Objective: To provide information on the role of pharmacists in nonsteroidal anti-inflammatory drug (NSAID) avoidance in high-risk patients.

Summary: Nonprescription analgesics such as ibuprofen and naproxen are widely used by Americans. These nonsteroidal anti-inflammatory drugs (NSAIDs) are available in large quantities in pharmacies and also in wholesale stores, gas stations, and convenience stores. In addition, more than 111 million people use prescription NSAIDs each year, including many older Americans. NSAIDs may seem innocuous, but they carry a significant risk of disrupting blood flow to the kidneys and thus precipitating acute kidney injury (AKI). Episodes of AKI can lead to costly hospitalizations and long-term consequences such as new-onset chronic kidney disease (CKD) or more rapid progression of existing CKD. Most cases of NSAID-induced AKI can be avoided by recognizing high-risk patients and counseling them on appropriate use of these medications. Community pharmacy–based NSAID counseling and education at the point of prescription dispensing or nonprescription purchase could complement and augment NSAID-induced AKI education provided by other members of the health care team to high-risk patients.

Conclusion: NSAID use is widespread and severely compromises effective renal perfusion in high-risk patients. The community pharmacist can play a pivotal role in NSAID avoidance education to prevent potential episodes of AKI that have long-term consequences for patients.
An estimated 36 million Americans use nonprescription analgesics on a daily basis, and more than 111 million nonsteroidal anti-inflammatory drug (NSAID) prescriptions are dispensed each year.1–2 NSAIDs are one of the most common medication classes inappropriately prescribed to older Americans.3

In primary care settings, NSAID prescriptions account for approximately 6% of prescriptions; however, NSAID exposure is likely much higher because of the use of non-prescription drug products.4 A recent analysis showed that among a cohort of 12,065 participants with documented kidney disease in the cross-sectional National Health and Nutrition Examination Survey, 5% reported using nonprescription NSAIDs regularly, and 66.1% of those patients had used these agents for 1 year or longer.5

NSAIDs such as ibuprofen and naproxen are widely available in large quantities in pharmacies and also in wholesale stores, gas stations, and convenience stores. Patients may not report using nonprescription NSAID use during medication reviews with their physicians.

These highly accessible medications may seem innocuous, but they carry a significant risk of disrupting blood flow to the kidneys, precipitating acute kidney injury (AKI). Episodes of AKI can lead to costly hospitalizations.

Recently, the long-term consequences of AKI have been recognized; they include new-onset chronic kidney disease (CKD) or more rapid progression of existing CKD. Importantly, most cases of NSAID-induced AKI can be avoided by recognizing high-risk patients and counseling on the appropriate use of these medications.

**Chronic kidney disease: A public health epidemic**

CKD is a public health epidemic that is principally caused by diabetes mellitus and hypertension and, therefore, largely preventable. Approximately 26 million Americans have CKD, and another 20 million are at risk for developing the disease.6 The usual definition of CKD is based on either evidence of reduced kidney function or evidence of kidney damage. Since the kidney operates as a filter, a functional definition of CKD is based on a decrease in kidney function or filtration as evidenced by an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m².7,8

The eGFR is different than creatinine clearance (e.g., the Cockcroft and Gault method) because it is derived using an equation and measurement of actual glomerular filtration instead of being estimated from 24-hour urine creatinine clearance.9 However, it is important to note that eGFR is still not as accurate as measured GFR.

Two common equations are used to calculate the eGFR—the Modification of Diet in Renal Disease (MDRD) equation and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Online calculators for both equations are widely available. These equations use several variables to estimate GFR, including serum creatinine, age, gender, and race. The National Kidney Disease Education Program (NKDEP) of the National Institutes of Health (NIH) supported an initiative to include automatic eGFR reporting every time a serum creatinine is ordered to increase awareness of CKD. This reporting system has been adopted by a large number of laboratories in the United States.10

