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- medical specialty and professional societies;
- researchers;
- federal, state and local government health care policy makers and specialists; and
- employee benefit managers.

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Health Care Guideline:
Assessment and Management of Acute Pain

Assessment Algorithm

1. Patient has pain or is likely to have pain
   AD

2. Critical first steps: Detailed history
   Focused physical exam
   AD

3. Pain assessment
   AD

4. Is source of pain:
   - Migraine?
   - Low back?
   - Ankle sprain?
   - Chest pain?
   - Dyspepsia?
   yes
   See ICSI guidelines
   no

5. Determine mechanism of pain
   (Patient may experience more than one type of pain)
   AD

6. Arrange diagnostic work-up
   and treat pain as appropriate per information available
   A

7. AD

8. Patient reports localized pin prick, sharp or stabbing pain
   Somatic Pain
   (See page 2 Treatment Algorithm)
   AD

9. Patient reports generalized ache or pressure
   Visceral Pain
   (See page 2 Treatment Algorithm)
   AD

10. Patient reports radiating or specific burning, tingling, or lancinating pain
    Neuropathic Pain
    (See page 2 Treatment Algorithm)
    AD

These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.
Acute Pain Treatment Algorithm

1. **Somatic pain**
   - Treatment choices include:
     - Tactile stimulation
     - Cold packs
     - Acetaminophen
     - NSAIDs
     - Opioids (via any route)
     - Local anesthetic (topical or infiltration)

2. **Visceral pain**
   - Treatment choices include:
     - Opioid (via any route)
     - NSAIDs
     - Intraspinal local anesthetic agents

3. **Neuropathic pain**
   - Treatment choices include:
     - Anticonvulsants
     - Tricyclic antidepressants
     - Neural blockade
     - Opioids

4. **Patient education**
   - Medication dose titration
   - Further diagnostic work-up
   - Specialty consult (if indicated)
   - Procedures
   - Adjuvant therapy
   - Behavioral and cognitive interventions
   - Clinical pearls

5. **Select an alternate treatment choice**

6. **Still confident of pain mechanism?**
   - yes
   - no

7. **Adequate pain relief?**
   - yes
   - no

8. **Intolerable symptoms secondary to analgesia other than pain?**
   - yes
   - no

9. **Follow-up instructions**

10. **Return to box 6 on previous page**

11. **Side effect management**

12. **A**
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SCOPE AND TARGET POPULATION

This guideline has been developed for patients of all ages (from infant to very elderly) who have acute pain or may be experiencing acute pain in the future (i.e., planned surgery). We acknowledge that assessments of pain in the pre-verbal, non-English speaking and cognitively impaired are challenging. As a result relevant recommendations will be made in order to enhance assessment of an intervention for all patients. The following definitions are assumed:

**Pain** is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

**Acute pain** states can be brief, lasting moments or hours, or they can be persistent, lasting weeks or several months until the disease or injury heals. (Chapman RC, Syrjala KL. “Measurement of pain.” In The Management of Pain, 2nd ed. Bonica JJ, ed. Philadelphia: Lea and Febiger, 1990:580-94.)

**Chronic pain**, in contrast, is an enduring condition that has become a stable element in the daily life of the patient. This definition excludes most forms of cancer pain but includes pain associated with chronic musculoskeletal, neuropathic, visceral, and degenerative disorders and pain problems with behavioral components. Its sensory characteristics are often but not always multifocal and vague, sometimes inappropriate for the organic pathology evident, and relatively constant. (Ibid)

(This guideline excludes patients with acute cancer pain, labor pain and migraine headache although many of the guideline’s recommendations apply to those groups as well.)

Rather than focus on the cause of the pain (a comprehensive list would fill a textbook) or the setting where the pain is treated (inpatient or outpatient), this guideline focuses on effective treatment based on the physiologic mechanisms of pain transmission (e.g., somatic, visceral, neuropathic). Understanding this should allow clinicians to apply this algorithm to almost any kind of acute pain (no matter what the cause) and in any setting.

RELATED ICSI SCIENTIFIC GUIDELINES

Other ICSI guidelines whose scope and/or recommendations are closely related to the content of this guideline are:

1. Adult Low Back Pain
2. Ankle Sprain
3. Diagnosis of Chest Pain
4. Dyspepsia
5. Migraine Headache

CLINICAL HIGHLIGHTS FOR INDIVIDUAL CLINICIANS

1. Determine the mechanism of pain (i.e. - somatic, visceral, neuropathic) based on the physical examination and detailed history. *(Annotation #6)*

2. Patients often experience more than one type of pain. *(Annotation #6)*
3. Intensity of pain is assessed prior to initiation of appropriate treatment and continually reassessed throughout duration of treatment. (Annotation #3)

4. Somatic pain is well-localized and may be responsive to cold packs, tactile stimulation, NSAIDs, acetaminophen, opioids, and localized anesthetic (topical or infiltrate). (Annotations #8, 9, 10)

5. Visceral pain is more generalized and is most responsive to opioid treatment. (Annotations #11, 12, 13)

6. Neuropathic pain may be resistant to opioid therapy and consideration should be given to adjuvant therapy such as tricyclic antidepressants and anticonvulsants. (Annotations #14, 15, 16)

**Priority Aims and Suggested Measures for Health Care Systems**

1. Improve pain management through assessment of all patients throughout hospitalization including on admission, ongoing assessment, and at discharge or during an outpatient visit.

