

Assessment and management of chronic pain in the older adult

James W. Cooper and Allison H. Burfield

Abstract

Objective: To review the assessment and recommended management of mild to moderate chronic pain in the older adult.

Data sources: Medline search using the terms *pain*, *older adult*, and *analgesics*, current national guidelines, and authors' case experiences.

Data synthesis: Assessing pain in cognitively intact and impaired older adults is essential to safe use of psychoactive medications. Following the guidelines of the American Geriatrics Society for persistent pain in the older adult provides guidance to the safe use of analgesics and other psychoactive drugs. Dosing of acetaminophen should be limited to avoid liver toxicity, and topical analgesics are preferred for focal pain. Full-dose nonsteroidal anti-inflammatory drugs should not be used for more than short periods, in order to avoid gastrointestinal, renal, and cardiovascular complications. Potentially inappropriate opioid analgesics and safer alternatives are encouraged. A description of other psychoactive medications for neuropathic pain and the role of vitamin D and depression in chronic pain is provided.

Conclusion: The assessment of pain and use of analgesics in the older adult should benefit and not increase drug-related morbidity and mortality.

Keywords: Pain management, pain (chronic), elderly, opioid analgesics, medication management, adverse drug effects.

Pharmacy Today. 2010(May);50(5):31-43.

James W. Cooper, BPharm, PhD, BCPS, CGP, FASCP, FASHP, is Emeritus Professor and Consultant Pharmacist, College of Pharmacy, University of Georgia, Athens, and Clinical Assistant Professor of Family Medicine, Medical College of Georgia, Augusta. Allison H. Burfield, RN, PhD, is Assistant Professor, School of Nursing, College of Health and Human Services, University of North Carolina, Charlotte.

Correspondence: James W. Cooper, BPharm, PhD, BCPS, CGP, FASCP, FASHP, 1200 Colliers Creek Rd., Watkinsville, GA 30677. E-mail: jcooper@mail.rx.uga.edu

Published concurrently in *Pharmacy Today* and the *Journal of the American Pharmacists Association* (available online at www.japha.org).

Accreditation Information

Provider: American Pharmacists Association

Target audience: Pharmacists

Release date: May 1, 2010

Expiration date: May 1, 2013

ACPE number: 202-000-10-127-H01-P

CPE credit hours: 2.0 hours (0.2 CEUs)

ACPE activity type: Knowledge-based

Fee: There is no fee associated with this activity for members of the American Pharmacists Association. There is a \$15 fee for nonmembers



The American Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education as a provider of CPE. The ACPE Universal Activity Number assigned to the program by the accredited provider is 202-000-10-127-H01-P.

Disclosure: Other than continuing education programs developed by the authors or APHA and mentioned as resources for more information, the authors and APHA's editorial staff declare no conflicts of interest or financial interests in any products or services mentioned in this article, including grants, employment, gifts, stock holdings, or honoraria.

Learning objectives

At the completion of this activity, the pharmacist will be able to:

- Review the most common causes and comorbidities of chronic pain in the older adult.
- Discuss assessment techniques for pain assessment in the cognitively intact and impaired older adult.
- Differentiate the safest and most effective pharmacologic treatments for chronic pain in the older adult.
- Delineate inappropriate pain medications and detail alternatives to these medications to minimize the risk of adverse drug reactions to these medications.
- Estimate the risk of long-term full-dose NSAIDs and the significance of adverse drug reactions that occur with these agents.

Acute versus chronic pain: Overview

Most acute pain in the geriatric patient is from acute trauma (e.g., fall, contusion, incident fracture, fragility fracture, accident fracture) and may require multiple modalities of therapy, both pharmacologic and nonpharmacologic. Most chronic pain is from single to multiple causes, including osteoarthritis of hands, shoulders, hips, and knees, rheumatoid arthritis of the hands and spinal column, peripheral neuropathy from diabetes, peripheral vascular disease (PVD) or postherpetic neuralgia after acute herpes zoster (shingles) infection, muscle disuse or myopathy that may be associated with hypolipidemic agents, or incident/fragility fracture (e.g., vertebral compression and collapse sequelae or “failed back” syndrome).¹⁻³

The key first question in chronic pain management is to determine the frequency with which as-needed analgesics are used on a daily basis. If they are used, then setting up a regular schedule of the preferred first-step agent, acetaminophen (*N*-acetyl-*p*-aminophenol [APAP]), is important (Cooper JW, Burfield AH, unpublished observations).¹⁻⁹ APAP could be given as 500 to 650 mg four times a day or as 500 mg every 4 hours at 6:00 am, 10:00 am, 2:00 pm, 6:00 pm, and 10:00 pm, with the sixth dose saved for use if the patient wakes up during the night. The maximum daily dose should not exceed 2.6 g. APAP may be taken as eight doses of the 325-mg strength or five doses of the 500-mg strength. Often, patients or their caregivers state that APAP does not help their pain; however, a careful history usually will reveal that patients only took an occasional dose of APAP. When APAP is taken on a continual basis for 24 to 48 hours, marked relief of chronic pain typically results.¹

At a Glance

Synopsis: The current work reviews the assessment and management of chronic pain in the older adult. The latest American Geriatrics Society guidelines are used as an outline for appropriate medication use. Avoiding inappropriate drugs or drug combinations is essential to the pharmacists’ role in optimizing drug use in the older adult.

Analysis: *Visual analog scales can be used to assess pain in coherent patients, whereas nonverbal scales may be needed for cognitively impaired patients. Acetaminophen should be considered as initial and ongoing treatment of persistent pain, particularly musculoskeletal pain, because of its demonstrated safety and effectiveness. Because full-dose oral nonsteroidal anti-inflammatory drugs markedly increase fluid retention and blood pressure and risk of congestive heart failure, myocardial infarction, and stroke risk, they should be considered rarely and with extreme caution in selected patients. Potentially inappropriate medications, especially propoxyphene, should be avoided as much as possible.*

Case 1 and self-assessment questions

An 81-year-old man with mild to moderate osteoarthritis pain of the hands, hips, and knees complains to his pharmacist that he is “not helped at all” by APAP. You suspect that he has only tried single 325- to 500-mg doses once or twice a day. He is well oriented to time, place, and person.