Evidence of kidney damage includes history of abnormal biopsy, an imaging study showing an absent or damaged kidney, or other markers of kidney abnormalities such as hematuria. However, in most cases, proteinuria is the finding that indicates kidney damage. Generally, a urine albumin:creatinine ratio greater than 30 mg/g is considered abnormal and may be considered evidence that a patient has CKD. An individual patient may have decreased kidney function, evidence of kidney damage, or both. In 2002, the Kidney Disease Quality Outcome Initiative proposed staging for kidney disease using the eGFR and markers of kidney damage. Recently, Kidney Disease Global Outcomes, a global organization that develops and implements evidence-based clinical practice guidelines in kidney disease, published a new staging approach that uses both eGFR and urine protein assessments to determine the prognosis of CKD.9 Table 1 lists the stages of CKD.

With approximately 45% of Americans receiving at least one prescription medication, approximately 10%–15% of patients picking up a prescription have some degree of CKD. Despite increased awareness regarding CKD over the past 10 years, the prevalence of CKD continues to rise at an alarming rate, with a projected 800,000 Americans requiring renal replacement therapies by 2020.5,7,11 Although national objectives for CKD were included for the first time in Healthy People 2010, minimal progress has been made in the screening, diagnosis, and treatment of CKD, especially in high-risk populations.12,13 By definition, CKD indicates that the kidneys are damaged and not functioning optimally. Thus, patients with CKD are at very high risk for drug-induced kidney injury, usually caused by medications that

<table>
<thead>
<tr>
<th>GFR category</th>
<th>GFR (mL/min/1.73m²)</th>
<th>Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>≥90</td>
<td>Normal</td>
</tr>
<tr>
<td>G2</td>
<td>60–89</td>
<td>Mildly decreased</td>
</tr>
<tr>
<td>G3a</td>
<td>45–59</td>
<td>Mildly to moderately decreased</td>
</tr>
<tr>
<td>G3b</td>
<td>30–44</td>
<td>Moderately to severely decreased</td>
</tr>
<tr>
<td>G4</td>
<td>15–29</td>
<td>Severely decreased</td>
</tr>
<tr>
<td>G5</td>
<td>&lt;15</td>
<td>Kidney failure</td>
</tr>
</tbody>
</table>

Adapted from reference 8.
affect blood flow through the kidneys (i.e., hemodynamic changes).

**Community-acquired acute kidney injury and CKD**

Community-acquired acute kidney injury (CA-AKI) is a rapid decline in kidney function that occurs in the outpatient setting assessed most commonly by creatinine clearance. Because of the rapidity of onset of AKI, symptoms may be worse than those experienced by patients with CKD. Early symptoms reported by patients can include fatigue, reduced urine output, and edema, especially in the lower extremities.14

Recent analyses have shown that the incidence of CA-AKI is higher than with hospital-acquired (HA) AKI, with rates among those hospitalized and discharged with the AKI ICD-9 code at nearly 80%.15 Although duration of hospitalization and mortality rate is lower among CA-AKI patients than in those with hospital-acquired AKI, recovery of renal function is incomplete and similar long-term outcomes on kidney function are apparent, with nearly 40% developing new-onset or progression of CKD.15-17

A recent cohort analysis of Veterans Affairs (VA) hospital patients in upstate New York found CA-AKI was 3.5 times higher than HA-AKI.16 In a large cohort study performed in the United Kingdom, significantly more patients with CA-AKI were diagnosed with new renal impairment within 14 months of the AKI episode. Approximately 15% of patients had no notation of renal impairment or planned follow-up at discharge.17 A retrospective analysis of AKI admissions at a VA hospital in Kentucky found that documented outpatient NSAID use was higher in the CA-AKI group than the HA-AKI (64 of 335 patients versus 10 of 87 patients).16

The most common causes of CA-AKI are listed in Table 2. The common element among these factors is that they all reduce blood flow through the kidneys. As noted earlier, patients who develop CA-AKI have poor outcomes similar to those with nosocomial AKI (e.g., from trauma or sepsis).15 Thus, strategies to limit the risk of CA-AKI are likely to have a substantial impact on health care costs and patient care.16

