

# OTC Advisor

Self-Care for Pain

Monograph 4

A continuing  
pharmacy  
education activity  
for pharmacists



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### ACTIVITY PREVIEW

Americans spend more than \$2.7 billion each year on nonprescription analgesics. Pharmacists are the logical health care professionals to assist patients with self-care decisions related to pain, because pharmacists are available at the point of purchase and are the only health care professionals who receive in-depth formal education and skill development in nonprescription pharmacotherapy.

This monograph addresses self-care for common pain conditions: musculoskeletal injuries, low back pain, osteoarthritis, headaches, and dysmenorrhea. Each condition is defined, and its pathophysiology is reviewed. Exclusions for self-treatment are presented and explained. Self-care options—nonprescription medications and nonpharmacologic interventions—are discussed in the context of a self-treatment algorithm. Each section of the monograph concludes with a list of Points to Remember that provides a quick summary of the major concepts and recommendations.

### LEARNING OBJECTIVES

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

1. Compare and contrast salicylates, nonsteroidal anti-inflammatory drugs, and acetaminophen in terms of mechanism of action and safety considerations.
2. Identify topical counterirritants that may be useful in the treatment of pain.
3. Describe the types of musculoskeletal pain and disorders, headaches, and dysmenorrhea that are amenable to self-treatment and identify symptoms and situations that indicate the need for medical evaluation.
4. Describe nonpharmacologic self-care strategies for patients with musculoskeletal pain, osteoarthritis, headaches, and dysmenorrhea.
5. Discuss the role of nonprescription analgesics in the management of musculoskeletal pain, osteoarthritis, headaches, and dysmenorrhea, including product selection considerations, correct dosing and administration, contraindications, and adverse effects.

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## INTRODUCTION

Systemic and topical analgesics are among the most widely used non-prescription medications in the United States. Americans spend more than \$2.7 billion each year on nonprescription analgesics. Nearly 80% of adults admit to taking a pain reliever at least once a week, with many taking these products inappropriately.

Many common pain conditions are amenable to self-treatment with non-prescription analgesics. This monograph begins with an overview of pain and descriptions of frequently used systemic and topical analgesic products. It concludes with discussions of the use of nonprescription analgesics for pain associated with:

- Minor musculoskeletal injuries.
- Acute low back pain.
- Osteoarthritis.
- Headaches.
- Dysmenorrhea.

## TYPES OF PAIN

The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” Pain is a perception, not a sensation; it may or may not correlate with an identifiable source of injury.

Common types of pain can be categorized broadly as nociceptive or neuropathic.

### Nociceptive Pain

Nociceptive pain arises from the activation of nociceptors: peripheral nerve endings that are activated by noxious mechanical, thermal, or chemical stimuli. “Nociception” is the term applied to the neural processes through which pain becomes a conscious experience. These processes include:

- Stimulation—transformation of noxious stimuli into electrical impulses.
- Transmission—movement of impulses from the site of stimulation to the brain.
- Perception—the process of recognizing, defining, and responding to pain.

- Modulation—activation of systems that exaggerate or reduce the perception of and response to pain.

Nociceptive pain may be classified as somatic or visceral. Somatic pain (also referred to as musculoskeletal pain) arises from bone, joint, muscle, skin, or connective tissue; it usually is described as aching, squeezing, stabbing, or throbbing. Visceral pain arises from internal organs such as the large intestine or pancreas. Obstruction of a hollow organ tends to produce deep pain that is cramping or gnawing, while injury to the organ capsule or other structures often is more localized and sharp. Either type of nociceptive pain may be localized or referred to remote sites.

Nociceptive pain may involve acute or chronic inflammation. Inflammation can be viewed as a shift from the prevention of tissue damage to the promotion of healing (e.g., in surgical wounds or after traumatic injury). Prostaglandins produced by damaged tissues lower the threshold to noxious stimulation, making the area more sensitive to pain. This heightened response discourages movement of and contact with the injured area, thereby allowing healing to progress.

### Neuropathic Pain

Neuropathic pain arises as a direct consequence of a lesion or disease affecting the central or peripheral somatosensory system. Although neuropathic pain may be influenced by ongoing tissue injury, it is likely that

the primary mechanisms sustaining the pain become independent of an ongoing injury.

Neuropathic pain usually is described as burning, tingling, or shock-like; it may have a shooting quality. Examples include diabetic neuropathy and postherpetic neuralgia. Neuropathic pain tends to respond poorly to traditional analgesics.

## SYSTEMIC NONPRESCRIPTION ANALGESICS

Systemic nonprescription analgesics include:

- Salicylates—aspirin, magnesium salicylate, and sodium salicylate.
- Nonsteroidal anti-inflammatory drugs (NSAIDs)—ibuprofen and naproxen sodium.
- Acetaminophen.

Recommended adult and pediatric dosages of these agents are listed in TABLES 1 AND 2. At these dosages, the nonprescription analgesics are considered to be essentially interchangeable in terms of analgesic efficacy for most conditions amenable to self-treatment. Some products include more than one nonprescription analgesic or combine nonprescription analgesics with caffeine.

It should be noted that aspirin and other salicylates technically are NSAIDs. However, in this monograph, the term “NSAIDs” will be used primarily to refer to nonsalicylate agents.

**Table 1. Recommended Adult Dosages of Nonprescription Analgesics**

Agent	Usual Adult Dosage	Maximum Daily Dosage
Acetaminophen	325–1,000 mg every 4 to 6 h	4,000 mg
Aspirin	650–1,000 mg every 4 to 6 h	4,000 mg
Ibuprofen	200–400 mg every 4 to 6 h	1,200 mg
Magnesium salicylate	650 mg every 4 h or 1,000 mg every 6 h	4,000 mg
Naproxen sodium	220 mg every 8 to 12 h	660 mg

**Table 2. Recommended Pediatric Dosages of Nonprescription Analgesics**

Agent	Dose by Body Weight (mg/kg)	Weight or Age	Single Dose (mg) <sup>a,b</sup>
Acetaminophen	10–15	6–11 lb	40 <sup>c</sup>
		12–17 lb	80 <sup>c</sup>
		18–23 lb	120 <sup>c</sup>
		24–35 lb	160
		36–47 lb	240
		48–59 lb	320
		60–71 lb	400
		72–95 lb	480
≥96 lb	650		
Aspirin <sup>d</sup>	10–15	<24 lb	As directed by primary care provider
		24–35 lb	162 <sup>c</sup>
		36–47 lb	243 <sup>c</sup>
		48–59 lb	324 <sup>c</sup>
		60–71 lb	405 <sup>c</sup>
		72–95 lb	486 <sup>c</sup>
		≥96 lb	648 <sup>c</sup>
Ibuprofen	7.5	6–11 lb	Not recommended
		12–17 lb	50
		18–23 lb	75
		24–35 lb	100
		36–47 lb	150
		48–59 lb	200
		60–71 lb	250
		72–95 lb	300
		≥96 lb	200–400 mg (maximum 1,200 mg/day)
Naproxen sodium	—	<12 y	Not recommended
		≥12 y	220–440 mg initially, then 220 mg every 8 to 12 h (maximum 660 mg/day)

<sup>a</sup> Individual doses of acetaminophen or aspirin may be repeated every 4 to 6 hours as needed, not to exceed five doses in 24 hours.

<sup>b</sup> Individual doses of ibuprofen may be repeated every 6 to 8 hours as needed, not to exceed four doses in 24 hours.

<sup>c</sup> This dose is not included in the approved nonprescription labeling; it is provided to assist pharmacists in determining appropriate doses.

<sup>d</sup> Because of the risk of Reye's syndrome when aspirin is administered to children with influenza (type A or B) or varicella zoster (e.g., chickenpox), many clinicians recommend a conservative approach of avoiding aspirin use altogether in children 15 years of age or younger.

### Acetylated and Nonacetylated Salicylates

Aspirin and the nonacetylated salicylates (i.e., magnesium salicylate and sodium salicylate) inhibit prostaglandin synthesis by inhibiting both isoforms of the enzyme cyclooxygenase (COX-1 and COX-2). The resulting decrease in prostaglandins reduces the sensitivity of nociceptors to the initiation of pain impulses at sites of inflammation and

trauma. Although some evidence suggests that aspirin also produces analgesia through a central mechanism, its site of action is primarily peripheral.

Salicylates are useful for managing mild to moderate pain of nonvisceral origin. They also have antipyretic and anti-inflammatory activity. However, the dosage of aspirin needed to produce anti-inflammatory effects often is in the range of 4–6 g/day. Because the

maximum nonprescription dosage for aspirin is 4 g/day (TABLE 1), anti-inflammatory activity often will not occur unless the drug is used at the high end of the acceptable dosage range.

### Gastrointestinal Adverse Effects

Minor upper gastrointestinal (GI) symptoms such as dyspepsia, epigastric discomfort, nausea, and vomiting affect between 10% and 60% of people who take aspirin and other NSAIDs. These adverse effects may be minimized by administering aspirin with food.

Aspirin is capable of damaging the GI mucosa by penetrating the protective mucous and bicarbonate layers and permitting back diffusion of acid, thereby causing cellular and vascular erosion. Two distinct mechanisms cause this problem: (1) a local irritant effect resulting from the drug contacting the gastric mucosa and (2) a systemic effect from prostaglandin inhibition. Gastric petechiae and erosions are evident as soon as 1 to 2 hours after ingestion of a single 600-mg dose of aspirin. Endoscopic studies of patients receiving aspirin 300 mg/day for 14 days have shown gastric and duodenal petechiae, erosions, and endoscopic ulcers with this smaller dose.

GI blood loss associated with aspirin use is dose dependent. Healthy subjects with no aspirin exposure have blood loss of approximately 0.5 mL/day in the stool. Moderate aspirin intake increases this amount to 2–6 mL/day, and as many as 15% of patients will lose more than 10 mL/day. Chronic GI bleeding of this magnitude can deplete total body iron and produce iron deficiency anemia. Patients who have any of the following risk factors for upper GI bleeding should avoid self-treatment with aspirin:

- Age 60 years or older.
- Concomitant use of alcohol.
- Concomitant use of other NSAIDs, anticoagulants, antiplatelet agents, bisphosphonates, selective serotonin reuptake inhibitors, or systemic corticosteroids.
- History of uncomplicated or bleeding peptic ulcer.
- Infection with *Helicobacter pylori*.
- NSAID-related dyspepsia.
- Rheumatoid arthritis.

Aspirin has been formulated as both enteric-coated and buffered products in an attempt to reduce the potential for GI toxicity. Enteric coating may decrease the local gastric irritation produced by aspirin, making it a preferred dosage form for patients requiring chronic therapy with medium to high doses. However, the risk of major upper GI bleeding that results in hematemesis or melena appears to be similar with plain and enteric-coated aspirin products. Endoscopic evaluation comparing gastric damage produced by buffered and nonbuffered aspirin products also suggests similar rates of gastric damage.

The nonacetylated salicylates are associated with a lower incidence of GI effects than aspirin.

