

Kidneys also have endocrine and metabolic functions. They produce renin, which helps maintain vascular volume, and erythropoietin, which helps maintain red blood cell volume. Other vital processes, including the conversion of 25-hydroxyvitamin D to active vitamin D, gluconeogenesis, and the metabolism of drugs and endogenous substances such as insulin, also occur in the kidney.

Most people have two kidneys. Each kidney consists of approximately 1 million functioning units called nephrons. Blood flows into each nephron through the glomerulus, a cluster of capillaries that serves as the filter of the nephron. Filtrate from the glomerulus flows into a cup-like structure known as Bowman's capsule, then through the proximal tubule, the loop of Henle, and the distal tubule. This series of tubules modifies the filtrate primarily by reabsorbing water and needed electrolytes into the bloodstream through the arteriovenous capillary bed, which surrounds the tubules. The modified filtrate (urine) then flows into the collecting duct, which joins larger and larger ducts and eventually drains into the renal pelvis. From the renal pelvis, the urine drains through the ureter into the bladder. (See Figure 1.)

Each glomerulus is itself supplied by an arteriolar capillary involving an afferent arteriole, which carries blood into the glomerulus, and an efferent arteriole, which carries blood away. Both have a muscular layer that allows for variable tone. The tone of the afferent and efferent arterioles determines the pressure within the glomerulus, allowing changes to the filtration rate. Various factors can influence such tone. For example, both angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) decrease efferent arteriolar tone, reducing glomerular pressure.

Figure 1. The Nephron



Blood flows into the nephron through the glomerulus. Filtrate from the glomerulus flows into Bowman's capsule, then through the proximal tubule, the loop of Henle, and the distal tubule, a series of tubules that modifies the filtrate primarily by reabsorbing water and needed electrolytes into the bloodstream. The modified filtrate (urine) then flows into the collecting duct and eventually drains into the renal pelvis. All figures courtesy of the National Kidney Disease Education Program and the National Institute of Diabetes and Digestive and Kidney Diseases.

IDENTIFYING CKD

CKD is typically a progressive disease. Because the millions of nephrons within each kidney constitute a considerable physiologic reserve, the slow nephron loss that occurs in most forms of CKD may not be noticeable until significant kidney function is lost. In the early stages of the disease, most patients have no symptoms. While urine volume usually doesn't change, urine composition does. The only way to identify early-stage CKD is through laboratory testing.

CKD has been defined by the Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice

guideline as "abnormalities of kidney structure or function, present for more than three months, with implications for health."[8] CKD can be diagnosed based on evidence of reduced function (reduced GFR) or kidney damage, or both.[8] Markers of kidney damage include certain pathologic abnormalities revealed on histologic studies, electrolyte abnormalities associated with renal tubular disorders, structural abnormalities revealed on imaging studies, a history of abnormal biopsy or kidney transplantation, and urine sedimentation abnormalities such as hematuria.[8] But in most cases, kidney damage presents as proteinuria or, more specifically, albuminuria.

CKD is detected and monitored by assessing kidney function using the estimated GFR (eGFR) and by assessing kidney damage using the urine albumin-to-creatinine ratio (UACR). Accordingly, CKD is specifically defined as an eGFR of less than 60 mL/min/1.73 m^2 or a UACR greater than 30 mg/g, or both, for at least three months.[8] Kidney failure is typically defined as an eGFR of less than 15 mL/min/1.73 m^2.[8]

Because CKD is often asymptomatic in the early stages, its presence may not be obvious to the patient until the disease has advanced. Some patients may have trouble accepting a CKD diagnosis in the absence of symptoms. This may be exacerbated by fear associated with the diagnosis,[11] which may cause patients to avoid education or care.

GFR. The GFR reflects total filtration in all functioning nephrons. To put GFR in context, consider that the cardiac output is about 6 L/min in a healthy person. Approximately 20% of the cardiac output—about 1.2 L/min—goes to the kidneys. However, the kidneys filter plasma rather than whole blood. Plasma accounts for about 50% of blood volume, or about 600 mL/min of the cardiac output. The kidneys filter about 20% of the plasma that passes through the glomerulus, at a rate of about 120 mL/min in a healthy person.