Self-assessment questions

- 1. What do you do as your next step?**
 - a. Inquire about how he has been using APAP and whether any other analgesics are being used or are available for his use.
 - b. Recommend a continual schedule of 500 to 650 mg up to 2,600 mg/day for a 24- to 48-hour trial.
 - c. Ask the patient to call you back after a 2-day trial of continual APAP and report on how this has helped his pain.
 - d. All of the above alternatives are correct.
- 2. The patient states on recheck in 2 days that he takes 500 mg APAP four to five times a day but still has pain that has decreased his ability to perform his activities of daily living, including bathing, dressing, performing household chores, and walking his dog. What is your next recommendation?**
 - a. Topical nonsteroidal anti-inflammatory drug (NSAID) to focal pain areas
 - b. Glucosamine and chondroitin orally on a continual basis
 - c. Alternatives a and b and exercise as tolerated
 - d. Adding propoxyphene to his APAP

Answer key: 1. d; 2. c

For osteoarthritis-related pain, using daily glucosamine 1,500 mg and chondroitin 1,200 mg may decrease the need for oral analgesics beyond APAP given on a continual basis, but this regimen takes several weeks to have an effect. Controversy exists¹⁰ regarding whether glucosamine and chondroitin are of benefit, which may arise from several areas: a dearth of literature attesting to the value of glucosamine and chondroitin, inadequate dosing, inconsistent drug product bioavailability, and unrealistic patient expectations of how soon they will experience pain relief from glucosamine and chondroitin. Patients should be counseled to adhere to their drug regimen because results from glucosamine and chondroitin may take up to 1 month to appear. For focal pain (i.e., not diffuse or over large areas) of joints and muscles, also consider topical NSAIDs (creams, gels, or lotions [e.g., 1% diclofenac (Voltaren Gel—Novartis)]), then compounded ketoprofen gel 5% to 15% applied topically two to three times daily to focal affected areas. However, oral NSAID use should be avoided. Recent Food and Drug Administration (FDA) warnings on the liver toxicity from topical NSAIDs can be found at www.fda.gov/medwatch. For diffuse pain or pain over large areas of the skin, large amounts of topical NSAIDs should be avoided and opiates may be needed if pain is moderate to severe. Lidocaine cream (Lidoderm—Endo, Americaine—Heritage) or patch (Flector—

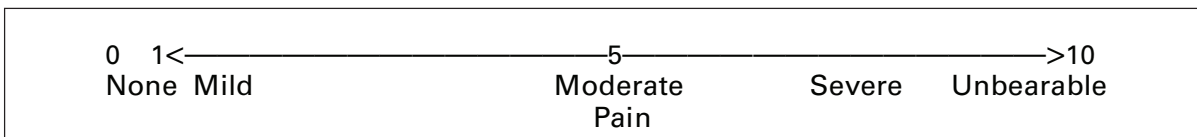


Figure 1. Visual analog scale for pain

King) and capsaicin cream (Zostrix—Hi-Tech) also may be useful for focal neuropathic pain, such as that seen in shingles postherpetic neuralgia and diabetic neuropathy of the hands and feet.¹ Do not spread NSAIDs or lidocaine cream, ointment, or gel over large areas of skin when pain is diffuse (i.e., covering large areas). Little to no evidence supports using topical glucosamine, chondroitin, or methylsulfonylmethane for focal or diffuse chronic pain.¹⁻³

Assessing pain

Visual analog scales (VASs; Figure 1) can be used to assess pain in coherent patients. Nonverbal scales (Figure 2) can be used for cognitively impaired (i.e., no orientation to time, place, or person) patients or those with mini-mental state exam⁴ scores less than 15 (possible 30 total) or global deterioration scale⁵ scores of 5 or more (1–7 scale).

Ask coherent patients to place their finger on the VAS or to tell you where they are on the VAS in relation to the worst (10) pain they have ever felt versus the faintest perceptible pain (1) or no pain (0). Another way to assess pain is that mild pain may require peripheral analgesics on an occasional basis but does not impair ones ability to function. Moderate pain requires life-style modifications and perhaps occasional opioid or narcotic analgesics. Severe pain is debilitating and requires peripherally acting (oral APAP, topical NSAIDs) and central nervous system (CNS)-active (narcotic/opioid analgesics) drugs. If the severe pain has a neuropathic origin (e.g., diabetic or postherpetic neuropathy), other usually neuroactive medications such as antidepressants (e.g., selective serotonin reuptake inhibitors [SSRIs]/serotonin–norepinephrine reuptake inhibitors [SNRIs], duloxetine) and/or anticonvulsants (e.g., pregabalin, gabapentin) may be needed in addition to the peripherally acting and CNS-active agents.¹⁻³

Patients may have mild to moderate or moderate to severe pain. The VAS may also be used to ascertain patients’ response to analgesics. For example, patients with osteoarthritis pain may state that their pain is 4 to 7 when not taking APAP and 2 to 4 when taking APAP.

Check nonverbal signs and symptoms (Figure 2) if patients have a diagnosis of dementia and are approaching 5 or more on a 1 to 7 global deterioration scale (i.e., little orientation to time, place, or person and requires assistance with activities of daily living, especially dressing, feeding, and toileting, or simply does not have orientation to time, place, and/or person).⁴

Case 2 and self-assessment questions

An 85-year-old patient with diagnosis of dementia taking mementine and donepezil has a history of osteoarthritis and three

fractures from falls while taking anxiolytics and antipsychotics that are now stopped. You receive a propoxyphene/APAP prescription from his caregiver but are reluctant to fill it as a result of past experiences with patients who get more confused and delirious when taking propoxyphene, and the drug is also on the “inappropriate drugs” list for older adults (Table 1).^{8,9}

Self-assessment questions

- 1. Which pain scale should be used?**
 - a. VAS
 - b. Nonverbal pain scale
 - c. Either alternative a or b is correct.
 - d. Neither alternative a nor b is correct.

- 2. Which analgesic should be started first if chronic pain is suspected?**
 - a. APAP
 - b. Oral NSAID
 - c. Topical NSAID
 - d. Oral opioid or narcotic

Answer key: 1. b; 2. a

Guidelines for appropriate assessment and treatment of pain

The key considerations for safe drug therapy for chronic pain in the older adult are best summarized by the recent final recommendations of the American Geriatrics Society (AGS).⁹ The AGS Panel on Pharmacological Management of Persistent Pain in Older Persons provided the recommendations listed below.

AGS recommendations for nonopioids

I. APAP should be considered as initial and ongoing pharmacotherapy in the treatment of persistent pain, particularly musculoskeletal pain, because of its demonstrated effectiveness and good safety profile (high quality of evidence, strong recommendation).

Propoxyphene
Indomethacin ^a
Ketorolac ^a
All full-dose NSAIDs for more than several days to 2 weeks
Pentazocine ^a
Meperidine ^a

Abbreviation used: NSAID, nonsteroidal anti-inflammatory drug.
^aAlso inappropriate in injectable dosage forms.
 Of note, propoxyphene may be scheduled to be removed from the market in the United States.²⁷

For those with cognitive impairment, observe patient at rest and with movement for the following:

1. Vocal nonverbal complaints: groans, moans, cries, gasps, sighs
2. Facial movements: grimaces, winces, furrowed brow, tightened lips, clenched teeth, distorted expressions
3. Bracing or holding on to side rails, bed, walkers, or canes or favoring affected area on movement
4. Restlessness to include constant changing of position, rocking, inability to keep still, akathisia-type movements; rule out tardive dyskinesia with abnormal involuntary movement scale⁶ if taking metoclopramide or antipsychotics
5. Rubbing or massaging affected areas with or without verbal complaints
6. Vocal complaints of discomfort or pain (e.g., "ouch," "that hurts") or abusive language when moved
7. Agitation and behavioral disturbances

First-step intervention. Acetaminophen intervention as a regularly scheduled medication at 2.5 g/day (e.g., 500 mg every 4 hours [6:00 am, 10:00 am, 2:00 pm, 6:00 pm, and 10:00 pm]) has been shown to markedly decrease CNVPB score, especially agitation behaviors.⁷

Note that a score of 6 or greater or agitation at rest or with movement may indicate need for regular schedule of acetaminophen intervention. Give 1 point for each "yes," whether at rest and/or with movement, and no points for "no."