### Reye's Syndrome

Reye's syndrome is an acute, potentially fatal illness that occurs almost exclusively in children 15 years of age or younger. It is characterized by progressive neurologic damage, hepatic injury (fatty liver with encephalopathy), and hypoglycemia; the mortality rate may be as high as 50%. Although the cause of Reye's syndrome is unknown, the onset usually follows a viral infection with influenza (type A or B) or varicella zoster (e.g., chickenpox). Using salicylates during these viral illnesses increases the risk of developing Reye's syndrome by as much as 35-fold.

The use of aspirin during simple viral upper respiratory infections such as the common cold is not contraindicated. However, because it can be difficult to differentiate various viral infections, many clinicians recommend a conservative approach of avoiding aspirin use in children 15 years of age or younger.

### Salicylate Intoxication

Mild salicylate intoxication (salicylism) occurs with chronic therapy that produces toxic plasma salicylate concentrations. Chronic intoxication in adults generally requires salicylate doses of 90–100 mg/kg per day for at least 2 days. Conditions that predispose patients to salicylate toxicity include:

- Marked renal or hepatic impairment (e.g., uremia, cirrhosis, hepatitis).

- Metabolic disorders (e.g., hypoxia, hypothyroidism).
- Unstable disease (e.g., cardiac arrhythmias, intractable epilepsy, brittle diabetes).
- Status asthmaticus.
- Multiple comorbidities.

Symptoms of mild salicylate toxicity include headache, dizziness, tinnitus, difficulty in hearing, dimness of vision, mental confusion, lassitude, drowsiness, sweating, thirst, hyperventilation, nausea, vomiting, and occasional diarrhea. These symptoms can be reversed by lowering the plasma concentration to a therapeutic range. Although tinnitus typically is one of the early signs of toxicity, it should not be used as a sole indicator of salicylate toxicity.

### Aspirin Intolerance

Aspirin intolerance generally manifests as urticarial symptoms (including angioedema) or bronchospastic symptoms (including difficulty in breathing) that occur within 3 hours of aspirin ingestion. Severity of the intolerance is variable, ranging from minor to severe. Clinically important aspirin intolerance is uncommon; risk factors include chronic urticaria and asthma with nasal polyps.

The cross-reaction rates for ibuprofen and naproxen in patients with documented aspirin intolerance are 98% and 100%, respectively. High cross-reaction rates in aspirin-intolerant patients also are reported with some prescription NSAIDs. Thus, patients with a history of aspirin intolerance should be advised to avoid all aspirin- and NSAID-containing products. Acetaminophen has a low cross-reaction rate (7%) and is the preferred nonprescription analgesic for self-medication in patients with aspirin intolerance.

### Other Safety Considerations

All salicylates—but aspirin in particular—can impair hemostasis. A single 650-mg dose of aspirin can double bleeding time; low doses also increase bleeding time. Because of the effect on hemostasis, aspirin is contraindicated in patients with a history of any bleeding disorder (e.g., hypoprothrombinemia, vitamin K deficiency, hemophilia) or a history of peptic ulcer disease.

Patients with renal impairment should exercise caution when using salicylates. Clinically important alterations in renal blood flow resulting in acute reduction in renal function can result from use of even short courses of salicylates.

All salicylates have dose-related effects on renal uric acid handling and thus should be avoided in patients with a history of gout or hyperuricemia. Dosages of 1–2 g/day inhibit renal tubular uric acid secretion without affecting reabsorption and may increase plasma uric acid levels.

### Nonsteroidal Anti-inflammatory Drugs

Like salicylates, NSAIDs cause peripheral inhibition of COX and subsequent inhibition of prostaglandin synthesis. Also like salicylates, NSAIDs have analgesic, antipyretic, and anti-inflammatory activity. They are useful for managing mild to moderate pain of nonvisceral origin.

The most frequent adverse effects of NSAIDs involve the GI tract and include dyspepsia, heartburn, nausea, anorexia, and epigastric pain—even among children using pediatric formulations. These agents produce less GI upset and bleeding than aspirin. Taking a dose with food, milk, or antacids can minimize the possibility of stomach upset.

Other possible adverse effects of NSAID therapy include dizziness, fatigue, headache, or nervousness. Rashes or itching may occur in some patients, and some cases of photosensitivity have been reported. However, these effects usually are rare at normal nonprescription doses.

GI ulceration, perforation, and bleeding are uncommon but potentially serious complications of NSAID use. Risk factors include:

- Ingestion of larger doses or longer duration of treatment.
- Age 60 years or older.
- Previous ulcer disease or GI bleeding.
- Concurrent use of anticoagulants (including aspirin).
- Moderate use of alcohol (i.e., three or more drinks per day).

NSAIDs (with the exception of aspirin) are associated with an increased risk for myocardial infarction, heart failure,

## Emerging Issues: Systemic Nonprescription Pain Relievers/ Fever Reducers

On April 28, 2009, the FDA issued a final rule requiring manufacturers of nonprescription analgesic/antipyretic products to revise their labeling to include new safety information. Of note, the word “acetaminophen” or “NSAID” (for products containing salicylates, ibuprofen, or naproxen sodium) must appear highlighted or in bold type in a prominent font size on both the product container and outer carton. This change applies to single-ingredient products as well as products that contain acetaminophen or NSAIDs in combination with other active ingredients. In addition, the product container and outer carton must include a warning about the risk of severe liver damage when using acetaminophen or the risk of severe stomach bleeding when using NSAIDs. Manufacturers are required to implement all of the changes listed in the final rule by April 28, 2010.

On June 29 and 30, 2009, three FDA advisory committees considered a series of options for further reducing the incidence of liver injury associated with acetaminophen use that exceeds the maximum recommended daily dose (4 g/day). Their recommendations included:

- Limiting the amount of acetaminophen in nonprescription products to 325 mg per tablet (650 mg recommended dose).
- Lowering the maximum recommended daily dose of acetaminophen.
- Standardizing the concentration of liquid acetaminophen products for pediatric use.

The FDA had not taken any action on these recommendations at the time this monograph was finalized.

hypertension, and stroke. The cardiovascular risk appears to be dependent on both dose and duration of therapy. Although naproxen is considered to be a safer choice than ibuprofen, the American Heart Association recommends that patients with or at high risk for cardiovascular disease (i.e., hyperlipidemia, hypertension, diabetes, or other macrovascular disease) avoid NSAIDs altogether. Patients at lower risk should use NSAIDs cautiously—at the lowest dose and for the shortest duration possible to control symptoms.

Patients with a history of impaired renal function, congestive heart failure, or diseases that compromise renal hemodynamics should not self-medicate with NSAIDs. These agents may decrease renal blood flow and glomerular filtration rate as a result of inhibition of renal prostaglandin synthesis. Consequently, increased blood urea nitrogen and serum creatinine concentrations can occur, often with concomitant sodium and water retention. Advanced age, hypertension, diabetes, atherosclerotic cardiovascular

disease, and use of diuretics appear to increase risk of renal toxicity with ibuprofen use.

Overdoses of NSAIDs usually produce minimal symptoms of toxicity and are rarely fatal.

### Acetaminophen

Acetaminophen is effective in relieving mild to moderate pain of nonvisceral origin. In contrast to salicylates and NSAIDs, acetaminophen produces analgesia through a central rather than a peripheral inhibition of prostaglandin synthesis. Acetaminophen is an effective analgesic and antipyretic, but does not possess anti-inflammatory activity.

Acetaminophen is associated with few adverse effects at recommended nonprescription dosages. It is considered to be safe for use during both pregnancy and breastfeeding. Acetaminophen also is generally recognized as the nonprescription analgesic of choice in older adults.

Acetaminophen is potentially hepatotoxic in doses exceeding 4 g/day, especially with chronic use. Notably, unintended chronic overdose

comprises about half of all cases of acetaminophen-induced acute liver failure. Hepatotoxicity is caused by an intermediate metabolite of the parent compound that is detoxified by glutathione. Patients should be cautioned against exceeding the recommended maximum daily dosage of 4 g from all prescription and nonprescription products. More conservative dosing (i.e., 2 g/day or less) or avoidance may be warranted in patients at increased risk for acetaminophen-induced hepatotoxicity, including patients with:

- Concurrent use of other potentially hepatotoxic drugs (e.g., isoniazid, phenytoin, zidovudine).
- Ingestion of three or more alcoholic drinks per day.
- Poor nutritional intake.

Patients with glucose-6-phosphate dehydrogenase deficiency—a genetic disorder that results in the breakdown of red blood cells when the person is exposed to certain drugs or the stress of infection—also should use acetaminophen with caution.

### Drug Interactions

Clinically important drug interactions with nonprescription analgesic agents are listed in TABLE 3. Because most of these interactions involve salicylates or NSAIDs, acetaminophen generally is the safest nonprescription analgesic choice for patients receiving concomitant drug therapy.

Since 1999, the U.S. Food and Drug Administration (FDA) has required a warning regarding alcohol use on all nonprescription analgesic/antipyretic products for adult use. Concomitant use of ethanol with salicylates or NSAIDs may increase the risk of GI bleeding; concomitant use of ethanol with acetaminophen may increase the risk of hepatotoxicity. Patients who consume three or more alcoholic drinks per day should use nonprescription analgesics only under the direction of a primary care provider.

### Considerations in Pediatric Patients

Not all nonprescription analgesics are appropriate for all pediatric patients. As discussed in the ACETYLATED AND NONACETYLATED SALICYLATES section, aspirin or aspirin-containing products should not be administered

**Table 3. Clinically Important Drug Interactions With Nonprescription Analgesic Agents**

<b>Analgesic/Antipyretic</b>	<b>Drug</b>	<b>Potential Interaction</b>	<b>Management/Preventive Measure</b>
Acetaminophen	Alcohol	Increased risk of hepatotoxicity	Avoid concurrent use if possible; minimize alcohol intake when using acetaminophen
Acetaminophen	Warfarin	Increased risk of bleeding (elevations in INR)	Limit acetaminophen to occasional use; monitor INR for several weeks when acetaminophen 2–4 g/day is added or discontinued in patients taking warfarin
Aspirin	Valproic acid	Displacement from protein-binding sites and inhibition of oxidation of valproic acid	Avoid concurrent use; use naproxen instead of aspirin (no interaction)
Aspirin	NSAIDs, including COX-2 inhibitors	Increased risk of gastroduodenal ulcers and bleeding	Avoid concurrent use if possible; consider use of gastroprotective agents (e.g., PPIs)
Ibuprofen	Aspirin	Decreased antiplatelet effect of aspirin	Aspirin should be taken at least 30 minutes before or 8 hours after ibuprofen; use acetaminophen (or other analgesic) instead of ibuprofen
Ibuprofen	Phenytoin	Displacement from protein-binding sites	Monitor free phenytoin levels; adjust dose as indicated
NSAIDs (several)	Bisphosphonates	Increased risk of GI or esophageal ulceration	Use caution with concomitant use
NSAIDs (several)	Digoxin	Inhibited renal clearance of digoxin	Monitor digoxin levels; adjust dose as indicated
Salicylates and NSAIDs (several)	Antihypertensive agents, $\beta$ -blockers, ACE inhibitors, vasodilators, diuretics	Antihypertensive effect inhibited; possible hyperkalemia with potassium-sparing diuretics and ACE inhibitors	Monitor blood pressure, cardiac function, and potassium levels
Salicylates and NSAIDs	Anticoagulants	Increased risk of bleeding, especially GI	Avoid concurrent use, if possible; lowest risk with salsalate and choline magnesium trisalicylate
Salicylates and NSAIDs	Alcohol	Increased risk of GI bleeding	Avoid concurrent use, if possible; minimize alcohol intake when using salicylates and NSAIDs
Salicylates and NSAIDs (several)	Methotrexate	Decreased methotrexate clearance	Avoid salicylates and NSAIDs with high-dose methotrexate therapy; monitor levels with concurrent treatment
Salicylates (moderate to high doses)	Sulfonylureas	Increased risk of hypoglycemia	Avoid concurrent use, if possible; monitor blood glucose levels when changing salicylate dose

ACE = angiotensin-converting enzyme; COX = cyclooxygenase; GI = gastrointestinal; INR = international normalized ratio; NSAID = nonsteroidal anti-inflammatory drug; PPI = proton pump inhibitor.