It isn't feasible to routinely measure GFR in the clinical setting. Direct GFR measurement is generally restricted to research settings. Instead, clinicians calculate an eGFR using an estimating equation. Results over 60 mL/min/1.73 m^2 cannot reliably be distinguished from normal because of the limitations of the estimating equations,[12] and thus are generally reported as normal.

The two most common GFR estimating equations—the Modification of Diet in Renal Disease (MDRD) Study equation[13] and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation[12]—are based on serum creatinine levels. Creatinine is a waste product of muscle metabolism that is excreted by the kidneys. In general, higher serum creatinine levels reflect lower kidney function. However, because muscle mass—and therefore serum creatinine levels—vary across age, sex, and race, mild to moderate kidney injury is poorly inferred from serum creatinine alone. For example, a creatinine level of 1.2 mg/dL in a 28-year-old African American man reflects an eGFR in the normal range of greater than 60 mL/min/1.73 m^2. However, the same serum creatinine level in a 78-year-old white woman reflects a significantly reduced eGFR of 43 mL/min/1.73 m^2. To account for this variation, both the MDRD Study and CKD-EPI equations include age, sex, and race as variables.[12, 13] The resulting estimate is normalized to an average body surface area of 1.73 m^2.[12, 13]

It's worth noting that creatinine-based eGFRs based on MDRD Study or CKD-EPI equations have significant limitations. Creatinine-based eGFRs do not accurately reflect kidney function in people with changing creatinine levels, as occurs in acute kidney injury, or in those who have greatly increased or decreased muscle mass, as occurs in cachexia.[12, 13] Moreover, certain medications (for example, trimethoprim) may alter serum creatinine without actually changing the GFR.

In clinical care, it's important to remember that eGFR is not actual GFR. Population-based estimating equations like the MDRD Study and CKD-EPI equations were developed through analysis of clinical data for large groups of people in studies in which GFR was measured. Applying these equations to a given patient's clinical data provides only an estimate of that patient's GFR. Current estimating equations provide eGFRs that have about an 85% chance of being within 30% of measured GFR.[12, 14]

Other GFR estimating equations have been developed that may be more valid in specific subpopulations.[15, 16] And newer equations that incorporate serum levels of markers such as cystatin C are in development.[17] Cystatin C, a protein produced by all nucleated cells, isn't affected by diet or muscle mass; but standardized laboratory methods for measuring cystatin C have not been widely implemented.

Many clinicians find explaining GFR to patients daunting, but it needn't be; GFR isn't a complicated concept. The case study of Anna Lowry, a 49-year-old woman with CKD, will be used throughout this article for illustration, offering specific guidance in helping patients to better understand and manage their CKD. (See *Case Study: Addressing eGFR Results*; this case is a composite based on the authors' experience.)

The National Kidney Disease Education Program, a program of the National Institute of Diabetes and Digestive and Kidney Diseases, has valuable resources on CKD. For a clinical tool that can help nurses explain GFR and UACR to their patients, visit www.niddk.nih.gov and search using the phrase "Explaining Your Kidney Test Results."

UACR. In healthy people, most of the protein in the filtrate is reabsorbed by the nephron tubules, leaving very small amounts in the urine. But in people with CKD, glomerular permeability increases, allowing

protein to cross the filtration barrier in greater quantities than normal, resulting in protein in the urine.[18] Because elevated protein levels in the tubules can exacerbate kidney damage, proteinuria may be not only a sign of kidney damage but also a cause.[19]

Albumin is the predominant protein in the urine of people with CKD; because total protein measurement cannot be standardized, the urine albumin level is the preferred measure of kidney damage. Elevated urine albumin is a marker for glomerular disease, as well as cardiovascular disease (CVD),[20] and might also be a marker for generalized endothelial dysfunction.[21, 22]

Since urine albumin levels are subject to variation in urine volume and concentration, urine albumin is best assessed by determining the UACR using a spot (random) urine specimen. The UACR (also called the

Case Study: Addressing GFR Results

Anna Lowry, age 49, has type 2 diabetes and a history of gestational diabetes at age 30.

Problem list:
- Type 2 diabetes
- Hypertension
- Dyslipidemia
- Retinopathy

Family history: Both parents had diabetes; mother is on dialysis.