At rest and/or with movement

1. Vocal nonverbal ____
2. Facial expressions ____
3. Bracing ____
4. Restlessness ____
5. Rubbing area ____
6. Vocal complaints ____
7. Agitation ____
- Total score ____ (0–14)

Medications currently taken (watch for psychotropics, which may mask pain):

Patient name Date Assessor name and notes

Figure 2. Checklist of CNVPBs¹

Abbreviation used: CNVPB, chronic nonverbal pain behavior.
 Figure 2 is not copyrighted; pharmacists can use in practice.

A. APAP absolute contraindications: liver failure (high quality of evidence, strong recommendation). Of important note, APAP is the leading cause of acute liver failure, especially in overdose, particularly unintended overdose. An FDA report from May 2009 suggested that products containing APAP carry stronger label warnings about the drug's potential for liver damage. Despite label changes and public awareness campaigns during the previous decade, an FDA working group stated that patients still might not be aware of the danger and may take multiple products that contain APAP or ingest the drug with alcohol.

"There is extensive evidence that hepatotoxicity caused by acetaminophen use may result from lack of consumer awareness that acetaminophen can cause severe liver injury," according to the report. The panel of outside advisers recommended to FDA that the name "acetaminophen" be displayed prominently on the package of any medication containing it. The group also suggested that the label warn patients to not take more than one acetaminophen-containing medication

(more information available at www.fda.gov/medwatch/acetaminophen).

Case 3 and self-assessment questions

A 79-year-old man taking APAP 650 mg four to six times a day for "joint pain" that was 5 to 6 on a 10-point VAS for pain (Figure 1) was seen by his community pharmacist on a home care visit to review his medications. The pharmacist also inquired about what the patient was taking for sleep and discovered that he was taking an additional 1,000 mg APAP with an antihistamine for sleep every night. The patient was noted by the pharmacist to have some pain under his right rib cage and suspected liver tenderness and was referred to his primary care provider (PCP). His PCP discovered that he had early stages of liver impairment and told the patient to discontinue the bedtime APAP/antihistamine combination and change his sleep habits to avoid long naps during the day and caffeine after noon. He was also encouraged to walk for 15 to 30 minutes per day.

The PCP referred the patient back to his pharmacist after his liver function tests were normal with a prescription for compounded ketoprofen 5% gel to be applied “sparingly” to affected joints three times a day. The patient was also warned to consume no more than 2,000 mg APAP per day and told to use no oral alcohol. He was instructed to ask his pharmacist to inquire about his pain and sleep medication use on each refill of any prescription or purchase of over-the-counter (OTC) medications. The patient has done well on ketoprofen gel daily use and occasional APAP, with pain scores of 1 to 2 on a 10-point VAS and 7 to 8 hours of sleep every night with few daytime naps. The patient can now walk up to 1 hour per day with a cane at his local mall.

Self-assessment questions

1. This case suggests the need for all health care providers to

- Perform a thorough drug history of both prescribed and OTC medications on each visit.
- Inquire about pain relief with agents being used and evaluate need for additional agents if inadequate pain relief is evident.
- Recommend changes in medication agent and/or dosage if unsafe use is evident.
- All of the above alternatives are correct.

2. This patient may derive better pain relief from

- A regular schedule of a lower total daily dose of APAP.
- A topical NSAID to the affected joints.
- Alternatives a and b are correct.
- An opioid with no APAP.

Answer key: 1. d; 2. c

B. AGS relative contraindications and cautions for APAP: hepatic insufficiency, chronic alcohol abuse/dependence (moderate quality of evidence, strong recommendation). Since 1998, OTC APAP products have carried the warning that if three or more alcoholic drinks are consumed each day, patients should ask their physician whether APAP or other pain relievers/fever reducers should be taken.

According to a May 2009 FDA report, APAP product labeling should be strengthened to warn specifically about liver damage risk for those who have three or more drinks a day. In a study combining data from 22 specialty medical centers in the United States, APAP-related liver injury was the leading cause of acute liver failure for 1998 through 2003. According to the report, from 1991 to 2001, 56,000 emergency department visits, 26,000 hospitalizations, and 458 deaths resulted each year from APAP overdoses.

C. AGS recommends that the maximum daily recommended APAP dosages of 4 g per 24 hours should not be exceeded and must include “hidden sources” such as combination pills (moderate quality of evidence, strong recommendation). The AGS recommendation has been superseded by an August 2009 FDA advisory committee report that suggested lowering the maximum adult daily dose to no more than 2,600 mg (the equivalent of eight “regular-strength” 325-mg tablets or capsules or five

Table 2. Key counseling points for safe APAP use

Advise patients to check all medications for pain, allergy, cold and cough, and sleep for APAP.

Ensure that the daily dose of APAP does not exceed 2,600 mg if patients do not have liver problems (e.g., chronic hepatitis, other liver disease). If patients have liver problems, refer them to their PCP.

Advise patients that they should not drink alcohol with APAP for the safest use of the drug. Most APAP labels state that consumption of up to three drinks per day is acceptable.

Counsel patients that they will have to take APAP on a regular basis for best relief of chronic pain state.

APAP may not be safe to use with warfarin. If it is used or started, a follow-up measure of warfarin effect on the prothrombin time as measured by INR should be done within 1 to 2 weeks after APAP is started. As few as seven 325-mg APAP tablets per week have been found to markedly increase INR.¹²

Abbreviation used: APAP, acetaminophen; INR, international normalized ratio; PCP, primary care provider.

“extra-strength” 500-mg tablets or capsules). The maximum was a dose of 4,000 mg (eight extra-strength capsules) per day. The dose should be even lower than this for patients who consume three or more alcoholic drinks while on the medication. A more prudent recommendation by the authors may be the total avoidance of alcohol while using APAP because patients may misperceive acceptable or safe alcohol use with APAP. Whether the 2.6-g APAP recommendation will be implemented is unclear currently.¹¹

Case 4

A 48-year-old nurse taking 3 to 4 g APAP a day for chronic pain reported also regularly consuming one to three drinks per day. She complained of right upper quadrant gastrointestinal (GI) pain to her hospital pharmacist, was noted to be jaundiced on exam, and was referred to a gastroenterologist who found her in acute liver failure and in need of a liver transplant. On questioning by the alcohol and drug intake counselor at the transplant facility, who asked her to show the size of the one to three drinks she consumed with the APAP, the size was noted to be 8 to 12 oz per drink of distilled spirits. The recommended size for each standard drink of distilled spirits is 30 to 45 mL; this patient had consumed 240 to 360 mL per drink. The pretransplant diagnosis was alcohol and APAP-induced acute liver failure.