**Table 4. Classification of Nonprescription Counterirritant External Analgesics**

Group	Mechanism of Action	Ingredients	Concentration (%)
A	Rubefaciants	Allyl isothiocyanate	0.5–5.0
		Ammonia water	1.0–2.5
		Methyl salicylate	10–60
		Turpentine oil	6–50
B	Produce cooling sensation	Camphor	3–11
		Menthol	1.25–16.0
C	Cause vasodilation	Histamine dihydrochloride	0.025–0.1
		Methyl nicotinate	0.25–1.0
D	Incite irritation without rubefaction; are equal in potency to group A ingredients	Capsicum	0.025–0.25
		Capsicum oleoresin	0.025–0.25
		Capsaicin	0.025–0.25

to children 15 years of age or younger (unless such use is specified by a primary care provider) because of the risk of Reye’s syndrome. Aspirin products contain no dosing information for patients younger than 12 years of age (users are instructed to “ask a doctor.”) The NSAID naproxen sodium is approved for use only in patients at least 12 years of age. Thus, acetaminophen and ibuprofen are the primary nonprescription options for children younger than 12 years of age.

Weight-based dosing of acetaminophen and ibuprofen is considered to be more accurate than age-based dosing in pediatric patients. Rapidly growing infants quickly outgrow previous dose requirements. Pharmacists should assist parents and caregivers in recalculating doses based on the child’s current body weight at the time of each new treatment course.

Use of acetaminophen and ibuprofen in pediatric patients is complicated by the various available strengths and formulations. Both analgesics are available in concentrated liquid drops formulations intended for infants and young children:

- Acetaminophen drops 80 mg/0.8 mL for children who weigh up to 35 lb.
- Ibuprofen drops 50 mg/1.5 mL for children who weigh up to 23 lb.

Both products also are available as less concentrated suspensions (acetaminophen 160 mg/5 mL and ibuprofen 100 mg/5 mL) intended for older children. There is some overlap in the labeled weight ranges; unintended overdosing or underdosing can occur if parents switch between the infant drops and suspension formulation and assume that the products are the same concentration.

In general, nonprescription analgesics should be administered to children younger than 2 years of age only under the direction of a primary care provider. The labeling for acetaminophen products currently directs users to “ask a doctor” about dosing for children younger than 2 years of age (or weighing less than 24 lb). The labeling for ibuprofen concentrated liquid drops contains dosing information for children as young as 6 months of age (or weighing 12 lb or more).

### Considerations in Pregnancy and Breastfeeding

Salicylates and NSAIDs should be avoided in the last trimester of pregnancy. As potent inhibitors of prostaglandin synthesis, salicylates and NSAIDs can cause delayed parturition, prolonged labor, and increased postpartum bleeding. These agents also can have adverse fetal cardiovascular effects (e.g., premature closure of the ductus arteriosus).

Acetaminophen, ibuprofen, and naproxen are considered to be compatible with breastfeeding. Aspirin and other salicylates are excreted into breast milk in low concentrations and should be avoided in women who are breastfeeding.

## TOPICAL NONPRESCRIPTION ANALGESICS

The sites of action for topical analgesics are the soft tissues and peripheral nerves beneath the site of application. The topical products used most frequently for the treatment of minor musculoskeletal pain are counterirritants. Counterirritation is the paradoxical pain-relieving effect achieved by producing a less severe pain to counter a more intense one. When applied to the skin at pain sites, counterirritants excite and subsequently desensitize nociceptive sensory neurons. The sensations associated with these reactions—as well as sensations associated with rubbing or massaging the skin during product application—distract from the deep-seated pain in muscles, joints, and tendons.

The four general categories of counterirritants are listed in TABLE 4. Rubefaciants cause vasodilation of cutaneous vasculature, producing reactive hyperemia; it is hypothesized that this increase in blood pooling and/or flow is accompanied by an increase in localized skin temperature, which may then exert a counterirritant effect. Camphor and menthol are believed to act on heat- and cold-sensitive receptors within sensory neurons called transient receptor potential (TRP) cation channels. When applied topically, these agents trigger a sensation of cold that is followed quickly by a sensation of warmth. Capsicum preparations elicit a transient feeling of warmth through stimulation of the TRP vanilloid-1 receptor. In addition, capsicum preparations release and ultimately (after repeated application) deplete the neuropeptide substance P from peripheral sensory neurons—an effect that may be analogous to cutting or ligating a nerve.

Topical counterirritants are available as solutions, liniments, gels, lotions, ointments, creams, and

patches. Products often include active ingredients from more than one of the categories listed in TABLE 4. Ointments and oil-based liniments have increased absorption compared with solutions, gels, lotions, and creams, but they are greasy and generally less acceptable to patients. The use of patches is becoming more popular because of their simple application and duration of action, but their use eliminates any benefit of a therapeutic rubbing action.

Topical counterirritants generally should be applied no more than four times per day. The application site may be bandaged lightly; however, tight bandaging or occlusive dressing increases the risk of irritation, redness, or blistering. Simultaneous application of heat (e.g., with heating pads or heat wraps) can increase the percutaneous absorption of menthol and methyl salicylate in particular, causing full-thickness skin and muscle necrosis as well as persistent interstitial nephritis. Patients should be cautioned against using heating pads or other modes of heat therapy in conjunction with any topical analgesic preparation.

Capsaicin is used for long-term treatment of certain types of pain (e.g., osteoarthritis). Pain relief usually is noted within 14 days after therapy has begun, when substance P has been depleted. However, relief occasionally is delayed by as long as 4 to 6 weeks. Once capsaicin has begun to relieve pain, patients must continue to apply it regularly three or four times per day to keep the pain from returning. If capsaicin treatment is stopped and the pain returns, treatment can be resumed. Patients should be aware that local burning or stinging often occurs when treatment begins (and substance P is released) but abates with repeated applications.

## MUSCULOSKELETAL INJURIES AND ACUTE LOW BACK PAIN

The pain associated with minor acute musculoskeletal injuries and acute low back pain usually can be managed adequately with nonprescription analgesics. The self-treatment of these conditions is outlined in FIGURE 1.

### Musculoskeletal Injuries

Injuries to muscles, tendons (which attach muscle to bone), and ligaments (which connect adjacent bones to each other) can be divided broadly into acute injuries and overuse injuries. Acute traumatic injuries occur when ligaments, tendons, or muscles fail to cope with the demands placed on them (e.g., when the stretch capacity of a tendon is exceeded). These injuries include:

- Strains—stretching or tearing (rupture) of a muscle or tendon due to overextension.
- Sprains—stretching or tearing of a ligament due to joint overextension.
- Contusions—bruising of a muscle (e.g., by blunt trauma).

Patients with acute traumatic injuries usually present with pain and swelling of the affected area. Patients also may experience bruising, some loss of function, and gradual stiffening of the affected area.

Delayed-onset muscle soreness is a type of subacute muscle pain that occurs as a result of any unaccustomed vigorous exercise or physical activity, especially exercise or activity that involves eccentric muscle contraction. Symptoms typically begin 8 or more hours after and are prominent 24 to 48 hours after the exercise or activity. The pain, which generally is described as a dull ache, reflects muscle damage that presumably was initiated by force generated in the muscle fibers; the mechanism by which the pain is generated is unknown. Other symptoms may include muscle and joint stiffness, swelling, and decreased joint range of motion.

Overuse injuries arise from repetitive, submaximal loading of the muscles or tendons (overuse injuries to ligaments are rare). They develop gradually and generally do not have a clearly defined cause or onset. Both tendonitis (inflammation of a tendon) and bursitis (inflammation of the bursa, the small sac that acts as a cushion between moving structures) may occur as overuse injuries of the elbow (e.g., “tennis elbow”), shoulder, wrist, hip, knee, or ankle. Carpal tunnel syndrome also is a type of overuse injury. The pain associated with these condi-

tions may develop suddenly and be quite severe; it usually is made worse by movement.

### Acute Low Back Pain

Low back pain occurs posteriorly in the region between the lower rib margin and the proximal thighs. It is the most frequently reported musculoskeletal pain, as well as the most prevalent and common work-related injury in Western society. Acute low back pain frequently occurs as a result of lumbar strain or sprain. Although the majority of patients with acute low back pain recover within a few days to a few weeks with conservative treatment, relapses and recurrences affect as many as 40% of patients.

Sciatica is a condition in which a herniated or ruptured disc presses on the sciatic nerve. Compression of the nerve causes burning or shock-like low back pain that radiates down one leg to below the knee, sometimes all the way to the foot. Patients who complain of low back pain consistent with sciatica should be evaluated by a primary care provider.

### Exclusions for Self-Treatment

Self-treatment of musculoskeletal injuries and acute low back pain should be limited to patients with mild to moderate pain who do not exhibit any of the exclusions for self-treatment listed in FIGURE 1. Of note, patients with pain that has persisted for more than 2 weeks should use nonprescription analgesics only after being evaluated by a primary care provider.