Social history: Teacher's aide, married, one son. No alcohol or tobacco use.

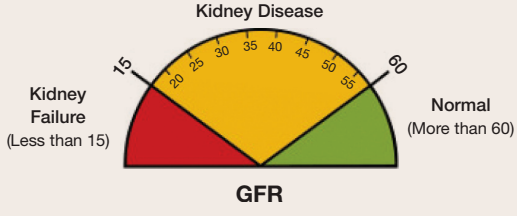
Medications:
- Insulin NPH/REG 70/30, 45 units twice daily
- Lisinopril 40 mg daily
- Simvastatin 40 mg daily
- Furosemide 20 mg daily
- Baby aspirin

Test	Initial	Reference Range* or Target
HbA_{1c}, %	10.1	< 8
Blood pressure, mmHg	138/67	< 140/90
LDL-C, mg/dL	146	0–100
HDL-C, mg/dL	23	> 40
Triglycerides, mg/dL	198	< 150
Creatinine, mg/dL	1.1	0.8–1.3
eGFR, mL/min/1.73 m^2	**53**	**> 60**
UACR, mg/g	**pending**	**< 30**
Weight, lbs	176	

* Reference ranges may vary.

Ms. Lowry, a 49-year-old teacher's aide, has type 2 diabetes and presents today for a routine follow-up visit. She is married with one son, and had gestational diabetes at age 30. There is a family history of diabetes on both sides, and her mother is currently on dialysis. Ms. Lowry does not use alcohol or tobacco. Her blood pressure is 138/67 mmHg. Her initial laboratory test results show that her glycated hemoglobin level is 10.1%, her low-density lipoprotein cholesterol level is 146 mg/dL, and her estimated glomerular filtration rate (eGFR) is 53 mL/min/1.73 m^2.

Ms. Lowry's primary care physician tells her that she had "an abnormal kidney test result" and says he wants to "run a few more tests to check on her kidneys." On hearing this, she becomes very concerned. She expresses fear that she will need dialysis, and tells the nurse, "I don't want to end up like my mother."



The nurse listens to Ms. Lowry's concerns and acknowledges her fears. Using the GFR dial from the National Kidney Disease Education Program's *Explaining Your Kidney Test Results* handout, she explains that eGFR is an estimate of kidney function, and shows Ms. Lowry that her eGFR indicates that her kidney function is just slightly below normal. The nurse further explains that neither dialysis nor transplantation is necessary until the eGFR reflects kidney failure (below 15 mL/min/1.73 m^2). She lets Ms. Lowry know that the additional tests will help her health care team understand how much kidney damage has occurred and determine whether her kidney function is staying the same or worsening.

microalbumin test, the urine albumin test, and the microalbumin-to-creatinine ratio) is usually reported as milligrams of albumin per gram of creatinine. Because most people excrete creatinine at a rate of about one gram per day, the UACR provides a good estimate of 24-hour urine albumin excretion. Thus the UACR in a spot specimen is assumed to reflect the UACR in a 24-hour collection specimen.

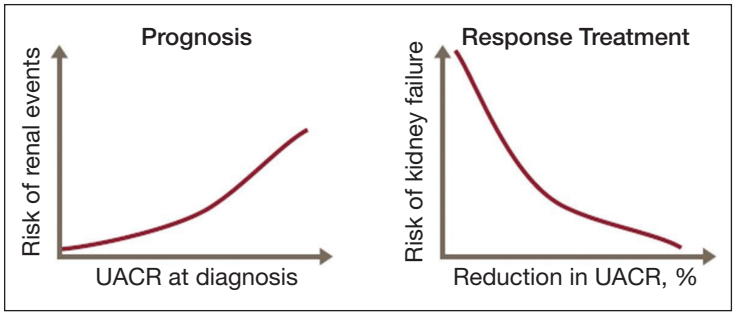
The urine albumin level varies continuously. The risk of associated adverse outcomes increases as this level rises. Historically, the terms *microalbuminuria* (UACR between 30 mg/g and 300 mg/g) and *macroalbuminuria* (UACR above 300 mg/g) have been used to categorize urine albumin levels. But these categories are based on the limited sensitivity of the traditional urine dipstick, which becomes positive for albumin at about 300 mg/g, rather than on any physiologic change that occurs at 300 mg/g. Over time, these terms are likely to fall out of use.