Until recently, serum creatinine was thought to return to baseline without long-term kidney complications in survivors of AKI.12 However, several large epidemiologic studies have shown that AKI is a strong risk factor for both new-onset CKD and faster progression of existing CKD.18,19 The relationship between AKI and CKD is affected by AKI severity, duration, and frequency. In fact, the Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Evaluation and Management of CKD states that “all people with CKD are considered to be at increased risk of AKI.”18

Conversely, AKI also is an important risk factor for the development of CKD.19 In patients older than 60 years who have normal age-related kidney function decline, there is a 3-fold to 8-fold, progressive, age-dependent increase in the frequency of CA-AKI.20,21 Recent data have also shown that AKI predisposes patients to progression and development of de novo CKD, with up to 70% of older patients who have an episode of AKI developing CKD within 2 years.72

NSAIDs have also been associated with more rapid progression of CKD. A large cohort of NSAID users 66 years of age or older from Alberta was followed for a median of 2.75 years. High-dose NSAID users had a 26% increase in the risk of having an eGFR decline of greater than 15 mL/min/1.73 m².22 This rate and extent of kidney function decline is clinically important and could result in progression to more advanced stages of CKD (Table 1).

In a nested case–control study of nearly 400,000 patients aged 50–84 years in the United Kingdom, current NSAID use was associated with a 3-fold higher risk of AKI. The risk of AKI declined among recent (31–365 days) and past (>365 days) users of NSAIDs (relative risk [RR], 1.71 and 1.26, respectively). The impact of NSAID discontinuation on AKI underscores the importance of education regarding appropriate NSAID use.23 An analysis of kidney function in 450 patients (35% of whom were older than 56 years) receiving NSAID prescriptions from a primary care center showed that only 14% of patients had kidney function determined before initiating therapy.4 This underscores that CKD and AKI risk are not part of routine assessment of those prescribed NSAIDs.

The NSAID Patient Safety Study (n = 687) evaluated NSAID use in primary care practices in Alabama. Among patients surveyed, 63% used both nonprescription and prescription NSAIDs, and only 13.7% patients recalled discussing NSAID use with a pharmacist. The authors concluded that pharmacists, pharmacy staff, and patients are missing an opportunity to avoid inappropriate and unsafe NSAID use.24

Provision of NSAID avoidance education to patients at risk of AKI is an important yet underappreciated counseling point for clinicians who care for these patients. Risk of AKI is underrecognized in the primary care setting.26 Community pharmacists are easily accessible to these patients and are uniquely suited to counsel on medications. Pharmacists also have access to medication profiles to identify high-risk patients and can monitor both prescription and nonprescription NSAID use.

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**Table 2. Diseases and medications that compromise kidney perfusion**

<table>
<thead>
<tr>
<th>Disease/Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Cirrhosis</td>
</tr>
<tr>
<td>Volume depletion (e.g., vomiting, diarrhea, aggressive diuresis)</td>
</tr>
<tr>
<td>ACE inhibitors and angiotensin II receptor blockers</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
</tr>
</tbody>
</table>

Abbreviation used: ACE, angiotensin converting enzyme.
Drug-induced kidney injury

The kidneys are a primary pathway for the elimination of many drugs and toxins. They receive 25% of cardiac output, which leads to extensive exposure to circulating drugs. Kidney hemodynamics can be significantly altered by commonly used medications. These factors result in enhanced susceptibility to drug-induced AKI.

Although there is no universal definition of CA-AKI, an increase in serum creatinine of 25%–30% above baseline values is a useful working definition. An estimated 15%–20% of hospitalized patients are diagnosed with AKI, depending on definitions applied. In an analysis of adverse events in hospitalized patients, kidney dysfunction accounted for 6.7% of drug-related complications. The true incidence of drug-induced CA-AKI is not known because of a lack of consistency in defining the condition and difficulty capturing data in the outpatient setting. The most common cause of drug-induced AKI in the community setting is disruption of kidney hemodynamics.