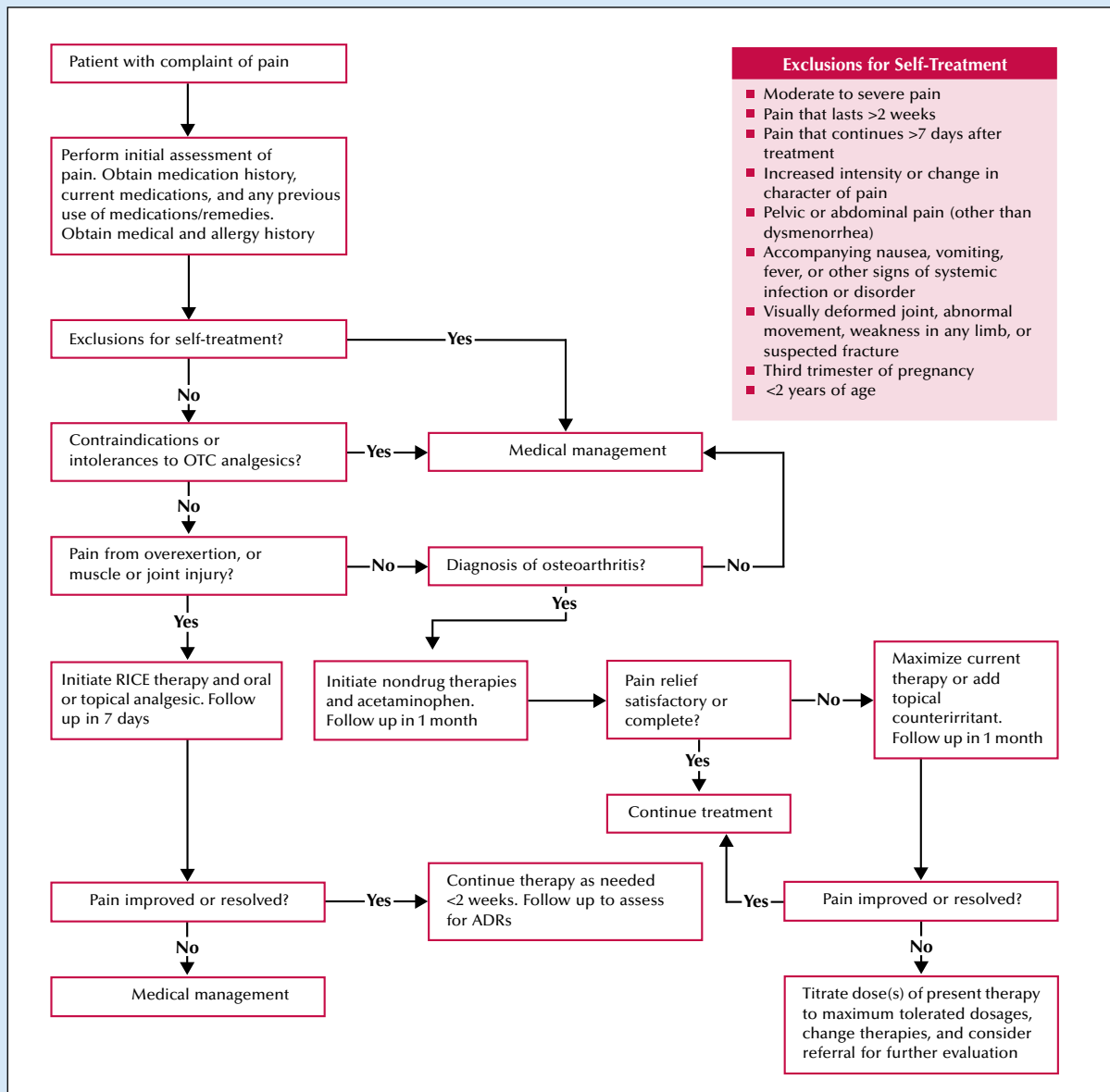
### Self-Treatment of Musculoskeletal Injuries and Acute Low Back Pain

The goals of self-treatment of musculoskeletal injuries and acute low back pain include the following:

- Decrease the subjective intensity (severity) and duration of pain.
- Restore function of the affected area.
- Prevent reinjury and disability.
- Prevent acute pain from becoming chronic persistent pain.

For acute traumatic injuries, these goals are accomplished initially with rest, ice, compression, and elevation (RICE) therapy in conjunction with systemic and/or topical nonprescrip-

**Figure 1. Algorithm for Self-Treatment of Musculoskeletal Injuries and Disorders**



ADR = adverse drug reaction; OTC = over-the-counter; RICE = rest, ice, compression, and elevation.

Source: Wright E. Musculoskeletal injuries and disorders. In: Berardi RR, Ferreri SP, Hume AL, et al. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care*. 16th ed. Washington, DC: American Pharmacists Association; 2009:99.

tion analgesics. Acute low back pain, delayed-onset muscle soreness, and overuse injuries may be treated with ice and/or heat therapy in conjunction with systemic and/or topical nonprescription analgesics. Gentle physical activity should be encouraged in patients with low back pain; bed rest alone may make back pain worse and delay recovery.

### RICE Therapy

RICE therapy promotes healing and helps reduce swelling and inflammation associated with muscle and joint injuries. Guidelines for RICE therapy are presented in TABLE 5.

Ice (e.g., ice cubes or chips in a plastic bag or damp cloth) should be applied as close to the injury time as possible and reapplied three to four times daily until the swelling

decreases. This generally takes 12 to 24 hours, but swelling may continue for 48 to 72 hours with more severe injuries (e.g., ankle sprains). Post-exercise icing often is appropriate to reduce the likelihood of inflammation and reduce pain.

Excessive icing can cause significant vasoconstriction and reduce vascular clearance of inflammatory mediators from the damaged area. To

## CASE 1. MUSCULOSKELETAL INJURIES AND DISORDERS

PC is a 52-year-old man who complains of knee pain. The pain has “come and gone for a while,” but it worsened 3 days ago following an 18-hole golf game.

Information obtained during a patient history and assessment includes the following:

- The right knee is swollen and moderately inflamed. A grinding sound is audible during movement of this knee.
- The left knee shows no signs of inflammation or crepitus.
- The patient plays golf regularly (averaging four times each month) and always walks the course. During the most recent golf game, the knee was bothersome, but the patient recalls no particular incident that would have caused the knee pain.
- The patient’s height is 5’ 9” and he weighs 220 lb.
- There is no relevant history of preexisting conditions.

Which of the following statements represents the best approach for this patient?

- a. The patient should initiate a course of RICE (rest, ice, compression, and elevation) therapy and consult a primary care provider in 2 weeks if the pain is not relieved.
- b. The patient should apply heat to the affected knee and consult a primary care provider in 2 weeks if the pain is not relieved.
- c. The patient may self-treat the pain with maximal nonprescription doses of aspirin (4 g/day) to obtain an anti-inflammatory effect. He should consult a primary care provider in 2 weeks if the pain is not relieved.
- d. The patient should be evaluated by a primary care provider to rule out osteoarthritis. He can initiate short-term self-treatment with ice and acetaminophen while awaiting the appointment; however, ongoing self-treatment should not continue unless a diagnosis is made.

*Case study responses appear on page 18.*

help prevent injury, individual applications of ice should not exceed 15 to 20 minutes. Patients also should place a barrier, such as a thin towel, between the ice pack and the skin.

According to the current American Heart Association and American Red Cross guidelines for first aid, refreezable gel packs are not as good as ice for cold application.

### Heat Therapy

Heat therapy is a treatment option for patients with noninflammatory pain. Although the mechanism of action is not fully understood, heat may help reduce pain by increasing blood flow to the affected area. Heat is applied for 15 to 20 minutes, three to four times daily. Heat therapy should not be used in the acute stages of inflammation or trauma (i.e., during the first 48 hours) because it can intensify vasodilation and exacerbate vascular leakage and tissue damage.

Traditionally, heat has been applied using moist compresses or devices such as electric heating pads or hot

water bottles. Newer heat-generating products (e.g., ThermaCare) emit continuous low-level heat for up to 12 hours. These heat wraps adhere to the skin and thus can be positioned easily over the targeted area. The design also permits patients to remain active while wearing the heat wrap. Heat wraps are a recommended therapy for low back pain. They also can be used for both the prevention and treatment of delayed-onset muscle soreness and may be more effective than ice therapy. Although heat wraps generally do not cause adverse effects, patients should be advised to remove the wrap immediately if they have any pain or discomfort, itching, or burning. Patients older than 55 years of age should apply heat wraps over a layer of clothing; all patients should avoid wearing heat wraps while sleeping.

Heat should not be applied over broken skin or in conjunction with topical analgesics, as discussed earlier. Heat therapy also should not be used in patients with diminished pain perception or on areas of the skin with

decreased sensation; severe burns may result.

### Nonprescription Analgesics

Acetaminophen or NSAIDs may be used in the initial treatment of musculoskeletal injuries. The recommended dosage should be administered at regularly scheduled intervals beginning early in the course of the injury, followed by downward tapering of the dosage and interval as the injury improves (generally in 1 to 3 days). Analgesic therapy should be limited to 7 days of self-care use.

### Follow-Up

The primary indicator of treatment effectiveness is the patient’s perception of pain relief. If pain persists or has worsened after 7 days of self-treatment, the patient should be referred to a primary care provider for further evaluation. Patients also should consult a primary care provider if their pain changes in character or severity or if new acute pain develops.

### Points to Remember

- Self-treatment of acute musculoskeletal injuries should include rest, ice, compression, and elevation (RICE therapy). Heat therapy also may provide benefit after swelling abates.
- Treatment with systemic nonprescription analgesics (acetaminophen or NSAIDs) should be started soon after a musculoskeletal injury and administered on a regular schedule.
- Topical counterirritants are useful for treatment of minor acute musculoskeletal injuries and as an adjunct in the treatment of chronic musculoskeletal disorders. Patients should be advised not to use heating devices with topical counterirritants or cover the counterirritant with a tight bandage.
- Patients should contact their primary care provider if their symptoms do not improve after 7 days of therapy with nonprescription analgesics or if their symptoms change or worsen.

**Table 5. Guidelines for RICE Therapy**

- Rest the injured area as soon as possible after the injury occurs and continue until pain is reduced (generally 1 to 2 days). Use slings, splints, or crutches if necessary.
- Apply ice as soon as possible to the injured area in 10- to 15-minute increments, three to four times per day. Continue the ice-pack therapy for 1 to 3 days, depending on the severity of the injury.
- Apply compression to the injured area with an elastic support or an elasticized bandage as follows:
  - Choose the appropriate size bandage for the injured body part. If preferred, purchase a product specifically designed for the injured body part.
  - Unwind about 12 to 18 inches of bandage at a time and allow the bandage to relax.
  - If ice also is being applied to the injured area, soak the bandage in water to aid the transfer of cold.
  - Wrap the injured area by overlapping the previous layer of bandage by about one third to one half its width.
  - Begin wrapping at the point most distal from the injury. For example, if the ankle is injured, begin wrapping just above the toes.
  - Decrease the tightness of the bandage as you continue to wrap. If the bandage feels tight or uncomfortable or circulation is impaired, remove the compression bandage and rewrap it. Cold toes or swollen fingers would indicate a bandage is too tight.
  - After using the bandage, wash it in lukewarm, soapy water; do not scrub it. Rinse the bandage thoroughly and allow to air dry on a flat surface.
  - Roll up the bandage to prevent wrinkles and store it in a cool, dry place. Do not iron the bandage to remove wrinkles.
- Elevate the injured area at or above the level of the heart 2 to 3 hours per day to decrease swelling and relieve pain.

RICE = rest, ice, compression, and elevation.

## OSTEOARTHRITIS

Osteoarthritis, the most common joint disorder in the United States, affects more than 26 million American adults. It is characterized by a gradual softening and destruction of articular cartilage in diarthrodial joints, with subsequent thickening of the subchondral bone and new bony outgrowths (osteophytes) at joint margins. Rearrangement of the joint architecture leads to pain, decreased or altered motion, crepitus, and possibly local inflammation that usually is mild or localized.