As with eGFR, explaining UACR to patients can help them better understand their disease and promote self-management. (See *Case Study: Addressing UACR Results*.) Increased albuminuria is often the first sign of CKD. Nurses are sometimes the first to identify a patient's CKD on the basis of persistent albuminuria. If a nurse encounters a patient with albuminuria who has not been diagnosed with CKD, the nurse should ask the patient what her or his primary care provider has said about the patient's kidneys. Often the answer is "nothing." The primary care provider may mention the kidneys, along with a list of other concerns, but with little explanation.

Diabetic kidney disease. Although a kidney biopsy is the best way to identify the cause of CKD, biopsies aren't always performed, especially in people with diabetes. In general, a clinical diagnosis of diabetic kidney disease is made if the patient with diabetes has[8, 9]

- a UACR greater than 300 mg/g, or
- a UACR greater than 30 mg/g, along with diabetic retinopathy or with type 1 diabetes for at least 10 years.

Figure 2. UACR, Risk of Renal Events, and Risk of Disease Progression



Data from the Chronic Renal Insufficiency Cohort Study (left) show that the risk of adverse kidney events (loss of half of estimated glomerular filtration rate, dialysis, or death) increases with increased levels of urine albumin at diagnosis.[32] Data from the RENAAL (Reduction in End Points in Noninsulin-Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan) Study (right) show that lowering urine albumin through treatment with a renin–angiotensin–aldosterone system antagonist may reduce the risk of chronic kidney disease progression to kidney failure.[33] UACR = urine albumin-to-creatinine ratio.

SLOWING DISEASE PROGRESSION

Strategies to slow the progression of CKD include controlling blood pressure and reducing albuminuria.[8] Additional measures may include making dietary modifications,[23, 24] managing diabetes,[25, 26] and avoiding acute kidney injury.[27]

Controlling blood pressure. Reducing blood pressure may be the most effective intervention to slow CKD progression. Despite the availability of various antihypertensive drugs, blood pressure remains poorly controlled in many patients with CKD; and as GFR decreases, the likelihood of uncontrolled hypertension increases.[28]

Despite strong evidence supporting the need for blood pressure control in patients with CKD, consensus has yet to be reached on the ideal blood pressure target.[29] In 2014, the Eighth Joint National Committee recommended a target of less than 140/90 mmHg for people with CKD.[30] But more recent results from the Systolic Blood Pressure Intervention Trial (SPRINT) suggest that an even lower target might be optimal.[31] Among the more than 2,600 patients who had CKD at baseline, those treated to a systolic blood pressure target of less than 120 mmHg had lower rates of cardiovascular events, though not renal outcomes, compared with those treated to a target of less than 140 mmHg. No patients with diabetes were included in SPRINT.

Reducing albuminuria. An elevated urine albumin level at the time of CKD diagnosis was associated with an increased risk of adverse kidney events in the Chronic Renal Insufficiency Cohort Study.[32] This risk was shown to decrease when albuminuria was reduced following treatment with an ARB in the RENAAL (Reduction in End Points in Noninsulin-Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan) Study.[33] (See Figure 2.[32, 33])

There are several known risk factors for albuminuria. Hypertension,[34, 35] diabetes,[34, 35] smoking,[34, 36] obesity,[34, 35] high sodium intake,[37, 38] excessive protein intake,[39] hyperlipidemia,[34, 35] and chronic inflammation[40] are associated with increased albuminuria. Aside from treatment with renin–angiotensin–aldosterone system (RAAS) blockers—which include ACE inhibitors and ARBs—interventions to reduce albuminuria include controlling blood pressure[41] and lowering sodium intake.[42, 43] Planned weight loss,[44] reducing excessive protein intake,[39] and smoking cessation[45] may also help reduce albuminuria.