Precision of kidney hemodynamics

NSAIDs inhibit the cyclo-oxygenase (COX) enzyme. Inhibition decreases vasodilatory renal prostaglandins in the afferent arteriole of the glomerulus. The vasodilatory effect of renal prostaglandins is augmented by angiotensin II–mediated vasoconstriction at the efferent arteriole. This autoregulation of glomerular perfusion pressure maintains normal blood flow and glomerular filtration rate.

Patient case

A 56-year-old man is admitted to the cardiology service for volume overload and decompensated CHF. He has gained 10 kg in the past 2 weeks and has 4+ pitting edema on his legs. His medications on admission include lisinopril 40 mg orally once daily, metoprolol succinate 200 mg once daily, and furosemide 40 mg orally twice daily. Two days before admission, he started taking ibuprofen for neck pain developed from sleeping in his living room chair.

Pertinent laboratory data on admission include serum creatinine 3.2 mg/dL (normal 0.9–1.2 mg/dL, patient’s baseline 2.2 mg/dL), blood urea nitrogen 40 mg/dL (normal 8–18 mg/dL), and potassium 5.2 meq/L (normal 3.5–5.0 meq/L).

Which of the following factor(s) likely contributed to the patient’s acute rise in serum creatinine?

a. Decompensated CHF
b. Lisinopril
c. Furosemide
d. Ibuprofen
e. All of the above alternatives are correct.

Answer: e. All of the above alternatives are correct.

A number of kidney-compromising effects are leading to this patient’s fluid overload. Decompensated CHF leads to poor cardiac output and decreased perfusion to kidney, increasing renin production. Lisinopril dilates the efferent arteriole, which decreases glomerular capillary pressure. Furosemide decreases effective perfusion to the kidney. Ibuprofen, especially with altered kidney hemodynamics, will produce constriction of the afferent arteriole.

Collectively, all of these factors affect kidney hemodynamics and reduce blood flow to the kidney, reducing filtration and resulting in acute kidney injury.
NSAIDs reduce glomerular perfusion pressure by blocking prostaglandin-mediated vasodilation. Patients with hypertension, preexisting CKD, congestive heart failure (CHF), liver disease, or atherosclerosis, and older patients are especially dependent on vasodilatory prostaglandins to maintain kidney perfusion and are therefore more vulnerable to NSAID-induced blockade.30,31

Other commonly used medications that affect blood flow to the kidney can increase the risk of NSAID-induced AKI. Diuretics decrease intravascular volume, and angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) dilate the efferent arteriole, leading to increased risk of AKI when used with NSAIDs.

### Adverse effects of NSAIDs

NSAIDs are used extensively worldwide. NSAIDs have accounted for more than 70 million prescriptions and 30 billion nonprescription purchases annually (Table 3).32

Adverse kidney effects secondary to NSAID use occur in 1%–5% of patients; older patients are at higher risk for NSAID-induced AKI.30,32

COX-2–selective inhibitors appear to have similar renal adverse event profiles as nonselective NSAIDs.33 A study completed while rofecoxib was still being marketed examined the incidence of adverse kidney experiences with that agent when used for osteoarthritis versus ibuprofen, diclofenac, and nabumetone in more than 5,000 patients.34 The incidence of adverse renovascular events—including the development of edema, CHF, hypertension, and elevated serum creatinine—was similar between groups, with no reported cases of fulminate AKI. However, this trial excluded high-risk patients with CKD.

Acute kidney compromise can occur with a single dose of an NSAID, and the risk escalates with increasing doses and duration of use.35–37 Patients typically present with elevated serum creatinine and blood urea nitrogen (BUN), weight gain, and diminished urine output. Patients receiving NSAIDs may also present with kidney dysfunction after the development or exacerbation of an event that compromises kidney blood flow (e.g., CHF or gastroenteritis with severe vomiting and diarrhea). NSAIDs inhibit prostaglandin-mediated renin release, impairing the excretion of potassium, and thus hyperkalemia is also commonly found in patients presenting with NSAID-induced AKI.37

Irreversible kidney failure secondary to prolonged kidney ischemia can occur in high-risk patients in whom kidney dysfunction is not recognized.37