Osteoarthritis most commonly affects the joints of the hands, knees, hips, and lumbar and cervical spine. The pain usually is described as a deep, dull ache that worsens with movement and improves with rest, especially during the early stages of the disease. In the later stages of the disease, patients may experience pain at rest or at night as well as morning stiffness with pain lasting up to 30 minutes.

Osteoarthritis pain may or may not correlate with the degree of joint damage. Pain is often referred, and proximal muscles could be involved if a person with osteoarthritis guards the affected joint (e.g., by changing the gait to reduce discomfort).

The prevalence and severity of osteoarthritis increase with age. Other risk factors include obesity, previous joint injury or trauma, and participation in activities that involve repetitive motion. Heredity also plays a role.

### Self-Treatment of Osteoarthritis

Patients with suspected osteoarthritis should undergo an initial evaluation by a primary care provider. The self-treatment of pain associated with diagnosed osteoarthritis is outlined in **FIGURE 1**.

#### Nonpharmacologic Measures

The American College of Rheumatology considers nonpharmacologic measures to be the cornerstone of osteoarthritis management. Nonpharmacologic measures that help to maintain or improve joint mobility and limit functional impairment include:

- Weight loss (if overweight) to reduce stress on weight-bearing joints.
- Aerobic exercise (e.g., walking) and muscle-strengthening exercises (including isometric and isotonic exercises) to improve joint flexibility and biomechanics.
- Use of assistive devices (e.g., canes) as needed for ambulation.

Many patients benefit from participating in self-management programs,

such as the Arthritis Self-Help Program available through the Arthritis Foundation.

Applications of ice or heat, as described in the previous section, can be used for the temporary relief of pain, stiffness, and occasional swelling associated with osteoarthritis. Patients may need to experiment with both ice and heat to determine which modality offers the greatest pain relief. For some patients, alternating between applications of heat and ice provides the greatest relief.

#### Nonprescription Analgesics

Clinical practice guidelines emphasize the initial use of acetaminophen for the control of mild to moderate pain in osteoarthritis, especially in older patients because decreased renal function and increased risk of upper GI bleeding are important considerations. The relief of mild to moderate pain often is comparable to that achievable with an NSAID, with fewer adverse effects. However, responses to analgesics vary from patient to patient; nonprescription doses of NSAIDs (e.g., ibuprofen 400 mg three times daily) may prove effective for patients who fail to achieve adequate pain relief from maximal doses of acetaminophen.

Topical products containing cap-

saicin can be used in addition to or instead of oral medications. The cream should be applied to the symptomatic joint four times daily; pain relief usually begins within 14 days of regular use. Topical products containing methyl salicylate also may be helpful.

### Glucosamine and Chondroitin

Glucosamine is a glycoprotein that is either derived from marine exoskeletons (shellfish chitin) or produced synthetically. It is produced naturally in the human body and used in the synthesis of components of articular cartilage, including glycosaminoglycans, proteoglycans, and hyaluronic acid. As a dietary supplement, glucosamine is available in both sulfate and hydrochloride salt forms.

Chondroitin sulfate is a glycosaminoglycan made from glucuronic acid and galactosamine present in animal cartilage. It currently is manufactured from natural sources (shark or beef cartilage, including bovine trachea) or by synthetic means. Like glucosamine, chondroitin sulfate serves as a building block for cartilage production; it also inhibits leukocyte elastase, an enzyme involved in cartilage degradation.

Most of the existing evidence for the use of these agents in the treatment of osteoarthritis comes from trials that used glucosamine sulfate alone or in combination with chondroitin sulfate (few trials have examined chondroitin monotherapy). In general, the trials show an overall positive effect on decreasing pain and improving joint function, particularly for osteoarthritis of the knee. A notable exception—the Glucosamine/chondroitin Arthritis Intervention Trial (GAIT), which was funded by the National Center for Complementary and Alternative Medicine and the National Institute of Arthritis and Musculoskeletal and Skin Diseases—found that glucosamine and chondroitin sulfate, alone or in combination, were not significantly better than placebo in reducing knee pain or preventing disease progression. However, because that study used glucosamine hydrochloride, the results are not considered to be generalizable to the more widely studied glucosamine sulfate. The GAIT results also were limited by a high rate of

response to placebo (60.1%) and the relatively mild degree of osteoarthritis pain among the participants; in a subgroup of patients with moderate to severe pain, combined treatment with glucosamine hydrochloride and chondroitin sulfate was found to reduce knee pain significantly.

The recommended dosage of glucosamine sulfate is 1,500 mg/day, administered orally as a single dose or divided doses. (Insufficient data exist to support topical application of glucosamine.) The recommended dosage of chondroitin sulfate is 1,200 mg/day, administered orally as a single dose or divided doses. Because chondroitin is the more expensive ingredient, it is prudent to advise interested patients to begin treatment with glucosamine sulfate alone. A combination product can be considered if some benefit is seen after 4 to 5 months of glucosamine monotherapy but symptoms remain bothersome. If no additional benefit is apparent after 3 to 5 months of combination therapy, the chondroitin sulfate should be discontinued.

Most trials have found the safety of glucosamine sulfate and chondroitin sulfate to be equal to that of placebo. Minor GI symptoms (e.g., nausea, stomach upset, constipation, diarrhea) have been reported with both agents. Patients with severe shellfish allergies should avoid glucosamine.

### Follow-Up

Pharmacists should plan to follow up with patients approximately 1 month after treatment with nondrug measures and acetaminophen is initi-

ated. If the patient reports unsatisfactory or incomplete pain relief at that time, possible interventions include increasing the dose of acetaminophen (as long as doing so will not exceed the maximum daily dosage of 4 g from all prescription and nonprescription sources) and adding topical capsaicin or methyl salicylate. If the patient's pain neither improves nor resolves after an additional 4 weeks of treatment, possible interventions include further increasing the dose of acetaminophen, switching to a different analgesic, and referring the patient to a primary care provider for further evaluation.

### HEADACHE

More than 90% of people experience headache at some time during their lives. Headaches generally are classified as primary or secondary. Primary headaches, which account for approximately 90% of headaches, are not associated with an underlying illness. Secondary headaches are symptoms of an underlying condition such as head trauma, vascular defects (e.g., infarction, intracerebral hemorrhage, aneurysm), substance abuse or withdrawal, bacterial and viral diseases, and disorders of craniofacial structures.

Three types of primary headache are amenable to self-treatment: tension-type headache, diagnosed migraine (vascular) headache, and sinus headache. These headaches can be differentiated by their characteristic signs and symptoms (TABLE 6).

### Points to Remember

- Self-treatment of arthritis pain is appropriate only for patients with a diagnosis of osteoarthritis. Patients with suspected osteoarthritis should be referred to a primary care provider.
- Optimal self-treatment of osteoarthritis includes both nonpharmacologic and pharmacologic therapies.
- Acetaminophen is the drug of first choice for mild to moderate osteoarthritis pain because it is associated with fewer adverse effects (particularly GI adverse events) than NSAIDs.
- Topical products containing capsaicin or methyl salicylate may be used in addition to or instead of systemic analgesics.
- Products containing glucosamine sulfate, with or without chondroitin sulfate, may be of benefit to patients with osteoarthritis.

**Table 6. Characteristics of Tension-Type, Migraine, and Sinus Headaches**

Characteristic	Tension-Type Headache	Migraine Headache	Sinus Headache
Location	Bilateral; over the top of the head, extending to the base of the skull	Usually unilateral	Face, forehead, or periorbital area
Nature	Varies from diffuse ache to tight, pressing, constricting pain	Throbbing; may be preceded by an aura	Pressure behind eyes or face; dull, bilateral pain; worse in the morning
Onset	Gradual	Sudden	Simultaneous with sinus symptoms, including purulent nasal discharge
Duration	Minutes to days	Hours to 3 days	Days (resolves with sinus symptoms)

### Tension-Type Headaches

Tension-type headaches—also called stress headaches—are the most common type of primary headache, with more than 75% of the U.S. population experiencing tension-type headaches at some time. They often manifest in response to stress, anxiety, depression, emotional conflicts, and other stimuli. Tension-type headaches can be episodic or chronic; chronic headaches occur at least 15 days per month for at least 6 months.

The pain of tension-type headaches typically is bilateral with a pressing or tightening (nonpulsating) quality, as if a band is constricting the head. The severity of the pain is variable; some headaches are mild enough not to require treatment, whereas others are severe enough to be disabling. Although tension-type headaches usually are not aggravated by routine physical activity such as walking or climbing stairs, shivering or cold temperatures may increase the pain.

### Migraine Headaches

Migraine headaches are recurrent headaches that manifest in attacks lasting 4 to 72 hours. They occur with or without focal neurological symptoms (aura) that may include shimmering or flashing areas or blind spots in the visual field, difficulty speaking, visual and auditory hallucinations, and

(usually) one-sided muscle weakness. Migraine without aura occurs almost twice as frequently as migraine with aura, although patients may have both types of headaches. When aura is present, it usually precedes the headache but may accompany it.

The pain of migraine headaches tends to be much more severe than that associated with tension-type headaches, with 80% of migraineurs reporting their pain as severe. The pain typically occurs unilaterally in a fronto-temporal area and has a pulsating quality. It is aggravated by or causes avoidance of routine physical activity. In addition to pain, patients may experience nausea, vomiting, photophobia, phonophobia, tinnitus, light-headedness, vertigo, and irritability. Some patients have a prodrome of a burst of energy or fatigue, extreme hunger, and nervousness.

As many as 70% of patients with migraine have family histories of migraine, suggesting that this disease is influenced by heredity. Onset usually begins in the first three decades of life, with greatest prevalence at approximately 40 years of age. Stress, fatigue, oversleeping, fasting or missing a meal, vasoactive substances in food, caffeine, alcohol, menses, and changes in barometric pressure and altitude may trigger migraine. Certain medications including reserpine,

nitrates, oral contraceptives, and postmenopausal hormones also are potential migraine triggers.

Although tension-type headache and migraine headache historically were thought to have separate pathologies, they appear to be more similar than distinct. It is possible that migraine and tension-type headaches represent different manifestations of a single pathophysiology.

### Sinus Headaches

Sinus headache is a frequently reported symptom in patients with acute sinusitis. It occurs when infection or blockage of the paranasal sinuses causes inflammation or distention of the sensitive sinus walls. Dull, pressure-like pain usually is localized to facial areas over the sinuses; bending forward in a stooping position or blowing the nose often intensifies the pain. Patients typically experience other sinus symptoms such as toothache in the upper teeth, facial pain, nasal stuffiness, and nasal discharge. Persistent sinus pain with or without discharge suggests possible infection and requires further medical evaluation.

It may be difficult to differentiate sinus headache from migraine without aura, especially because pathophysiologic mechanisms at work during migraine headache can produce prominent sinus congestion. As many as 90% of patients who believe they are suffering from sinus headache actually may be experiencing migraine headache.