Case Study: Addressing UACR Results

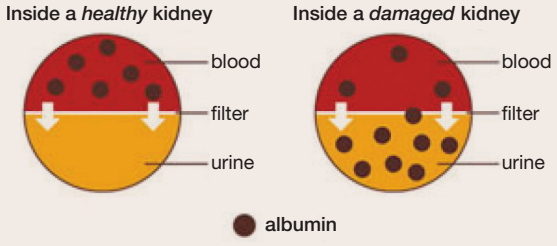
Problem list:
- Type 2 diabetes
- Hypertension
- Dyslipidemia
- Retinopathy
- **Albuminuria**

Medications:
- Insulin NPH/REG 70/30, 45 units twice daily
- Lisinopril 40 mg daily
- Simvastatin 40 mg daily
- Furosemide 20 mg daily
- Baby aspirin

Test	Initial	Reference Range* or Target
HbA_{1c}, %	10.1	< 8
Blood pressure, mmHg	138/67	< 140/90
LDL-C, mg/dL	146	0–100
HDL-C, mg/dL	23	> 40
Triglycerides, mg/dL	198	< 150
Creatinine, mg/dL	1.1	0.8–1.3
eGFR, mL/min/1.73 m^2	**53**	**> 60**
UACR, mg/g	**2,823**	**< 30**
Weight, lbs	176	

* Reference ranges may vary.

Additional testing reveals that Ms. Lowry's urine albumin-to-creatinine ratio (UACR) is nearly 3,000 mg/g. Even though her estimated glomerular filtration rate (eGFR) indicates only moderately reduced kidney function, her UACR is significantly elevated.



Using the National Kidney Disease Education Program's *Explaining Your Kidney Test Results* handout, the nurse explains to Ms. Lowry that the UACR shows how much protein is in her urine. She tells Ms. Lowry that her UACR result is above normal and that this is a sign of kidney damage. Ms. Lowry is upset by this news. The nurse comforts her and encourages her to continue sharing her concerns. When she's calmer, the nurse lets her know that high levels of protein in the urine can be predictive of a faster decline in kidney function. She also offers encouragement, explaining that there are many things the patient can do to slow further damage, such as managing diabetes and controlling blood pressure. The nurse advises Ms. Lowry to keep track of her eGFR and UACR test results over time, just as she does her glycated hemoglobin levels.

Treatment with RAAS blockers. Medications that block the RAAS can be helpful both in controlling blood pressure[46,47] and in reducing albuminuria[46,48] and are associated with slower CKD progression.[46,47,49] ACE inhibitors work by blocking the conversion of angiotensin I to angiotensin II; ARBs block the angiotensin II receptor.

Current guidelines for controlling blood pressure in patients with CKD recommend treatment with an ACE inhibitor or an ARB, either alone or in combination with other antihypertensive therapies.[8,30] After initiation of an ACE inhibitor or ARB, serum creatinine and electrolytes should be monitored.[8] Serum creatinine may increase as a result of lowered pressure within the nephron and a consequent drop in eGFR. Serum potassium levels may also rise, raising the risk of hyperkalemia.[50] In some cases, these drugs may have to be discontinued for safety reasons.[51] ACE inhibitors can cause a nonproductive cough in some patients; if this happens, an ARB may be substituted.

Pharmacists usually review medications with patients. Nurses can help clarify any areas of confusion and promote adherence to the regimen. Nurses may also be able to identify adherence issues that patients are embarrassed or reluctant to discuss with physicians. (See *Case Study: Medications*.)

Dietary management in patients with CKD is complex. Medical nutrition therapy with a registered

dietitian who is experienced in kidney disease is recommended, particularly as CKD progresses.

Reducing sodium intake. For patients with CKD, reducing sodium intake may improve blood pressure control, lower urine albumin levels, and increase the efficacy of RAAS blockers in managing both hypertension and albuminuria.[42, 43]

The average American consumes more than 3,400 mg of sodium per day—more than needed.[52] As with all dietary recommendations, the optimal amount of sodium must be individualized. That said, the *2015–2020 Dietary Guidelines for Americans*, issued jointly by the U.S. Department of Health and Human Services and the Department of Agriculture, recommends that adults and children ages 14 years and older limit sodium to less than 2,300 mg/day, and notes that adults with prehypertension or hypertension may benefit from further reducing sodium intake to 1,500 mg/day.[52] The current Nutrition Facts label on food items bases an item's "percent daily value" of sodium on the recommended limit of less than 2,400 mg/day, but will begin changing this to less than 2,300 mg/day starting in 2018.[53]