Patients with COX-2-inhibitor–induced AKI present with a clinical picture similar to AKI secondary to use of nonselective NSAIDs. Hyperkalemia, volume overload, and hyponatremia are common features of COX-2-inhibitor–induced AKI.33 The duration of COX-2 inhibitor use before patients present with AKI has been relatively short, within the range of 6–21 days.33

Prostaglandin inhibition by nonselective NSAIDs and COX-2 inhibitors rarely compromises kidney function in healthy patients receiving therapeutic doses of these agents on a short-term basis (e.g., 7–10 days).34 Patients at risk for AKI are those with diseases that reduce kidney perfusion and require a compensatory increase in kidney prostaglandins to promote vasodilation of the afferent arteriole to maintain adequate glomerular capillary pressure and filtration.

Older patients with age-related chronic kidney disease are at high risk for drug-induced AKI; the use of NSAIDs may increase the risk by up to 58% in patients older than 65 years.38 A greater risk of AKI has also been associated with total daily doses of ibuprofen of more than 1200 mg.38 Reported risk factors for COX-2-inhibitor–induced AKI are similar to NSAID-induced AKI, including age older than 60 years, CKD, and concomitant therapy with loop diuretics.39 ACE inhibition upregulates COX-2 expression, and patients dependent on angiotensin II for glomerular perfusion may be at increased risk of AKI when receiving concomitant ACE

<table>
<thead>
<tr>
<th>Medications</th>
<th>Trade names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celecoxib</td>
<td>Celebrex</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>Cataflam, Voltaren, Arthrotec (combined with misoprostol)</td>
</tr>
<tr>
<td>Diflunisal</td>
<td>Dolobid</td>
</tr>
<tr>
<td>Etodolac</td>
<td>Lodine, Lodine XL</td>
</tr>
<tr>
<td>Fenoprofen</td>
<td>Nalfon</td>
</tr>
<tr>
<td>Flurbiprofen</td>
<td>Ansaid</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Advil, Motrin, Tab-Profen, Vicoprofen (combined with hydrocodone), Combunox (combined with oxycode)</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>Indocin, Indocin SR</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>Orudis KT, Oruvail</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>Toradol</td>
</tr>
<tr>
<td>Mefenamic acid</td>
<td>Ponstel</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>Mobic</td>
</tr>
<tr>
<td>Nabumetone</td>
<td>Relafen</td>
</tr>
<tr>
<td>Naproxen</td>
<td>Aleve, Naprosyn, Anaprox, Anaprox DS, Naprelan, Naprapac (packaged with lansoprazole)</td>
</tr>
<tr>
<td>Oxaprozin</td>
<td>Daypro</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>Feldene</td>
</tr>
<tr>
<td>Sulindac</td>
<td>Clinoril</td>
</tr>
<tr>
<td>Meclofenamate sodium</td>
<td>Meclofenamate</td>
</tr>
<tr>
<td>Tolmetin sodium</td>
<td>Tolectin</td>
</tr>
</tbody>
</table>

Abbreviation used: NSAIDs, nonsteroidal anti-inflammatory drugs.
The majority of NSAID-induced AKI cases resolve promptly after discontinuation of the offending agent; however, hospitalization may be necessary to provide supportive management, particularly if volume overload or hyperkalemia are present. Rarely, hemodynamic-mediated deterioration of kidney function can lead to irreversible, long-term kidney failure, necessitating dialysis.

The majority of reported cases of COX-2-induced AKI also resolve quickly, within 2–8 days following discontinuation of the offending agent. Some patients may require short-term hemodialysis to manage hyperkalemia and volume overload. AKI can lead to development or progression of CKD; this link is often not fully appreciated in the outpatient setting.

### Counseling patients at high risk of AKI

#### Counseling strategies

Community pharmacists are in an optimal position to initiate counseling on NSAID avoidance in high-risk patients.