FDA also suggested limiting immediate-release tablets to a maximum of 325 mg (now 500 mg), which may also reduce intentional overdose. The agency also recommended limiting pediatric liquid formulations to one midstrength dose rather than the multiple-strength doses currently available. The May 2009 FDA report was issued a month before three advisory committees recommended to FDA that the warning labels for products such as Tylenol (McNeil) and Vicodin (APAP with hydrocodone—Abbott) should be updated. The joint advisory committee met June 29 and 30, 2009, to help FDA craft a risk minimization strategy. This will include a black box warning on all APAP products.¹¹

Table 3. Key points on NSAID use

<p>A matched case–control study of the relationship of NSAIDs and CHF hospitalization¹⁹ found the following: Use of NSAIDs in the week before admission doubled the risk of CHF admission. Longer half-life NSAIDs (naproxen and piroxicam) were more likely than shorter half-life agents (ibuprofen) to cause exacerbation of CHF. More than one in five CHF admissions were associated with NSAID use. NSAID use is the most common drug-induced cause of CHF and exacerbation in the elderly.¹⁹ The Rotterdam Study of 7,277 noninstitutionalized older adults (mean age 70 years, 62% women) found that use of any NSAID (not low-dose ASA) after diagnosis of CHF increased the relative risk of CHF relapse by 9.9. Of note, little OTC NSAID use occurred in the Netherlands at the time the study was conducted.²⁰ Nearly three-fourths (73%) of older patients hospitalized for GI bleeds received NSAIDs at some point after their discharge (Rotterdam Study), 51% low-dose ASA, 4% NSAID with oral anticoagulant but no antiulcer drug, 35% NSAID with antiulcer drug, and 8% NSAID with oral anticoagulant and antiulcer drug.²¹ When long-term NSAIDs including ASA were stopped, the risk of MIs in older adults increased.²¹ Oral glucocorticoids (e.g., prednisone), ASA, clopidogrel, prasugrel, oral bisphosphonates (alendronate, risedronate, and ibendronate), and antidepressants increased GI bleeding risk.^{14,17}</p>
<p>Assess ADR risk and importance to ensure informed safe use with the following: Fries et al.²³ NSAID gastropathy hospitalization or death risk scale. Of note, for non-COX-2 selective inhibitors, risk may be less than for COX-2 selective inhibitors (e.g., celecoxib). GI event score Age (years) 2 plus History NSAID adverse effects^a (add 50) plus Disability index (0–3) or American Rheumatology Association class 1 10 plus NSAID dose (% maximum) 15 plus Current oral glucocorticoid, ASA, clopidogrel, prasugrel, or oral bisphosphonate (any/all use add 40) equals Total score Hospitalization/death risk per year (score – 100)/40</p>

Abbreviation used: ADR, adverse drug reaction; ASA, aspirin; CHF, congestive heart failure; COX, cyclooxygenase; GI, gastrointestinal; MI, myocardial infarction; NSAID, nonsteroidal anti-inflammatory drug; OTC, over the counter.
^aNausea, vomiting, anemia, or GI bleeding.

liver disease and should be avoided completely in severe liver impairment (Table 2).

II. Nonselective NSAIDs and cyclooxygenase (COX)-2 selective inhibitors may be considered rarely and with extreme caution, in highly selected individuals (high quality of evidence, strong recommendation). The reasons for this strong recommendation are that full-dose oral NSAIDs markedly increase fluid retention and blood pressure and risk of congestive heart failure (CHF), myocardial infarction (MI), and stroke. Additional evidence on NSAIDs is provided below.

A. Patient selection for oral NSAIDs: other (safer) therapies have failed, evidence of continuing therapeutic goals has not emerged, and ongoing assessment of risks/complications is outweighed by therapeutic benefits (low quality of evidence, strong recommendation).

B. Absolute contraindications to oral NSAIDs: current active peptic ulcer disease (low quality of evidence, strong recommendation), chronic kidney disease (moderate level of evidence, strong recommendation), and heart failure (moderate level of evidence, weak recommendation).

C. Relative contraindications and cautions for oral NSAIDs: hypertension, *Helicobacter pylori* gut infection, history of peptic ulcer disease, and concomitant use of corticosteroids or SSRIs (moderate quality of evidence, strong recommendation).

III. Older patients taking long-term oral nonselective NSAIDs should use a proton pump inhibitor (PPI) or misoprostol for GI protection (high quality of evidence, strong recommendation).^{12–16}

IV. Patients taking an oral COX-2 selective inhibitor with aspirin (acetylsalicylic acid [ASA]) should use a PPI or misoprostol for GI protection (high quality of evidence, strong recommendation).^{12–16}

V. Patients should not take more than one nonselective NSAID/COX-2 selective inhibitor for pain control (low quality of evidence, strong recommendation). Patients taking ASA for cardioprophylaxis should not use ibuprofen (moderate quality of evidence, weak recommendation)—the reason for avoiding ibuprofen and perhaps other oral NSAIDs is that it prevents the antiplatelet effects of ASA.¹⁷

VI. All patients taking nonselective NSAIDs and COX-2 selective inhibitors should be routinely assessed for GI and renal toxicity, hypertension, heart failure, and other drug–drug and drug–disease interactions (weak quality of evidence, strong recommendation).

Additional evidence and recommendations for safe use of NSAIDs

For NSAIDs, long-term use (i.e., >2 weeks) of all full-dose oral agents should be avoided. Particularly, indomethacin (Indocin—Merck) should be avoided, as GI adverse effects are more serious with indomethacin than with other NSAIDs. CNS effects of lightheadedness and headache are also more common with indomethacin. Oral and injectable ketorolac should be avoided. Avoid use of all NSAIDs, both non-COX-2 and COX-2 selective inhibitors (celecoxib), for full-dose use greater than 7 to 14 days or sustained-release form. Other prescription and OTC oral NSAIDs

Additional evidence and guidelines for APAP use

Both the American Medical Directors Association (www.ama.com) and the American College of Rheumatology (www.acr.org) recommend APAP as first-step therapy for osteoarthritis in older patients. APAP is preferred for noninflammatory pain. The use of more than 2.6 g per day for several weeks may lead to liver damage.⁹ APAP should not exceed 1 to 1.3 g/day in early alcoholic

should be avoided, especially ibuprofen with ASA because ibuprofen may decrease ASA effect on platelet adhesion.¹⁷ The American Heart Association also has recommended avoiding all NSAIDs because of higher risk of fluid retention, CHF, MI, and stroke or cerebrovascular accident (CVA) risk and recurrence.