Most ingested sodium—about 75%—comes from processed and restaurant foods, with the rest coming from salt that is either naturally present or added during cooking or at the table.[54] Indeed, eating out may contribute substantially to daily sodium intake. According to the *2015–2020 Dietary Guidelines for Americans*, people ages two years and older get 21% of their daily sodium intake from burgers and sandwiches and another 14% from "protein foods," such as meat, poultry, eggs, and seafood.[52]

It's important for nurses to include sodium intake when discussing blood pressure management with patients. Teach patients to check food labels for sodium content. (For a useful guide, visit www.niddk.nih.gov and search using the phrase "Sodium: Tips for People with Chronic Kidney Disease.") Remind patients that the sodium content of sea salt is the same as that of table salt. Some people use salt substitutes in an effort to limit sodium. Salt substitutes containing potassium

Case Study: Medications

Notes:
- Ms. Lowry's eGFR is below 60.
- She is taking an ACE inhibitor.
- Her serum potassium level is normal.

Medications:
- Insulin NPH/REG 70/30, 45 units twice daily
- **Lisinopril 40 mg daily**
- Simvastatin 40 mg daily
- Furosemide 20 mg daily
- Baby aspirin

Test	Initial	6-Month Follow-Up	Reference Range* or Target
HbA_{1c}, %	10.1	9.4	< 8
Blood pressure, mmHg	138/67	150/92	< 140/90
Creatinine, mg/dL	1.1	1.3	0.8–1.3
eGFR, mL/min/1.73 m^2	**53**	**44**	**> 60**
UACR, mg/g	2,823	3,107	< 30
Potassium, mEq/L		**4.2**	**3.5–5**

* Reference ranges may vary.

Ms. Lowry is started on the angiotensin-converting enzyme inhibitor lisinopril. At her follow-up visit, her blood pressure is elevated, and the prescribing clinician increases her dosage.

The nurse asks Ms. Lowry whether she's taking lisinopril every day as prescribed. She reminds Ms. Lowry that taking it every day is one of the most important things she can do to slow progression of chronic kidney disease, because it helps to control blood pressure, which in turn helps protect the kidneys. She gives Ms. Lowry a blood pressure log for use in tracking her blood pressure at home.

The nurse also explains that increasing the lisinopril dosage can lead to unwanted complications, and gently asks again whether Ms. Lowry is taking the medication as prescribed. Ms. Lowry admits that she doesn't always take it because it makes her cough. The nurse thanks her for her honesty, and explains that the team will consider alternatives. The nurse flags the patient's lack of adherence and cough for the prescribing clinician, who decides to stop the lisinopril, switch Ms. Lowry to an angiotensin receptor blocker (ARB), and monitor her blood pressure closely for the next few weeks.

Ms. Lowry's serum potassium level is normal. The nurse makes a mental note to help her keep track of her potassium levels once she's taking the ARB regularly. She explains the symptoms of hyperkalemia (which include fatigue, weakness, numbness or tingling, nausea or vomiting, chest pains, and heart palpitations) to Ms. Lowry and encourages her to alert her primary care physician if any of these symptoms arise.

chloride are not recommended for patients with CKD because of the risk of elevated potassium levels. Similarly, many "reduced sodium" food products replace sodium chloride with potassium chloride, and should be avoided.

Reducing excessive protein intake. High protein diets are not recommended for people with CKD. Dietary protein—especially protein from animal sources—can temporarily increase both GFR and renal blood flow rate.[23] A higher intake of animal protein has been associated with elevated albuminuria in people with both hypertension and diabetes.[39] And dietary protein contains nitrogen, phosphorus, potassium, and metabolic acids that have to be filtered and excreted by the kidneys.

The optimal protein intake for people with CKD is still under debate. Most American adults eat more protein than recommended. According to data from the National Health and Nutrition Examination Survey (NHANES), the average protein intake for people ages 20 years and older in 2013–2014 was 70 g/day for women and about 98 g/day for men[55]—well above the Institute of Medicine's recommended 46 g/day for women and 56 g/day for men.[56] In general, the recommended daily protein allowance of 0.8 grams per kilogram of body weight[56] is considered adequate for people with CKD. For many patients, that level of protein intake may feel restrictive.