### Self-Treatment of Headache

Most patients with episodic headaches respond adequately to self-treatment with nonpharmacologic interventions (for migraine headaches in particular), nonprescription medications, or both therapies. The algorithm in FIGURE 2 outlines the self-treatment of headaches and lists exclusions for self-treatment. Some patients with episodic headaches and most with chronic headaches are candidates for prescription treatments; however, these patients often use nonprescription therapies adjunctively.

Health care professionals should be alert for patients who may be suffering from medication-overuse (rebound) headaches. These nearly

continuous headaches usually are associated with use of analgesic medications (i.e., acetaminophen, aspirin, caffeine, triptans, opioids, butalbital, or ergotamine formulations) for 3 months or longer. The headaches occur within hours of stopping the agent; readministration provides relief. When medication-overuse headache is suspected, use of the offending agent(s) should be tapered and subsequently eliminated. Prescription therapies may be needed to combat the increased headaches that temporarily ensue during the days to weeks of the withdrawal period.

### Nonpharmacologic Measures

General treatment measures for migraine include (1) maintaining a regular schedule for sleeping and eating meals to avoid fatigue, oversleeping, or hunger and (2) practicing methods for coping with stress. Some migraine patients benefit from use of ice (ice bags or cold packs) combined with pressure applied to the forehead or temple areas to reduce pain associated with acute migraine attacks.

Nutritional strategies intended to prevent migraine encompass:

- Dietary restriction of foods that contain triggers.
  - Avoidance of hunger and low blood glucose (a trigger of migraine).
  - Magnesium supplementation.
- Advocates of nutritional therapy recommend avoidance of foods with vasoactive substances such as nitrites, tyramine (found in red wine and aged cheese), phenylalanine (found in the artificial sweetener aspartame), monosodium glutamate (often used in Asian cuisine), caffeine (in coffee, tea, cola beverages, and chocolate), and theobromines (in chocolate). Any food allergen also can be a trigger.

### Nonprescription Analgesics

Episodic tension-type headaches often respond well to acetaminophen, NSAIDs, or salicylates. To be most effective, the analgesic should be taken as soon as the headache starts.

Taking an NSAID or salicylate at the onset of symptoms can abort a mild or moderate migraine headache. Analgesics are less effective once a migraine has evolved. Migraineurs

## CASE 2. HEADACHE

AB is a 39-year-old woman who visits the pharmacy looking for “something to help a headache.” She went out with some coworkers the previous evening and reports being “just a little hung over” after drinking three beers. The company AB works for has been experiencing financial difficulties, and there are rumors that some employees may need to be laid off.

The headache is bilateral over the temples and moderate in intensity. AB reports having experienced similar headaches before, but infrequently (two to three times per year). The patient history reveals no medications or conditions commonly associated with headache. AB denies excessive use of caffeine and has not taken any nonprescription medications during the past week; she is a former smoker (quit 2 years ago). AB reports no photophobia, aura, or other classic migraine symptoms.

Which of the following approaches is most appropriate for this patient?

- The patient should be advised to take both a nonprescription analgesic and a decongestant, because her symptoms are consistent with sinus headache.
- The patient should be evaluated by a primary care provider to rule out migraine headache.
- The patient may attempt self-treatment with a nonprescription analgesic. She should consult her primary care provider if the headache persists or worsens despite treatment.
- The patient should not attempt self-treatment with a nonprescription analgesic because of her recent use of alcohol.

*Case study responses appear on page 18.*

who can predict the occurrence of the headache (e.g., during menstruation) should take an analgesic (usually an NSAID) before the event known to trigger the headache as well as throughout the duration of the event.

Some patients have coexisting tension and migraine headaches. Treatment of the initiating headache type can abort the mixed headache problem; it is not always necessary to treat both types.

For patients with sinus headache, decongestants (e.g., pseudoephedrine) facilitate drainage of the sinuses. Concomitant use of nonprescription analgesics and decongestants can relieve the pain of sinus headache.

The use of nonprescription analgesics for any type of headache should be limited to 3 days per week. More frequent or continuous use of nonprescription analgesics increases a patient’s risk of both adverse effects and medication-overuse headache. Frequent use of analgesics also may signal the presence of a condition that should not be self-treated.

### Follow-Up

Appropriate follow-up depends on headache type, frequency, and sever-

ity and patient factors. For patients with episodic headaches, a trial of 6 to 12 weeks may be needed to assess the effectiveness of nonprescription analgesic therapy. Patients with chronic headache may require a trial of 4 to 6 weeks. Pharmacists should follow up with patients with severe headache pain within 10 days of initiation of self-treatment to assess efficacy and tolerability.

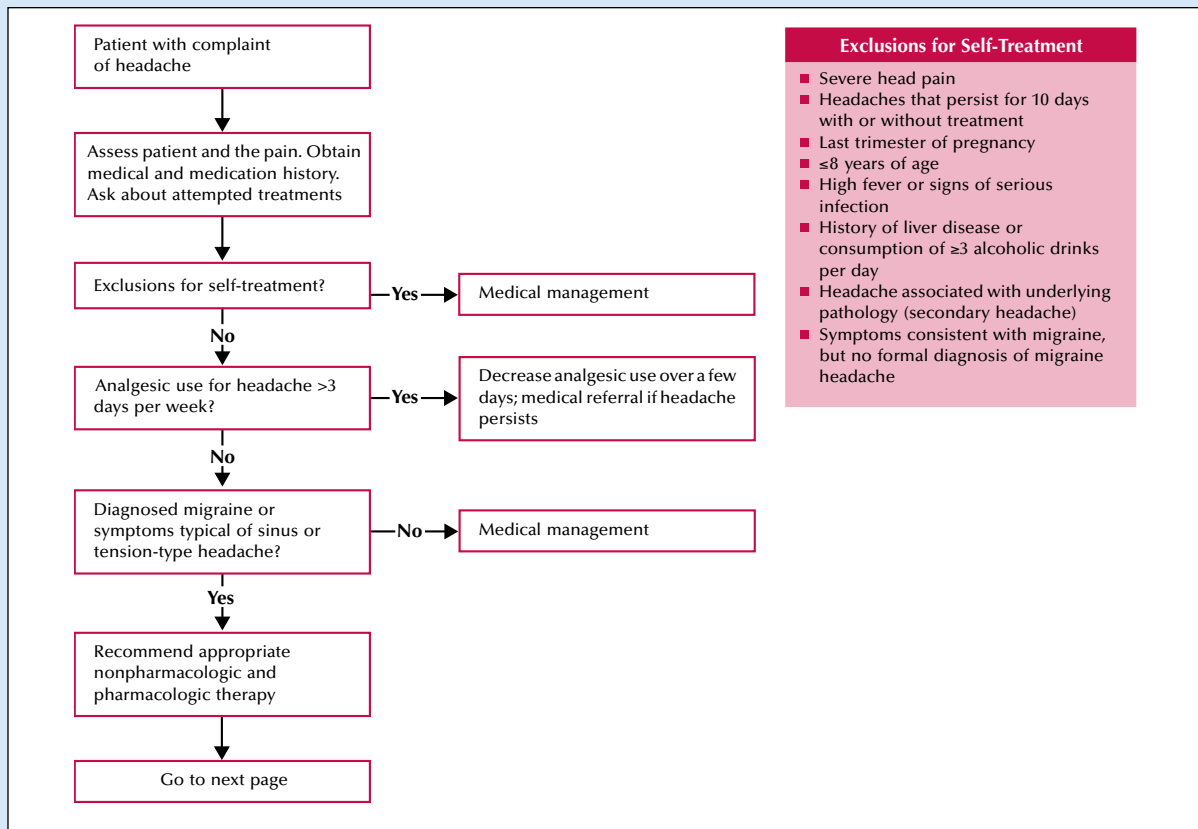
All patients should seek medical attention promptly if headaches persist longer than 10 days or worsen despite self-treatment. Patients should be advised that continuing or escalating pain can be a sign of a more serious problem.

More than half of patients suffering from migraine headache use only nonprescription medications, despite the severity of pain. Patients may need to be educated about the availability of effective prescription therapies that can limit pain and disability substantially.

## DYSMENORRHEA

Dysmenorrhea—difficult or painful menstruation—is one of the most common gynecologic problems in the United States. Dysmenorrhea is

**Figure 2. Algorithm for Self-Treatment of Headache**



divided into primary and secondary disorders (TABLE 7). Primary dysmenorrhea is idiopathic and associated with cramp-like abdominal pain at the time of menstruation in the absence of pelvic disease. Secondary dysmenor-

rhea usually is associated with pelvic pathology.

Primary dysmenorrhea typically develops within 6 to 12 months of menarche, generally affecting women during their teens and early 20s.

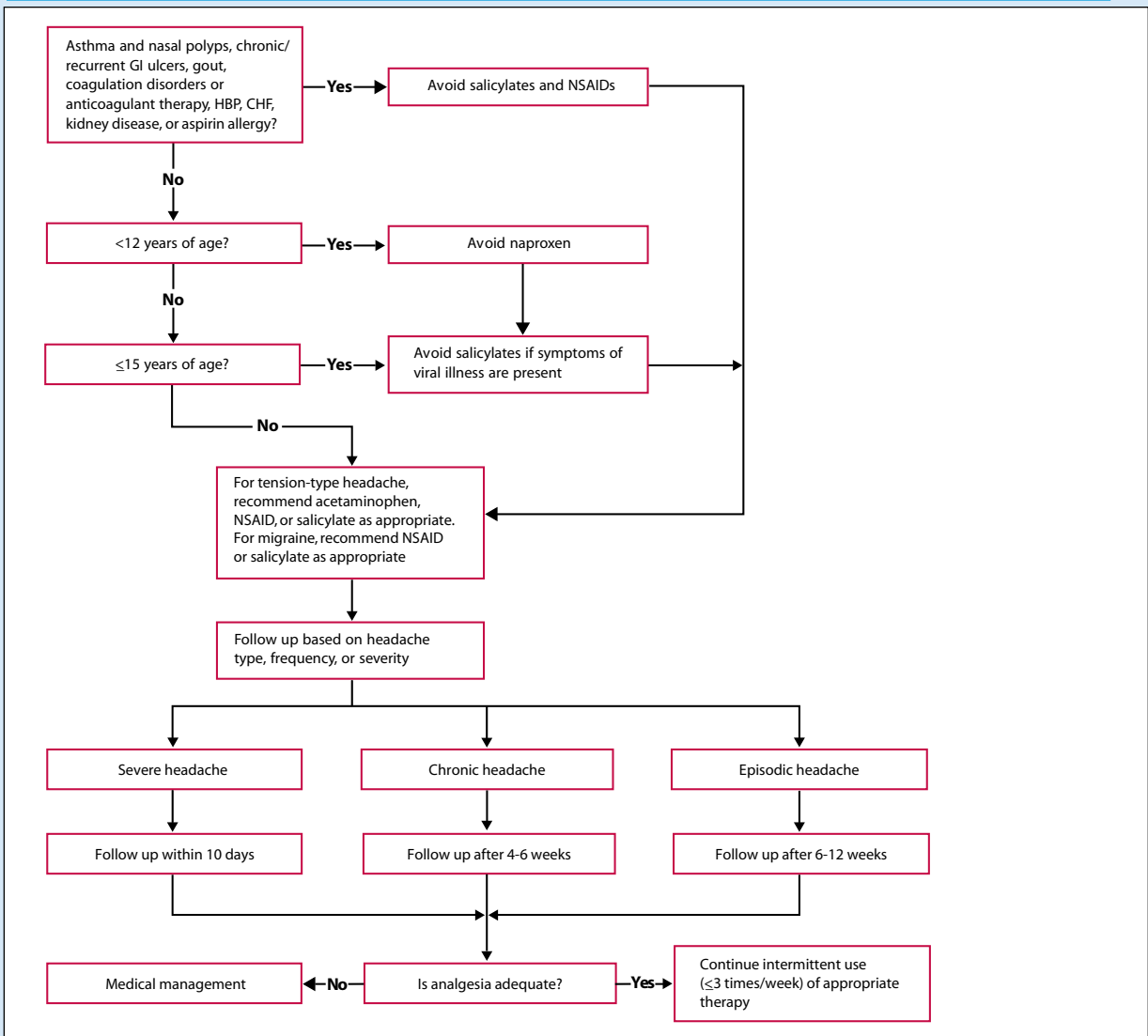
Primary dysmenorrhea occurs only during ovulatory cycles; therefore, its prevalence increases between early and older adolescence as the regularity of ovulation increases. The prevalence of dysmenorrhea decreases after the age of 25 years, in part because of oral contraceptive use and pregnancy.