Oral NSAIDs have a high incidence of gastropathy (heartburn and gastroesophageal reflux disease [GERD], gastritis, peptic ulcer disease, lower GI bleed, and perforation). Non-COX-2 selective NSAIDs cause anemia in one-half and GI bleed in 20% or more of chronic users, usually within the first 3 to 6 months.¹⁵ All NSAIDs affect clotting, water retention, and kidney function and may cause constipation.¹⁶ If NSAIDs must be used for short periods, an H₂ blocker (e.g., ranitidine) may prevent duodenal ulcers. PPIs (e.g., omeprazole) may prevent gastric or duodenal ulcers, and misoprostol may prevent gastric ulcers but is less effective than PPIs. Antacids and sucralfate do not prevent gastritis.

Gastroprotection costs

GI-protected older NSAIDs with PPI use may cost \$200 or more per month. Unprotected full-dose NSAID use may cost up to \$2,000 per month as a result of NSAID gastropathy-related hospitalizations.^{15,16} Again, patients should not use full-dose NSAIDs for longer than 7 to 14 days, especially if they have medications for high blood pressure, angina pectoris, MI, or CVA protection. NSAIDs should not be used with low-dose ASA, clopidogrel, or prasugrel without *H. pylori* eradication and continuous PPI. Never use ASA and clopidogrel or prasugrel with an NSAID. This may lead to a GI bleed in every 3 patient-months of use.¹⁸ See the gastropathy risk assessment below for estimation of adverse drug reaction (ADR) risk. Relabeling changes for all prescription and OTC NSAIDs are available at www.fda.gov/nsaids.

Cardiovascular and cerebrovascular effects

Weight should be monitored because a gain (3–5 lb or more) could indicate fluid retention and will increase blood pressure as a result of NSAIDs affecting the kidneys, especially for patients taking angiotensin-converting enzyme inhibitors or angiotensin receptor blockers for diabetes and for those who already have high blood pressure, CHF, a history of angina pectoris, or a history of MI (Table 3).

Case 5 and self-assessment questions

An 80-year-old man has a history of NSAID gastritis and MI and a disability index of 3. He is prescribed 2,400 mg/day ibuprofen (100% of maximum dose) and is also taking 5 mg/day prednisone and 325 mg/day ASA. Applying the Fries et al.²³ risk scale, the patient's risk is $80 - 2 = 160 + 50 + 20 + 15 + 40 = 285 - 100/40$ compared with 0 for non-NSAID users.

Self-assessment questions

1. What risk do you calculate?

- 2.6
- 4.6
- 6.6
- 8.6

Table 4. Algorithm for ADR significance assessment²⁴

ADR events	Yes (+1)	No (0)
Appropriate temporal sequence	Yes (+2)	No (-1)
Known ADR	Yes (+1)	No (0)
Alternative explanation available	Yes (-1)	No (+2)
Objective evidence of ADR	Yes (+1)	No (0)
Appropriate serum level or lab value	Yes (+1)	No (0)
Dechallenge improvement	Yes (+1)	No (0)
Rechallenge relapse	Yes (+2)	No (-1) ^a
Total score		

Abbreviation used: ADR, adverse drug reaction.

Scoring: Doubtful, <1; possible, 1–4; probable, 5–8; definite, 9–10.

^aIf rechallenge is not performed, value assigned is 0.

2. What actions do you take as his pharmacist?

- Recommend that he not take ibuprofen; regular-schedule APAP preferred
- Question the need for prednisone
- Suggest gastroprotection if he takes ASA and check his hemoglobin/hematocrit
- All of the above alternatives are correct.

Answer key: 1. b; 2. d

The algorithm for ADR significance assessment by Naranjo et al.²⁴ is used to establish the significance of clinical problems when an ADR caused by starting or withdrawing a drug is suspected (Table 4).

Case 6 and self-assessment questions

A 77-year-old woman starts naproxen 500 mg twice a day for osteoarthritis. During the next month, her hemoglobin and hematocrit decrease from 12 g/dL and 36% to 10 g/dL and 30%, respectively (normal 12–14 g/dL and 36–42%) and she has black tarry stools and persistent heartburn. She states that she has had three previous admissions to the hospital from taking 6 to 15 tablets a day of ASA 325 mg and piroxicam because of GI bleeds. Her celecoxib was stopped 1 month ago as a result of “drowsy” (CHF). The temporal sequence is logical (+2), and it is a known ADR (+1); there is no alternative explanation (such as use of concurrent alcohol, oral glucocorticosteroids, or ASA) (+2). Objective evidence of an ADR (+1) is present, and two lab tests are used to confirm ADR (+1). Dechallenge improvement is seen as her hemoglobin and hematocrit stabilized and increased to 11 g/dL and 33%, respectively, after celecoxib was stopped (+1), as well as no heartburn and rechallenge (+2) after the ASA ADR.

Self-assessment questions

1. The total score and significance of the ADR for this case are

- <1 and doubtful.
- 1–4 and possible.
- 5–8 and probable.
- 9–10 and definite.

2. What analgesic do you recommend for her osteoarthritis pain?

- a. APAP
- b. Other oral NSAIDs
- c. Propoxyphene
- d. Meperidine

Answer key: 1. c; 2. a

Of note, SSRIs (e.g., escitalopram, citalopram, sertraline, paroxetine), SSRIs/SNRIs (e.g., venlafaxine, duloxetine), and mirtazapine have recently been relabeled with a warning that they increase the risk of GI bleeds, especially when used with NSAIDs (see black box warning in product labeling for each agent).

Concurrent ASA use

A recent review confirmed previous assertions that ASA doses greater than 75 to 81 mg/day are not beneficial for the primary or secondary prevention of cardiovascular disease.²⁵ Doses greater than 75 to 81 mg/day do not enhance cardiovascular disease prevention efficacy but increase the risk of hemorrhagic events, primarily NSAID gastropathy and intracranial hemorrhages and, to a lesser extent, stroke and PVD. Preventive doses of ASA may be greater than 81 mg/day, but the risk of hemorrhagic events will be increased.

Pharmacists should always question ASA doses more than 81 to 325 mg/day and check hemoglobin periodically by physical assessment of lower eyelid redness and blood hemoglobin (>12 g/dL).

Related non-ASAs are less expensive but because of risk of salicisism at low dose, they are not preferred over APAP. GI blood loss is a concern in most patients taking ASA who have a history of GERD and/or peptic ulcer disease history and those with borderline anemia. Do not use hematinic without determination of anemia causation. The antiplatelet effect of ASA may also be of benefit in preventing recurrent MI and transient ischemic attack–related thrombotic strokes (CVA). Doses of as little as 81 mg daily or every other day, up to 325 mg/day, are acceptable.

Enteric coating does not decrease the chance of anemia and gastropathy. To prevent anemia to GI bleed, a regimen of ASA and clopidogrel is more gastropathic than PPI alone.¹⁸ Low-dose ASA may lose its antiplatelet effect if low-density lipoprotein is not reduced to less than 100 to 130 mg/dL.²⁶

Opioids per AGS guidelines

VIII. All patients with moderate to severe pain, pain-related functional impairment, or diminished quality of life resulting from pain should be considered for opioid therapy (low quality of evidence, strong recommendation); this does not include propoxyphene, pentazocine, or meperidine.^{8,9} The discussion of other opioids is beyond the scope of this article. Recently, removing propoxyphene from the U.S. market was recommended.²⁷

Case 7 and self-assessment questions

A new patient (69-year-old woman) complains of osteoarthritis-related pain and is taking as-needed propoxyphene napsylate/APAP combination (60 doses dispensed); she was to take one tablet every 6 hours as needed for pain and refill as needed.