Managing diabetes. Glucose affects the kidneys in complicated ways.[57, 58] Glucose is filtered from the blood in the glomerulus and is almost completely reabsorbed in the proximal tubule. When the amount of glucose in the filtrate exceeds the tubules' ability to reabsorb it (this happens at levels above approximately 180 to 200 mg/dL), glucose appears in the urine. Because glucose is coabsorbed with sodium, higher filtered loads of glucose may result in volume expansion, resulting in increased blood pressure.

There is some evidence that good diabetes control may prevent CKD from developing in people at higher risk for the disease.[26] There is limited evidence that once CKD is present, tighter control of diabetes, compared with poorer control, slows CKD progression.[25, 26] Good blood glucose control has been shown to lower the incidence of albuminuria in patients with diabetes and has been associated with a reduced risk of declining GFR in people with both diabetes and CKD.[25, 26]

In patients with CKD, the glycated hemoglobin (HbA_{1C}) goal level should be individualized. In general, among recently diagnosed people with diabetes, lowering the HbA_{1C} level to less than 7% may reduce microvascular complications (such as CKD) and long-term macrovascular complications (such as coronary artery disease).[59] But less stringent control may be indicated in people with CKD who have "a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, [or] extensive comorbid conditions."[59] The risk of hypoglycemia may increase as CKD progresses because of higher levels of circulating insulin as a result of reduced insulin catabolism.[60] Unexplained improvement in HbA_{1C} levels, an increased frequency of hypoglycemic episodes, or both, may indicate that CKD is progressing. As CKD progresses, the insulin dosage may need to be reduced and certain oral diabetes medications (including first- and second-generation sulfonylureas, biguanides, thiazolidinediones, and others) may have to change.[8] It's important to explain any such changes to patients, as some people with diabetic kidney disease might take the discontinuation of diabetes medications to mean they no longer have diabetes.

In treating hypoglycemia through diet, it's important not to increase potassium and phosphorus or phosphate intake. (Phosphorus is a naturally occurring mineral; phosphates are food additives derived from phosphorus. The terms are sometimes used interchangeably.) Juices with a high potassium content (including orange, grapefruit, and prune juice) should be avoided; this is even more important in patients taking ACE inhibitors or ARBs, because of the increased risk of hyperkalemia. Cranberry juice, which has a low potassium content, is a safer choice. Remind patients that a serving of juice is four ounces. Drinks with high phosphate levels (including many colas) should also be avoided.[8] Light-colored colas generally have lower phosphate levels and may be a safer option. Glucose tablets are effective in treating hypoglycemia without adding potassium, phosphorus, or phosphate.

Avoiding acute kidney injury. Acute kidney injury is a rapid loss of kidney function, as defined by an absolute increase in serum creatinine of 0.3 mg/dL or more, a percentage increase in serum creatinine of 50% or more, or a reduced urine output of less than 0.5 mL/kg/hr for more than six hours.[61] CKD patients have increased susceptibility to nephrotoxic medications and are at high risk for acute kidney injury. Such injury may accelerate CKD progression.[27] Nephrotoxic medications—including nonsteroidal antiinflammatory drugs (NSAIDs), quinolones, β-lactam antibiotics, and sulfonamides—and intravascular administration of iodinated contrast agents must be used with caution in these patients.

Nurses can educate patients on ways to lower their risk of acute kidney injury, such as avoiding over-the-counter and prescription NSAIDs (see *Case Study: Avoiding NSAIDs*). Nurses may also be able to help clinics implement "sick day rules," which encourage patients to stop taking RAAS blockers during periods of vomiting or diarrhea, when they're at higher risk for becoming hypovolemic and thus for experiencing acute kidney injury.

MANAGING CVD

Because CVD is the leading cause of morbidity and mortality in people with CKD, managing CVD is also

Case Study: Avoiding NSAIDs

Notes:
- Ms. Lowry's eGFR is below 60.
- She is taking an ARB.
- Her serum potassium level is slightly above normal.
- Her serum bicarbonate level is low.