Even in the absence of objective kidney function data (e.g., serum creatinine or creatinine clearance), patient profiles can be reviewed for those medications used for conditions that predispose patients to AKI or that have been identified as high-risk for AKI when used with NSAIDs. These include antihypertensive medications, since hypertension is a risk factor for CKD. Certain antihypertensive agents (i.e., ACE inhibitors, ARBs, aliskiren, and diuretics) carry an additional risk of AKI secondary to their effects on kidney hemodynamics (Table 2). Antidiabetic medications (oral or injectable) indicate the presence of diabetes, the primary cause of CKD in the United States. Digoxin in conjunction with other relevant medications (e.g., ACE inhibitors or ARBs) is often used in patients with CHF, a strong risk factor for AKI. Chronic liver disease can also be identified by use of medications commonly used to treat complications of liver failure (e.g., lactulose or rifaximin).

Strategies for initiating counseling in patients at risk for AKI could include placing brightly colored notes on prescription bags of high-risk patients to alert pharmacy staff to engage those patients in education of kidney safety issues with NSAIDs. An opportunity to discuss nonprescription pain relievers could present itself when conducting nondispensing activities such as during nonprescription consults, pharmacy blood pressure clinics, or other similar programs in the community pharmacy. In busy community pharmacies, student pharmacists can also engage patients in NSAID education when they are performing nonprescription medication consultations.

Because time may be limited, a simple list of education tips can be presented to the patient or available as a handout in the prescription pick-up area (Table 4). When counseling patients who intend to use NSAIDs for pain management, the patient’s history and symptomatology should be evaluated so that alternative therapies can be considered, if needed. For acute musculoskeletal injuries, nonpharmacologic interventions such as heat and cold applied to the injury may be appropriate. For chronic pain issues that have been under evaluation by a primary care provider, patients can also be directed to community resources such as support groups.

Recommendation of acetaminophen must be balanced with consideration of appropriate patient populations (e.g., exclusion of patients with liver disease) and counseling on maximum daily dose. Reliance on acetaminophen at high doses for long periods of time rarely has been associated with papillary necrosis secondary to kidney ischemia, which can lead to CKD. The pharmacist should use clinical judgment to dictate whether the patient should be counseled to be evaluated by their primary care provider.

Patients who are persistent about using NSAIDs despite...
because of known observation by the investigators. One ca-
to the Hawthorne effect, inducing patient behavior changes
the patient. However, the design of this study was susceptible
pared with simple advice with written material delivered to
dose and overall prescription NSAID use at 6 months com-
helping patient education interventions.46

Counseling tools and approaches
Patient education about kidney disease and kidney-related
risks described above should be advised to use the lowest
possible dose for a maximum of 10 days.46 High-risk patients,
especially older ones, should be counseled to seek medical
attention within 12–24 hours if experiencing severe vomit-
ing or diarrhea while on therapy. Informing the primary care
provider of NSAID use in high-risk patients is warranted to
ensure that NSAID use can be factored into clinical decisions
should an acute rise in serum creatinine occur.

Health literacy is an important consideration for patient
education programs and success of educational interven-
tions. Health literacy encompasses patients’ reading, writ-
ing, and numeracy skills, as well as cultural experiences and
understanding of health concepts.51 Patients often have poor
knowledge and literacy regarding kidney-related issues.46
Several national organizations provide resources to assist
in engaging patients in discussion of kidney-related issues
(Table 5). NKDEP, established in 2000 by NIH’s National
Institute of Diabetes and Digestive and Kidney Diseases, works
to reduce the burden of CKD, especially in communities
most affected by the disease. NKDEP seeks to raise aware-
ness among people at risk for CKD about the need for test-
ing; educates people with CKD about how to manage their
disease; and provides information, training, and tools that
help health professionals better identify and manage pa-
tients with CKD.

Conclusion
NSAID use is widespread and severely compromises effec-
tive renal perfusion in high-risk patients. The community
pharmacist can play a pivotal role in NSAID avoidance edu-
cation to prevent potential episodes of AKI that have long-
term consequences for patients.