She has a history of alcohol abuse and poor orientation to time, place, and person. Her VAS score for pain is 7 to 9. She also has a history of angina and MI but is not taking low-dose ASA. Lack of redness in her lower eyelid indicates anemia. She admits to a long-term dependence on propoxyphene and to taking three to five tablets per day.

Self-assessment questions

1. Regarding her propoxyphene, what do you recommend?

- a. Determine whether she is willing to give up her propoxyphene; if she is willing:
- b. Recommend a tapering of a daily dose per week and replace each dose with 325 to 500 mg APAP up to 2.6 g/day until she is totally off the propoxyphene in 3 to 5 weeks.
- c. Check for cognitive improvement as the propoxyphene is tapered and suggest oral glucosamine/chondroitin, topical NSAID gel, anemia assessment and treatment, and low-dose ASA, with PPI for gastroprotection after anemia is resolved.
- d. All of the above alternatives are correct.

2. Which is the safest analgesic to use in this patient?

- a. APAP
- b. Celecoxib
- c. Naproxen
- d. Ibuprofen

3. If celecoxib is used, how long should it be used with blood pressure and weight monitoring?

- a. 1–2 days
- b. 1–2 weeks
- c. 1–2 months
- d. Continually

4. Is a patient with a history of GI bleeds from any cause at risk for recurrent GI bleeds with any NSAID, even low-dose ASA and/or clopidogrel?

- a. Yes
- b. No

5. The newest guidelines for APAP use recommend what maximum daily dose in adults with no history of liver disease or alcohol use?

- a. 1 g
- b. 2 g
- c. 2.6 g
- d. 4 g

6. If daily oral iron is used to replenish blood lost, how long should therapy last?

- a. Until hemoglobin is 11–12 g/dL, then discontinue
- b. 1–2 weeks
- c. Forever
- d. 1–2 months

Answer key: 1. d; 2. a; 3. b; 4. a; 5. c; 6. a

IX. Patients with frequent or continuous pain on a daily basis may be treated with around-the-clock, time-contingent dosing aimed at achieving steady-state opioid therapy (low quality of evidence, weak recommendation). A recent review focused on opioids and their adverse effects.²⁷

X. Clinicians should anticipate, assess, and identify potential opioid-associated adverse effects (moderate quality of evidence, strong recommendation).

XI. Maximal safe doses of APAP or NSAIDs should not be exceeded when using fixed-dose opioid combination agents as part of an analgesic regimen (moderate quality of evidence, strong recommendation).

XII. When long-acting opioid preparations are prescribed, breakthrough pain should be anticipated, assessed, prevented, and/or treated using short-acting immediate-release opioid medications (moderate quality of evidence, strong recommendation).

XIII. Methadone should be initiated and titrated cautiously only by clinicians well versed in its use and risks (moderate quality of evidence, strong recommendation).

XIV. Patients taking opioid analgesics should be reassessed for ongoing attainment of therapeutic goals, adverse effects, and safe and responsible medication use (moderate quality of evidence, strong recommendation).

AGS guidelines for adjuvant drug therapy⁹

XV. All patients with neuropathic pain are candidates for adjuvant analgesics (strong quality of evidence, strong recommendation); this may include antidepressants and anticonvulsants, as well as vitamin D. Specific agents are beyond the scope of this article; however, antidepressants and vitamin D are discussed below.

XVI. Patients with fibromyalgia are candidates for a trial of approved adjuvant analgesics (moderate quality of evidence, strong recommendation).

XVII. Patients with other types of refractory persistent pain may be candidates for certain adjuvant analgesics (e.g., back pain, headache, diffuse bone pain, temporomandibular disorder) (low quality of evidence, weak recommendation).

XVIII. Tertiary tricyclic antidepressants (amitriptyline, imipramine, and doxepin) should be avoided because of higher risk for adverse effects (e.g., anticholinergic effects, cognitive impairment, falls) (moderate quality of evidence, strong recommendation).⁸

XIX. Agents may be used alone, but often the effects are enhanced when used in combination with other pain analgesics and/or nondrug strategies (moderate quality of evidence, strong recommendation).

XX. Adjuvant therapy should begin with the lowest possible dose and increased slowly based on response and adverse effects, with the caveat that some agents have a delayed onset of action and therapeutic benefits are slow to develop. For example, gabapentin may require 2 to 3 weeks for onset of efficacy (moderate quality of evidence, strong recommendation). Gabapentin levels should be assessed if the dose is no

more than 900 to 1,200 mg/day and an elevated serum creatinine (i.e., >1.5 mg/dL) or creatinine clearance less than 50 mL/minute is evident.

XXI. An adequate therapeutic trial should be conducted before discontinuing a seemingly ineffective treatment (weak quality of evidence, strong recommendation).

Other drugs⁹

XXII. Long-term systemic corticosteroids should be reserved for patients with pain-associated inflammatory disorders or metastatic bone pain. Osteoarthritis should not be considered an inflammatory disorder (moderate quality of evidence, strong recommendation). This area is beyond the scope of the current review.

XXIII. All patients with localized neuropathic pain are candidates for topical lidocaine (moderate quality of evidence, strong recommendation).

XXIV. Patients with localized nonneuropathic pain may be candidates for topical lidocaine (low quality of evidence, weak recommendation).

XXV. All patients with other localized nonneuropathic persistent pain may be candidates for topical NSAIDs (moderate quality of evidence, weak recommendation); this is discussed above.

XXVI. Other topical agents may be considered for regional pain syndromes, including capsaicin or menthol (moderate quality of evidence, weak recommendation).

XXVII. Many other agents for specific pain syndromes may require caution in older patients and merit further research (e.g., glucosamine, chondroitin, cannabinoids, botulinum toxin, alpha-2 adrenergic agonists, calcitonin, vitamin D, bisphosphonates, ketamine) (low quality of evidence, weak recommendation).