Medications:
- Insulin NPH/REG 70/30, 45 units twice daily
- **Losartan 100 mg daily**
- Simvastatin 40 mg daily
- Furosemide 20 mg daily
- Baby aspirin

Test	Initial	6-Month Follow-Up	12-Month Follow-Up	Reference Range* or Target
HbA_{1c}, %	10.1	9.4	8.7	< 8
Blood pressure, mmHg	138/67	150/92	136/77	< 140/90
Creatinine, mg/dL	1.1	1.3	1.6	0.8–1.3
eGFR, mL/min/1.73 m^2	**53**	**44**	**34**	**> 60**
UACR, mg/g	2,823	3,107	3,542	< 30
Potassium, mEq/L	--	**4.2**	**5.1**	**3.5–5**
HC03, mEq/L	--	--	**19**	**21–32**

* Reference ranges may vary.

Six months later, after a trip to the ED for a sprained ankle, Ms. Lowry comes in for her regular checkup. The nurse notices that Ms. Lowry's estimated glomerular filtration rate has decreased, her serum potassium level is borderline, and her serum bicarbonate level is low for the first time. The nurse sees that the ED physician prescribed Ms. Lowry 400-mg ibuprofen tablets for pain. The nurse has discussed nonsteroidal antiinflammatory drugs (NSAIDs) with Ms. Lowry in the past, and now asks about the ibuprofen prescription. Ms. Lowry reports that she knows she isn't supposed to take ibuprofen, but was too nervous to go against the ED physician's recommendation.

The nurse reminds Ms. Lowry that NSAIDs can be very harmful to her kidneys and gives her a list of common NSAIDs that should be avoided. She talks with Ms. Lowry about how important it is to speak up about one's health—even to physicians. Using role play, the nurse works with Ms. Lowry to help build her self-confidence in doing so.

Ms. Lowry returns for a follow-up visit one week later, after stopping NSAIDs. Her serum potassium and bicarbonate levels have returned to within normal ranges.

critical.[4] Patients with CKD have high prevalences of traditional CVD risk factors, including hypertension, diabetes, hyperlipidemia, tobacco use, older age, and inflammation.[62] Many comorbid conditions seen in people with CKD, including albuminuria,[20, 35, 40] anemia,[63] and abnormal calcium and phosphorus metabolism,[64] are also associated with increased CVD risk. NHANES data demonstrate that lipid abnormalities are associated with declining GFR.[62]

Statins are effective in reducing cholesterol synthesis in the liver, and have been shown to significantly reduce all-cause cardiovascular mortality in people with CKD.[65] Although statins do not appear to slow CKD progression, they may reduce proteinuria.[65]

IDENTIFYING PATIENTS AT HIGH RISK FOR PROGRESSION

Not all patients with decreased eGFR or low-grade albuminuria will progress to kidney failure. It's important to identify and slow disease progression in patients at higher risk for such progression; these patients may be identified by higher levels of albuminuria,[66, 67] progressive decreases in eGFR,[67] and poorly controlled hypertension.[66] But the imprecision of biomarkers for kidney function and damage, as well as individual variations in how CKD progresses, suggests that determining a patient's risk of progression must incorporate a variety of clinical characteristics. Until validated algorithms are available, clinicians are cautioned against offering a predictive prognosis based on any single biomarker measurement.

Referral to nephrology. Many CKD interventions are similar to those used in diabetes (for example, glucose control) and will be familiar to primary care practitioners; and other important interventions, such as screening for comorbidities, can be handled in primary care settings. However, appropriate referral to a nephrologist is associated with better CKD outcomes.[68, 69] Yet many patients with CKD aren't referred to a nephrologist soon enough.[4] Indeed, some patients may not be referred until they need

urgent kidney replacement therapy (which includes dialysis and transplantation). Late referral has been associated with more rapid disease progression,[68,69] poorer health status at dialysis initiation,[70] higher mortality after starting dialysis,[68] and decreased access to kidney transplantation.[71]

Clinicians may consider referral to a nephrologist to help prepare patients for kidney replacement therapy, especially in cases when eGFR is less than 30 mL/min/1.73 m^2. Referral may also help clinicians address diagnostic challenges in cases with rapidly decreasing eGFR; manage CKD-related complications such as blood pressure, anemia, abnormal mineral metabolism, bone disorders, hyperkalemia, hyperphosphatemia, malnutrition, and secondary hyperparathyroidism; and prevent or manage acute kidney injury. ▼

For six additional continuing education activities on topics related to kidney disease, go to www.nursingcenter.com/ce.

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