Table 5. Resources for counseling on CKD and AKI-related issues

<table>
<thead>
<tr>
<th>Organizations</th>
<th>Types of resources</th>
<th>Websites</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Kidney Disease Education Panel</td>
<td>Education on kidney disease, lifestyle management, medication use including NSAIDs</td>
<td><a href="http://nkdep.nih.gov/">http://nkdep.nih.gov/</a></td>
</tr>
<tr>
<td>Centers for Disease Control and Prevention</td>
<td>General kidney disease information for patients</td>
<td><a href="http://www.cdc.gov/">http://www.cdc.gov/</a></td>
</tr>
</tbody>
</table>

Abbreviations used: CKD, chronic kidney disease; AKI, acute kidney injury; NSAIDs, nonsteroidal anti-inflammatory drugs.


48. Cerulli J, Zeolla MM. Impact and feasibility of a community-pharmacist...
CPE assessment

Instructions: This exam must be taken online; please see “CPE information” for further instructions. The online system will present these questions in random order to help reinforce the learning opportunity. There is only one correct answer to each question.

1. Which of the following is involved with controlling blood flow through the kidney?
   a. Prostaglandins
   b. Epinephrine
   c. Aldosterone
   d. Estrogen

2. The kidneys are susceptible to drug-induced kidney injury because:
   a. They are responsible for most drug metabolism.
   b. They receive 25% of cardiac output.
   c. They do not clear water-soluble drugs.
   d. Their function is not affected by drugs.

3. Which of the following is an appropriate definition of acute kidney injury?
   a. Increase in blood urea nitrogen 25%–30% above baseline
   b. Patient requires dialysis
   c. Increase in serum creatinine 25%–30% above baseline
   d. Reduced urine output

4. NSAIDs affect kidney hemodynamics by:
   a. Increasing angiotensin-converting enzyme activity.
   b. Inhibition of afferent arteriole vasodilation.
   c. Increasing blood flow to the glomerulus.
   d. Constricting the efferent arteriole.

5. Congestive heart failure increases the risk of hemodynamically mediated acute kidney injury because:
   a. Effective perfusion to the kidney is decreased.
   b. Effective perfusion to the kidney is increased.
   c. Cardiac output is increased.
   d. Left ventricular mass is decreased.

6. In high-risk patients, NSAIDs can:
   a. Induce acute kidney injury only with long-term use.
   b. Induce acute kidney injury after a single dose.
   c. Prevent chronic kidney disease.
   d. Prevent acute kidney injury.

7. In comparison with nonselective NSAIDs, COX-2–selective inhibitors are:
   a. Not associated with a risk of acute kidney injury.
   b. Associated with higher risk of acute kidney injury.
   c. Associated with a similar risk of acute kidney injury.
   d. Safe in patients with chronic kidney disease.

8. The risk of NSAID-induced kidney injury increases with:
   a. Lower NSAID doses
   b. Concomitant use of ACE inhibitors
   c. Shorter duration of NSAID therapy
   d. Concomitant use of topical capsaicin

9. Consequences of AKI include which of the following?
   a. Increased mortality
   b. Increased cost of hospitalization
   c. Increased risk of kidney disease
   d. All of the above alternatives are correct.

10. Which of the following is true of NSAID-induced AKI?
    a. Most patients will require dialysis.
    b. The majority of cases occur in healthy individuals.
    c. The condition is always irreversible.
    d. Most cases can be avoided.

CPE information

To obtain 2.0 contact hours (0.2 CEUs) of CPE credit for this activity, you must complete the online Assessment, the Learning Evaluation, and Activity Evaluation. A Statement of Credit will be awarded for a passing grade of 70% or better on the Assessment. You will have two opportunities to successfully complete the CPE Assessment. Pharmacists who successfully complete this activity before December 1, 2017, can receive CPE credit. Your Statement of Credit will be available upon successful completion of the Assessment, Learning Evaluation, and Activity Evaluations and will be stored in your ‘My Training Page’ and on CPE Monitor for future viewing/printing.