Low vitamin D levels predispose to more chronic pain

Patients with chronic pain who have inadequate levels of vitamin D require almost twice the pain medications as similar patients who have adequate levels of vitamin D, according to a recent article in *Pain Medicine*.²⁸ Patients with levels of 20 ng/mL or less were considered to have inadequate levels of vitamin D, whereas patients with levels greater than 20 ng/mL were considered to have adequate levels of vitamin D. All patients who had inadequate levels of vitamin D were given vitamin D supplementation. Low 25-hydroxyvitamin D levels are common in adults. This study suggests a relationship between low vitamin D levels and pain perception, resulting in the need for higher narcotic doses. Based on the findings of this study, recommending vitamin D supplementation to better manage chronic pain might seem prudent. However, results of double-blind studies have been disappointing. Chronic diffuse pain can be a symptom of osteomalacia, and vitamin D supplementation may be beneficial in this setting. Low vitamin D levels increase the likelihood of osteoporosis, and supplementation should be considered in patients with low levels.^{28,29}

Explain to patients that there are three primary sources of vitamin D: sunlight, diet, and supplements. Generally speaking, 10 to 15 minutes of sun exposure three times per week is enough to maintain adequate vitamin D levels. Patients should also be encouraged to consume recommended daily allowances through foods that contain vitamin D (e.g., dairy products, fish, oysters, fortified cereals, margarine). Vitamin D supplements should only be considered for patients who do not get necessary vitamin D through sunlight and diet.^{28,29} A minimal daily dose of 1,000 to 1,500 units vitamin D₃ may be needed if supplements are given.^{28,29}

Treating depression and chronic pain in older primary care patients

Depression and pain are the most common mental and physical syndromes, respectively, found in older primary care patients. Researchers compared outcomes from an intervention and usual care in 250 patients from community-based or Department of Veterans Affairs clinics with pain (>3 months of lower back, hip, or knee pain) and depression (at least moderate severity). Intervention recipients received 12 weeks of optimized antidepressant treatment of depression, followed by six biweekly instructional sessions on the behavioral management of pain, then 6 months of relapse prevention. A nurse care manager, supervised by a psychiatrist, optimized antidepressant selection and dose (SNRI/venlafaxine or an SSRI/citalopram) in 93% of patients and led the behavioral sessions. At 12 months, considerably more intervention than control patients responded on a depression measure (>50% improvement; 37% vs. 16%), a composite pain measure (>30% reduction in pain and disability; 42% vs. 17%), and both measures (26% vs. 8%). Intervention recipients averaged 2.5 in-person contacts and 11.5 telephone contacts. They were more likely than control patients to use antidepressants (98% vs. 43%), to use antidepressants for longer periods (9 vs. 2 months), and to have an antidepressant switched or added (35% vs. 17% of a usual-care subgroup with medical record data).

In this collaborative care study, a short-term intervention optimizing antidepressants and providing brief behavioral pain treatment had sustained effects at 12 months on both depression and pain. Regarding depression response, the number needed to treat (NNT) was 4.8. This is comparable with the NNTs in studies of depressed patients without pain, but the absolute rates are closer to those found in medically ill depressed patients. Although a 30% reduction in pain is a modest threshold, the NNT of 4.1 also is excellent.³⁰ Of note, antidepressants increase the GI bleed risk of NSAIDs.

Summary

The current work has considered the assessment and treatment of chronic pain in the older adult, emphasizing the safe use of first-step agents, per recently revised guidelines of AGS. Appendix 1 (electronic version of this article, available online at www.japha.org) provides other resources for pharmacists to consider and pass on to patients.

References

- Cooper JW, Burfield AH. Pain management in "geriatric drug management." Accessed at www.cooperconsultantpress.com, April 14, 2010.
- Molony SL, Kobayashi M, Holleran EA, Mezey M. Assessing pain as a fifth vital sign in long-term care facilities: recommendations from the field. *J Gerontol Nurs*. 2005;31:16-24.
- Davis MP, Srivastava M. Demographics, assessment and management of pain in the elderly. *Drugs Aging*. 2003;20:23-57.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189-98.
- Reisberg B, Ferris SH, deLeon MJ, Crook T. The global deterioration scale for assessment of primary degenerative dementia. *Am J Psychiatry*. 1982;139:1136-9.
- National Institute of Mental Health. Abnormal involuntary movement scale. In Guy W, Ed. *ECDEU assessment manual for psychopharmacology*. DHEW publ. no 76-338. Rockville, MD: National Institute of Mental Health; 1976:534-7.
- Douzjian M, Wilson C, Schults M, et al. A program to use pain control medication to reduce psychotropic drug use in residents with difficult behavior. *Ann Longterm Care*. 1998;6(5):174-8.
- Fick DM, Cooper JW, Wade WE, et al. Updating the Beers criteria for potentially inappropriate medication use in older adults. *Arch Intern Med*. 2003;163:2716-24.
- AGS Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. Accessed at www.americangeriatrics.org/education/final_recommendations.pdf, July 3, 2009.
- Lee YH, Woo JH, Choi SJ, et al. Effect of glucosamine or chondroitin sulfate on the osteoarthritis progression: a meta-analysis. *Rheumatol Int*. 2010;30:357-63.
- Food and Drug Administration. Recommendations for FDA interventions to decrease the occurrence of acetaminophen hepatotoxicity. Accessed at www.fda.gov/downloads/AdvisoryCommittees/.../Drugs/.../UCM164898.pdf, May 29, 2009.
- Cooper JW, Wade WE, Mallet L. Anemia detection and treatment in a four geriatric long term care facility population. *Journal of Pharmacoepidemiology*. 1990;1(1):61-70.
- Cooper JW. Chronic constipation associations and laxative efficacy in a geriatric nursing home population. *Journal of Pharmacoepidemiology*. 1991;1(3-4):29-40.
- American Hospital Formulary Service. Drug information 2008;1971, 2234.
- Cooper JW. Consultant pharmacist effect on NSAID costs and gastropathy over a 5-year period. *Consult Pharm*. 1997;12:792-6.
- Cooper JW, Wade WE. Pharmacists interventions in geriatric nursing facility: NSAID therapy. *Consult Pharm*. 2005;20:492-7.
- American Hospital Formulary Service. Drug Information. 2008;2115.
- Eshaghian S, Kaul S, Amin S, et al. Role of clopidogrel in managing atherothrombotic cardiovascular disease. *Ann Intern Med*. 2007;146:434-41.
- Page J, Henry D. Consumption of NSAIDs and the development of congestive heart failure in elderly patients: an underrecognized public health problem. *Arch Intern Med*. 2000;160:777-84.
- Feenstra J, Heerdink ER, Grobbee DE, et al. Association of non-steroidal anti-inflammatory drugs with first occurrence of heart failure and with relapsing heart failure: the Rotterdam Study. *Arch Intern Med*. 2002;162:265-70.