The cause of primary dysmenorrhea is not fully understood, but prostaglandins and possibly leukotrienes and vasopressin are known or believed to be involved. Prostaglandin levels are two to four times greater in women with dysmenorrhea than in women without dysmenorrhea and are highest during the first 2 days of menses, when dysmenorrhea commonly occurs. Levels of leukotrienes and vasopressin also have been found to be elevated in women with dysmenorrhea. Prostaglandins, leukotrienes, and vasopressin may cause uterine contractions; elevated levels of these

### Points to Remember

- Many tension-type, migraine, and sinus headaches are amenable to treatment with nonprescription analgesics. Patients with symptoms suggestive of secondary or undiagnosed migraine headaches should be evaluated by a primary care provider.
- Nonprescription analgesics should be taken as early as possible in the evolution of a tension-type headache.
- Some migraine headaches can be aborted or prevented if an NSAID or salicylate is taken at the onset of headache pain or before the start of a predictable attack (e.g., a migraine headache that usually occurs during menstruation).
- Patients with sinus headache are likely to benefit from combination therapy with a nonprescription analgesic and decongestant.
- Patients should not use nonprescription analgesics for longer than 10 days or more frequently than 3 days per week, unless directed to do so by a primary care provider.

**Figure 2. Algorithm for Self-Treatment of Headache (Continued)**



CHF = congestive heart failure; GI = gastrointestinal; HBP = high blood pressure; NSAID = nonsteroidal anti-inflammatory drug; OTC = over-the-counter.

Source: Remington T. Headache. In: Berardi RR, Ferreri SP, Hume AL, et al. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care*. 16th ed. Washington, DC: American Pharmacists Association; 2009:67-8.

substances can amplify the uterine contractions and vasoconstriction that are a normal part of menstruation, resulting in uterine ischemia and pain.

Dysmenorrhea typically is experienced as a continuous dull aching pain with spasmodic cramping in the lower midabdominal or suprapubic region, which may radiate to the lower back and upper thighs. The pain begins several hours before or coincident with the onset of menses and usually lasts less than 48 hours, but may persist up to 72 hours. Uterine

contractions can force prostaglandins into the systemic circulation, causing additional symptoms such as nausea, vomiting, fatigue, dizziness, irritability, diarrhea, and headache.

### Self-Treatment of Dysmenorrhea

Self-treatment of dysmenorrhea is appropriate for the following types of patients:

- Otherwise healthy young women with a history consistent with primary dysmenorrhea who are not sexually active.

- Women who have been diagnosed with primary dysmenorrhea (TABLE 7). Adolescents with pelvic pain who are sexually active (and therefore at risk for pelvic inflammatory disease) and women with characteristics indicating secondary dysmenorrhea should be evaluated by a primary care provider.

FIGURE 3 presents an algorithm for managing primary dysmenorrhea, along with exclusions for self-care. The nonsalicylate NSAIDs ibuprofen and naproxen sodium are the principal nonprescription analgesics for treating

### Points to Remember

- Self-care is appropriate for an otherwise healthy young woman with a history consistent with primary dysmenorrhea who is not sexually active, or any woman diagnosed with primary dysmenorrhea. Adolescents with pelvic pain who are sexually active (at risk for pelvic inflammatory disease) and women with characteristics indicating secondary dysmenorrhea should be evaluated by a primary care provider.
- Nonsalicylate NSAIDs are the drugs of choice for the management of primary dysmenorrhea. These medications should be taken at the onset of or just prior to menses and used in scheduled doses for several days for optimal reduction in pain and cramping.
- The use of local topical heat can provide relief from dysmenorrhea. Its analgesic effect has a faster onset than drug therapy, and it can add to the relief provided by an NSAID. Nondrug therapy may be especially useful for women who cannot tolerate or who do not respond to nonprescription NSAIDs.

primary dysmenorrhea. Nonpharmacologic measures often serve as adjuncts to drug therapy. Nonpharmacologic options may be especially useful for the estimated 15% of women who cannot tolerate or do not respond to nonprescription medications.

#### Nonpharmacologic Measures

**Heat Therapy.** Topical heat therapy is a commonly recommended

nonpharmacologic treatment for dysmenorrhea; it may be adequate as the sole treatment for some women. An abdominal heat wrap (i.e., Therma-Care) that emits continuous, low-level heat was shown to be significantly better (14% greater pain relief) than placebo and acetaminophen in relieving pain and cramping. The heat wrap provided a faster onset of analgesic effect

than drug therapy did, and it added to the relief provided by ibuprofen.

**Lifestyle Modifications.** Lifestyle modifications may alleviate dysmenorrhea symptoms to varying degrees. Smoking and exposure to second-hand smoke have been associated with more severe dysmenorrhea; the severity reportedly increases with the number of cigarettes smoked per day. Although the basis for this effect is unknown, it has been hypothesized that nicotine-induced vasoconstriction is involved.

Participation in regular exercise may lessen the symptoms of primary dysmenorrhea for some women. However, evidence regarding the benefit of exercise is conflicting.

Some women may benefit from increased consumption of either (1) fish such as tuna, salmon, sardines, herring, and mackerel or (2) fish oil supplements that are rich in omega-3 polyunsaturated fatty acids. The American diet is high in omega-6 fatty acids such as arachadonic acid, which are precursors to both prostaglandins and leukotrienes. Omega-3 fatty acids compete with omega-6 fatty acids for the production of prostaglandins and leukotrienes; adding omega-3 fatty acids to the diet may result in the production of less potent prostaglandins and leukotrienes.

#### Nonprescription Analgesics

The nonprescription NSAIDs ibuprofen and naproxen sodium are the preferred agents for treating primary dysmenorrhea. Although aspirin and acetaminophen also may be used to treat the symptoms of dysmenorrhea, they are less potent inhibitors of prostaglandin synthesis and generally are effective only for mild symptoms.

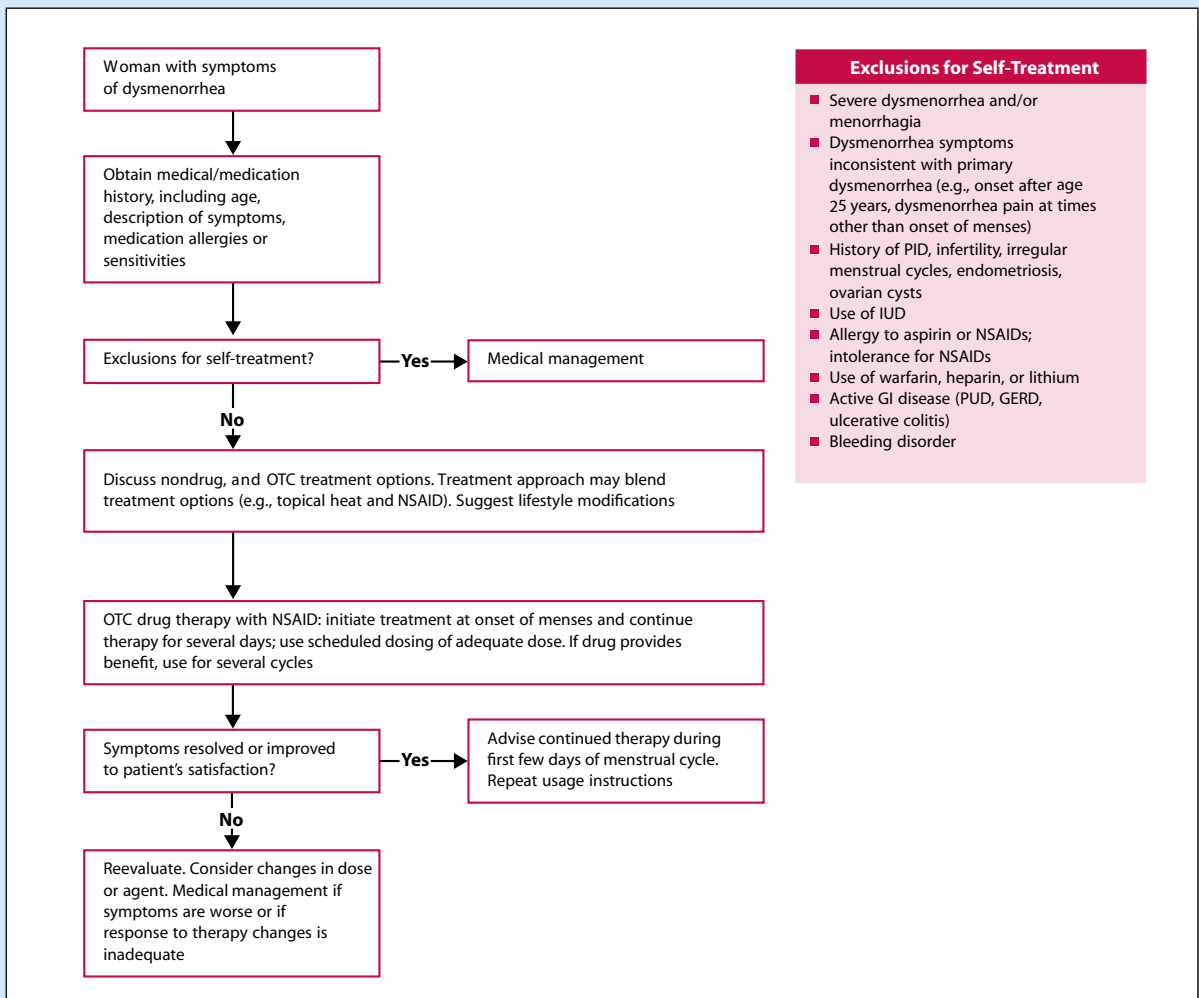
NSAIDs are used as much to prevent cramps as to relieve pain. The selected agent should be administered as soon as possible at the onset of menses or pain and continued on a scheduled basis (every 4 to 6 hours for ibuprofen, every 8 to 12 hours for naproxen) for the first 48 to 72 hours of menstrual flow. Delaying initiation of drug therapy may result in inadequate treatment or treatment failure. A therapeutic effect usually is apparent within

**Table 7. Differentiation of Primary and Secondary Dysmenorrhea**

Characteristic	Primary Dysmenorrhea	Secondary Dysmenorrhea
Age at onset of dysmenorrhea	Typically 6 to 12 months after menarche (age 12 to 13 years for most girls)	Mid- to late 20s through 30s and 40s
Menses	More likely to be regular with normal blood loss	More likely to be irregular; menorrhagia more common
Pattern and duration of dysmenorrhea	Onset just prior to or coincident with onset of menses; pain with each or most menses; lasting 2 to 3 days	Vary according to cause; change in pain pattern or intensity also may indicate secondary disease
Pain at other times of menstrual cycle	No	Yes; may occur before, during, or after menses
Response to NSAIDs and/or oral contraceptives	Yes	No
Other symptoms	Nausea, vomiting, fatigue, dizziness, irritability, diarrhea, and headache may occur at same time as dysmenorrhea	Vary according to cause; may include dyspareunia and pelvic tenderness

NSAIDs = nonsteroidal anti-inflammatory drugs.