CPE instructions:
1. Log in or create an account at pharmacist.com and select LEARN from the top of the page; select Continuing Education, then Home Study CPE to access the Library.
2. Enter the title of this article or the ACPE number to search for the article and click on the title of the article to start the home study.
3. To receive CPE credit, select Enroll Now or Add to Cart from the left navigation and successfully complete the Assessment (with randomized questions), Learning Evaluation, and Activity Evaluation.
4. To get your Statement of Credit, click “Claim” on the right side of the page. You will need to provide your NABP e-profile ID number to obtain and print your Statement of Credit.

Live step-by-step assistance is available Monday through Friday from 8:30 am to 5:00 pm ET at APhA Member Services at 800-237-APhA (2742) or by e-mailing education@aphanet.com.
11. Recent data show which of the following with regard to community-acquired AKI (CA-AKI) in comparison with hospital-acquired AKI?  
   a. CA-AKI occurs less frequently.  
   b. Both have similar long-term consequences.  
   c. Hospital-acquired AKI is more avoidable.  
   d. CA-AKI is well-defined.

12. A 62-year-old man with cirrhosis from alcohol abuse is taking propranolol 10 mg three times daily and rifaximin 500 mg twice daily. He has severe ascites and brings in a prescription for furosemide 40 mg twice daily. Which of the following place the patient at risk for CA-AKI?  
   a. Male gender  
   b. Propranolol use  
   c. Furosemide use  
   d. Liver disease diet

13. ACE inhibitors and angiotensin II receptor blockers increase the risk for NSAID-induced AKI by:  
   a. Increasing efferent arteriole vasoconstriction.  
   b. Increasing efferent arteriole vasodilation.  
   c. Increasing glomerular perfusion pressure.  
   d. Increasing protein in the urine.

Questions 14–16 pertain to the following case: The patient is an 87-year-old woman who lives in a nursing home. After a visit from her grandchildren, she develops severe gastroenteritis with vomiting and diarrhea. She has hypertension and chronic kidney disease. Her medications include verapamil 120 mg daily, lisinopril 40 mg once daily, and furosemide 40 mg twice daily.

14. Which of the following places this patient at risk for NSAID-induced AKI?  
   a. Change in usual daily routine  
   b. Diuretic use  
   c. Dehydration  
   d. Calcium-channel blocker use

15. On day 2, the patient develops a fever. What is the best approach to treating her fever?  
   a. Ibuprofen  
   b. Acetaminophen  
   c. Aspirin  
   d. Cold compresses

16. The patient’s blood pressure is 110/60 mm Hg, and she has a very dry mouth. Which best describes the basis of her symptoms and is considered a risk factor for AKI?  
   a. Hypovolemia  
   b. Heartburn  
   c. Well-controlled blood pressure  
   d. Diabetes

17. Which of the following is an important consideration for counseling patients on NSAID avoidance?  
   a. Education level  
   b. Advanced reading skills  
   c. Cultural experiences  
   d. All of the above alternatives are correct.

18. Which of the following is the most appropriate alternative for a patient at high risk for NSAID-induced AKI after an acute musculoskeletal injury?  
   a. Naproxen  
   b. Capsaicin cream  
   c. Ice applied to injury  
   d. Acetaminophen

19. Which of the following is not a relevant teaching point on NSAID avoidance?  
   a. NSAIDs are over-the-counter pain relievers.  
   b. Aspirin is a safer alternative to ibuprofen.  
   c. NSAIDs may not be good in people at risk for kidney disease because they may harm the kidneys by lowering blood supply to the kidney.  
   d. Adding NSAIDs to some blood pressure medicines can increase the possibility of harm to the kidney through decreased blood flow.

20. A 62-year-old man on multiple medications for diabetes and hypertension comes to the pharmacy to pick up his prescriptions. He wants to also purchase a bottle of 1,000 ibuprofen tablets and Advil PM. Which of the following would be an appropriate course of action?  
   a. No counseling is needed, as the patient does not have kidney disease.  
   b. Open a dialog about kidney safety risks of NSAIDs.  
   c. Refuse to allow purchase of the nonprescription products.  
   d. Counsel the patient on safe use of ibuprofen and Advil PM together.