21. Visser LE, Graatsma HH, Stricker BH. Contraindicated NSAIDs are frequently prescribed to elderly patients with peptic ulcer disease. *Br J Clin Pharmacol*. 2002;53:183–8.
22. Fischer LM, Schlienger RG, Matter CM, et al. Discontinuation of nonsteroidal anti-inflammatory drug therapy and risk of acute myocardial infarction. *Arch Intern Med*. 2004;164:2472–6.
23. Fries JF, Williams CA, Bloch DA, Michel BA. Nonsteroidal anti-inflammatory drug-associated gastropathy: incidence and risk factor models. *Am J Med*. 1991;91:213–22.
24. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30:239–45.
25. Campbell CL, Smyth S, Montalescot G, Steinhubl SR. Aspirin dose for the prevention of cardiovascular disease: a systematic review. *JAMA*. 2007;297:2018–24.
26. Boncler M, Gresner P, Nocun M, et al. Elevated cholesterol reduces acetylsalicylic acid-mediated platelet acetylation. *Biochim Biophys Acta*. 2007;1770:1651–9.
27. Guay DRP. Opioid analgesics for persistent pain in the older patient: part 1. *Clin Geriatr*. 2010;18(3):37–46.
28. Turner MK, Hooten WM, Schmidt JE, et al. Prevalence and clinical correlates of vitamin D inadequacy among patients with chronic pain. *Pain Med*. 2008;9:979–84.
29. Straube S, Moore AR, Derry S, McQuay HJ. Vitamin D and chronic pain. *Pain*. 2009;141:10–3.
30. Kroenke K, Bair MJ, Damush TM, et al. Optimized antidepressant therapy and pain self-management in primary care patients with depression and musculoskeletal pain: a randomized controlled trial. *JAMA*. 2009;301:2099–110.

Assessment questions

Instructions: The assessment test for this activity must be taken online; please see “CPE processing” below for further instructions. There is only one correct answer to each question. This CPE will be available at www.pharmacist.com no later than May 31, 2010.

1. **Most chronic pain in the older adult results from**
 - a. Single causes.
 - b. Multiple causes.
 - c. Single to multiple causes.
 - d. None of the above alternatives is correct.
2. **Acetaminophen (APAP) use in the older adult may be**
 - a. Underused.
 - b. Overused as a result of patients not reading labels of multiple over-the-counter medications.
 - c. Misused because of patient failure to realize the need for a regular schedule for chronic pain relief.
 - d. All of the above alternatives are correct.
3. **Pain in older patients who are taking drugs for dementia will more than likely need to be assessed by which of the following?**
 - a. Visual analog scale
 - b. Nonverbal pain behavior scale
4. **The first-step analgesic for most older adults should be a regular schedule of**
 - a. Propoxyphene.
 - b. APAP.
 - c. Tramadol.
 - d. Full-dose nonsteroidal anti-inflammatory drugs (NSAIDs).
5. **Inappropriate analgesics for the older adult include**
 - a. Meperidine.
 - b. Pentazocine.
 - c. Propoxyphene
 - d. All of the above alternatives are correct.
6. **Liver toxicity from APAP may result from**
 - a. Failure to check labels of all medications taken.
 - b. Concurrent alcohol use.
 - c. A daily maximum dose that is too high.
 - d. All of the above alternatives are correct.
7. **Controversy exists regarding whether glucosamine and chondroitin are of benefit, possibly as a result of**
 - a. Inadequate dosing of these agents.
 - b. Inconsistent drug product bioavailability.
 - c. Unrealistic patient expectations of how soon they can get pain relief from glucosamine and chondroitin.
 - d. All of the above alternatives may be correct.
8. **NSAIDs other than low-dose aspirin (ASA) should be used in the older adult for chronic focal pain only by which of the following routes?**
 - a. Topical
 - b. Oral
 - c. Injectable
 - d. NSAIDs are not safe by any route.
9. **The maximum daily APAP dose per recently revised Food and Drug Administration guidelines in those with no liver problems or alcohol intake is**
 - a. 4 g.
 - b. 3 g.
 - c. 2.6 g.
 - d. 2 g.
10. **Full-dose oral NSAIDs may markedly increase the risk of fluid retention leading to or worsening**
 - a. High blood pressure.
 - b. Congestive heart failure.
 - c. Myocardial infarction (MI) and stroke.
 - d. All of the above alternatives are correct.
11. **All patients taking long-term oral full-dose NSAIDs may, in addition to developing cardiovascular and cerebrovascular problems, develop or worsen which of the following gastrointestinal (GI) problems?**
 - a. Gastroesophageal reflux disease
 - b. Peptic ulcer disease
 - c. Constipation
 - d. All of the above alternatives are correct.
12. **If one must use any oral NSAID for short periods, which of the following are true?**
 - a. An H₂ blocker (e.g., ranitidine) may prevent only duodenal ulcers.
 - b. PPIs (e.g., omeprazole) may prevent gastric or duodenal ulcers, and misoprostol may prevent gastric ulcers but is less effective than PPIs.
 - c. Antacids and sucralfate do not prevent gastritis.
 - d. All of the above alternatives are correct.
13. **When long-term NSAIDs, including ASA, are stopped, an increased risk of MIs in older adults may result.**
 - a. True
 - b. False

14. Which of the following increase GI bleeding risk?

- Oral glucocorticoids (e.g., prednisone)
- ASA, clopidogrel, prasugrel, oral bisphosphonates (alendronate, risedronate, and ibendronate), and antidepressants
- Antidepressants
- All of the above alternatives are correct.

15. A recent review confirmed previous assertions that daily ASA doses greater than which of the following are not beneficial for the primary or secondary prevention of cardiovascular disease and may increase GI bleeding risk?

- 75–81 mg
- 81–160 mg
- 160–325 mg
- >325 mg

16. Methadone should be initiated and titrated cautiously only by clinicians well versed in its use and risks.

- True
- False

17. Adjuvant drugs for chronic pain relief may include

- Anticonvulsants.
- Antidepressants.
- Vitamin D and glucosamine/chondroitin.
- All of the above alternatives are correct.

18. Long-term systemic corticosteroids should be reserved

- For pain-associated inflammatory disorders (e.g., polymyalgia rheumatica).
- For metastatic bone pain from cancer.
- For osteoarthritis.
- Alternatives a and b are correct.

19. Tertiary tricyclic antidepressants (amitriptyline, imipramine, and doxepin) should be avoided in older adults because of higher risk for adverse effects such as

- Anticholinergic effects on heart rate.
- Cognitive impairment.
- Falls.
- All of the above alternatives are correct.

20. The preferred class(es) of antidepressant drugs to treat depression in chronic pain in the older adult is

- SNRI.
- SSRI.
- Alternatives a and b are correct.
- Neither alternative a nor b is correct.

CPE Information

To obtain 2.0 contact hours of CPE credit (0.2 CEUs) for this activity, complete the CPE exam and submit it online at www.pharmacist.com/education. A Statement of Credit will be awarded for a passing grade of 70% or better. You will have two opportunities to successfully complete the CPE exam. Pharmacists who successfully complete this activity before May 1, 2013, can receive credit.

Your Statement of Credit will be available online immediately upon successful completion of the CPE exam.

CPE instructions: Get your documentation of credit now! Completing a posttest at www.pharmacist.com/education is as easy as 1-2-3.

- Go to Online CE Quick List and click on the title of this activity.
- Log in. APhA members enter your user name and password. Not an APhA member? Just click "Create one now" to open an account. No fee is required to register.
- Successfully complete the CPE exam and evaluation form to gain immediate access to your documentation of credit.

Live step-by-step assistance is available Monday through Friday 8:30 am to 5:00 pm ET at APhA Member Services at 800-237-APhA (2742) or by e-mailing InfoCenter@pharmacist.com.