**Figure 3. Algorithm for Self-Treatment of Dysmenorrhea**



- Exclusions for Self-Treatment**
- Severe dysmenorrhea and/or menorrhagia
  - Dysmenorrhea symptoms inconsistent with primary dysmenorrhea (e.g., onset after age 25 years, dysmenorrhea pain at times other than onset of menses)
  - History of PID, infertility, irregular menstrual cycles, endometriosis, ovarian cysts
  - Use of IUD
  - Allergy to aspirin or NSAIDs; intolerance for NSAIDs
  - Use of warfarin, heparin, or lithium
  - Active GI disease (PUD, GERD, ulcerative colitis)
  - Bleeding disorder

GERD = gastroesophageal reflux disease; GI = gastrointestinal; IUD = intrauterine device; NSAID = nonsteroidal anti-inflammatory drug; OTC = over-the-counter; PID = pelvic inflammatory disease; PUD = peptic ulcer disease.

Source: Shimp LA. Disorders related to menstruation. In: Berardi RR, Ferreri SP, Hume AL, et al. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care*. 16th ed. Washington, DC: American Pharmacists Association; 2009:141.

30 to 60 minutes; optimal benefits are realized with continued regular dosing. Many women need to take the maximum recommended nonprescription dose at the maximum suggested frequency of use.

If pain relief is inadequate, beginning treatment 1 to 2 days before expected menses may help. (If there is any possibility that the patient is pregnant, therapy should be initiated only after menses begins.) Patients may respond better to one NSAID than to another. If the maximum nonpre-

scription dosage of the selected agent does not provide adequate symptom relief, a trial with another agent is recommended. The analgesic effect for most of these NSAIDs plateaus, so further dose increases may increase the risk of adverse drug effects rather than provide more benefit.

**Follow-Up**

Therapy with non-salicylate NSAIDs should be undertaken for three to six menstrual cycles—with changes made in the agent, dosage, or both—before

judging the effectiveness of these agents. Women who fail to obtain adequate relief from non-salicylate NSAIDs should be referred to a primary care provider. The currently labeled prescription dosages of NSAIDs for the treatment of dysmenorrhea usually are higher than the maximum non-prescription dosages; patients may require prescription NSAID therapy or treatment with other agents (e.g., combined oral contraceptives).

## CASE STUDY RESPONSES

### Case 1. Musculoskeletal Injuries and Disorders

- a. The patient should initiate a course of RICE (rest, ice, compression, and elevation) therapy and consult a primary care provider in 2 weeks if the pain is not relieved.  
Incorrect. The patient's symptoms appear to be consistent with osteoarthritis rather than an acute traumatic injury. He should be evaluated by a primary care provider.
- b. The patient should apply heat to the affected knee and consult a primary care provider in 2 weeks if the pain is not relieved.  
Incorrect. The patient's symptoms appear to be consistent with osteoarthritis rather than an acute traumatic injury. He should be evaluated by a primary care provider. Also, RICE therapy usually is preferable to heat when inflammation is present.
- c. The patient may self-treat the pain with maximal nonprescription doses of aspirin (4 g/day) to obtain an anti-inflammatory effect. He should consult a primary care provider in 2 weeks if the pain is not relieved.  
Incorrect. The patient's symptoms appear to be consistent with osteoarthritis. Self-treatment of pain is appropriate once the diagnosis has been made, but acetaminophen is recommended for initial therapy. The patient's age puts him at increased risk of adverse GI events from aspirin use.
- d. The patient should be evaluated by a primary care provider to rule out osteoarthritis. He can initiate short-term self-treatment with ice and acetaminophen while awaiting the appointment; however, ongoing self-treatment should not continue unless a diagnosis is made.**  
***Correct. The patient's symptoms appear to be consistent with osteoarthritis. Self-treatment of pain is appropriate once the diagnosis has been made; acetaminophen is recommended for initial therapy.***

### Case 2. Headache

- a. The patient should be advised to take both a nonprescription analgesic and a decongestant, because her symptoms are consistent with sinus headache.  
Incorrect. AB's symptoms are not consistent with sinus headache.
- b. The patient should be evaluated by a primary care provider to rule out migraine headache.  
Incorrect. AB reports no symptoms consistent with migraine.
- c. The patient may attempt self-treatment with a nonprescription analgesic. She should consult her primary care provider if the headache persists or worsens despite treatment.**  
***Correct. AB's symptoms are consistent with tension-type headache, and she reports no exclusions for self-treatment.***
- d. The patient should not attempt self-treatment with a nonprescription analgesic because of her recent use of alcohol.  
Incorrect. The alcohol-related exclusion for self-treatment is consumption of three or more drinks per day. However, AB should be educated about potentially increased risks if she uses an analgesic in conjunction with moderate amounts of alcohol.

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## CPE EXAM

Instructions: The assessment questions printed below allow you to preview the online CPE exam. Please review all of your answers to be sure you have marked the proper letter on the online CPE exam. There is only one correct answer to each question.

- Which of the following best characterizes the relative analgesic potency of the listed nonprescription analgesics?
  - Aspirin > acetaminophen > ibuprofen.
  - Acetaminophen > ibuprofen > aspirin.
  - Ibuprofen > aspirin > acetaminophen.
  - The nonprescription analgesics are considered to be essentially interchangeable at usual nonprescription dosages.
- Which of the following patients has an increased risk of upper GI bleeding with aspirin?
  - A 45-year-old woman.
  - A patient with osteoarthritis.
  - A patient who also is being treated with a selective serotonin reuptake inhibitor.
  - All of the above.
- Because of the risk of Reye's syndrome, the use of aspirin generally should be avoided in children who are \_\_\_\_\_ years of age or younger.
  - 6.
  - 8.
  - 12.
  - 15.
- Which of the following represents a major advantage of ibuprofen or naproxen, compared with salicylate analgesics?
  - They are associated with less GI upset and bleeding.
  - They can be used by aspirin-intolerant patients.
  - They have antipyretic activity as well as analgesic activity.
  - They have no effect on renal blood flow.
- Which of the following nonprescription analgesics does *not* exhibit anti-inflammatory activity at doses commonly used for self-treatment?
  - Acetaminophen.
  - Aspirin
  - Ibuprofen.
  - Magnesium salicylate.
- The correct dose of acetaminophen for a child who weighs 23 lb is:
  - 40 mg.
  - 80 mg.
  - 120 mg.
  - 160 mg.
- A parent who needs to administer the dose indicated in question 6—using acetaminophen suspension (160 mg/5 mL)—should measure out:
  - 1.25 mL.
  - 2.5 mL.
  - 3.75 mL.
  - 5 mL.
- The correct dose of ibuprofen for a child who weighs 38 lb is:
  - 50 mg
  - 75 mg.
  - 100 mg.
  - 150 mg.
- Patients who consume \_\_\_\_\_ or more alcoholic drinks per day should consult a primary care provider before using nonprescription analgesics.
  - One.
  - Three.
  - Five.
  - Patients who consume alcoholic drinks do not need to be concerned about using nonprescription analgesics.
- The topical products used most frequently for the treatment of minor musculoskeletal pain are classified as:
  - Analgesics.
  - Anesthetics.
  - Antipruritics.
  - Counterirritants.
- An acute traumatic injury to a ligament is known as:
  - A contusion.
  - A sprain.
  - A strain.
  - Tendonitis.
- Exclusions for self-treatment of musculoskeletal injuries and disorders include all of the following *except*:
  - First trimester of pregnancy.
  - Pain that lasts longer than 14 days.
  - Signs of systemic infection.
  - Visually deformed joint.
- In RICE therapy for acute musculoskeletal injuries, ice should be applied:
  - Continuously until there is a noticeable decrease in the degree of local inflammation.
  - For 30 minutes every hour for the first 48 hours after injury.
  - In 10- to 15-minute increments, three to four times per day.
  - Until the area being iced becomes numb to the touch.
- Heat therapy may be particularly beneficial for patients with which of the following musculoskeletal conditions?
  - Delayed onset muscle soreness.
  - Low back pain.
  - Osteoarthritis.
  - All of the above.

15. The nonprescription analgesic of first choice for the treatment of osteoarthritis is:
  - a. Acetaminophen.
  - b. Aspirin.
  - c. Ibuprofen.
  - d. Naproxen.
16. A patient who complains of diffuse, aching head pain that came on gradually and is felt most intensely over the top of the head has symptoms most consistent with:
  - a. Migraine headache.
  - b. Sinus headache.
  - c. Secondary headache.
  - d. Tension-type headache.
17. Which of the following is *not* an exclusion for self-treatment of headache?
  - a. Diagnosed migraine headache.
  - b. High fever.
  - c. History of liver disease.
  - d. Severe head pain.
18. To decrease the risk of developing medication overuse headache, patients should refrain from using nonprescription analgesics more frequently than:
  - a. 3 days per week.
  - b. 6 days per week.
  - c. 10 days per month.
  - d. 14 days per month.
19. Which of the following measures may help to lessen the symptoms of dysmenorrhea?
  - a. Fish oil supplements.
  - b. Heat therapy.
  - c. Smoking cessation.
  - d. All of the above.
20. Women with dysmenorrhea generally experience the greatest pain relief with:
  - a. Acetaminophen.
  - b. Aspirin.
  - c. A nonacetylated salicylate.
  - d. An NSAID.

## CPE INSTRUCTIONS

Completing a posttest at [www.pharmacist.com/education](http://www.pharmacist.com/education) is as easy as 1-2-3...

1. Go to **Online CPE Quick List** and click on the title of this activity.
2. **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.
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