   Possible measures of accomplishing this aim:
   a. Percentage of patients with initial assessment for pain using a formal assessment tool.
   b. Percentage of patients with documentation of pain rating on the vital sign sheet (5th vital sign).
   c. Percentage of patients with discharge plan identifying patient’s continuing needs for pain management and orders to meet these needs.

2. Improve the appropriate selection and dosing of pain management treatment.

   Possible measures of accomplishing this aim:
   a. Percentage of patients taking NSAID with continued pain (> 4/10 on pain scale or exceeding patient’s pain goal) who are prescribed an opioid.
   b. Percentage of all patients who receive meperidine.
   c. After 48 hours, the percentage of patients reporting pain at either a level > 4 or at unacceptable level to patient.
   d. Percentage of patients reporting good or very good satisfaction with the approach to pain control.
   e. Percentage of patients with a diagnosis consistent with neuropathic pain (see Appendix A for clinical examples) who are given a trial of either anticonvulsants or tricyclic antidepressants.
3. Increase the involvement of patients in pain management.

   Possible measure of accomplishing this aim:

   a. Percentage of patients with acute pain with documentation of patient-reported pain, intensity, and degree of relief after intervention.

   b. Percentage of patients reporting an understanding of the need to communicate unrelieved pain.

   c. Percentage of inpatients prescribed an opioid who are assessed within one hour for parenteral administration or within two hours for oral therapy for symptoms secondary to analgesia (e.g., decreased mental status, confusion, delirium, nausea, vomiting).

   d. Percentage of patients with documentation of an intervention to reduce pain, of those patients who have a pain level > 4/10 or at unacceptable level to patient.

   e. Percentage of inpatients with documentation of patient’s goal for pain control on admission.

   f. Percentage of patients with documentation of receiving education on the pain assessment scale and on goals of pain management.

**Evidence Grading**

Individual research reports are assigned a letter indicating the class of report based on design type: A, B, C, D, M, R, X.

Key conclusions are assigned a conclusion grade: I, II, III, or Grade Not Assignable.

A full explanation of these designators is found in the Discussion and References section of the guideline.
ALGORITHM ANNOTATIONS

1. Patient Has Pain or Is Likely to Have Pain

Pain is undertreated by many practitioners, which leads to serious clinical consequences. This guideline encourages aggressive assessment, treatment and reassessment of pain. Specific recommendations include: 1) parameters within which ketorolac (e.g., Toradol) should be used, 2) caution against use of meperidine (e.g., Demerol) except for limited dosing in healthy persons, and 3) use of adjunct medications for neuropathic pain.

Evidence supporting this recommendation is of classes: B, D, R, X

2. Critical First Steps

Acute pain is not a diagnosis; it is a symptom. Frequently its cause is obvious such as after surgery or an acute trauma. Many times, however, the exact underlying etiology is not clear and a diagnostic work-up is necessary. Our work group believes that an interview with the patient or a responsible caregiver is essential. The interview and examination should cover the following:

General History
- History of present illness (HPI)
- Current medications
- Medication allergies
- Past medical history
- Social history

Pain History
- Onset
- Duration
- Quality, character
- Ameliorating and provoking factors
- Patient rating if possible (see Annotation #3)

Clinical Exam
- Observation of response to pain (pre-verbal or cognitively impaired patients): e.g., rubbing a particular area, guarding, facial expression. (See "Observer/Caregiver Ratings of Pain and Pain Relief" in Discussion #2.)

Evidence supporting this recommendation is of classes: C, D
- Focused physical exam (part of body or region in pain), especially pulse, respiratory rate, blood pressure.
- Functional assessment (see Annotation and Discussion #3, "Pain Assessment").
Diagnostic Studies
Lab studies, x-rays or other diagnostic tests may be needed, depending on the results of the history and physical examination.

Specialty Consult
General surgical, orthopedic, anesthesiological or other consultation may be deemed necessary.

Key Patient Education Messages
- The patient and/or caregiver play a critical role in the assessment and management of pain.
- Assessing the type and amount of pain is important to good pain control. This is done by describing and rating the pain. Educate the patient and/or caregiver in the selection and use of an appropriate pain scale.
- Parents can help assess pain in children by what their child says, what their child is doing, and how their child’s body is reacting.

3. Pain Assessment
Based on the assumption that patient self-reporting is the “most reliable indicator of the existence and intensity of pain” (National Institutes of Health) ...the ideal tool for pain will identify the presence of pain and its evolution over time. In addition, tools should be applicable to any person regardless of age, race, creed, socioeconomic status, and psychological or emotional background.

The single dimensional scales measure only pain intensity and by their nature are self-report. The multidimensional scales measure not only the intensity but also the nature and location of the pain and in some cases the impact the pain is having on activity or mood. See Table 1, "Assessment Tools for Adults," and Table 2, "Assessment Tools for Children."

Evidence supporting this recommendation is of classes: A, B, C, D, R, X

Reassessment
Inpatients:
- Within one hour for parenteral administration
- Within two hours for oral therapy

Outpatients: Instruct patient on when and how to contact care provider regarding efficacy of pain therapy.
Table 1. Assessment Tools for Adults

<table>
<thead>
<tr>
<th>Scale</th>
<th>Administration</th>
<th>Validated in</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual analog scale (VAS)</td>
<td>visual</td>
<td>chronic pain</td>
<td>Poor reproducibility with cognitive dysfunction, post-op or dementia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>rheumatic disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>children &gt; 5</td>
<td></td>
</tr>
<tr>
<td>Numeric rating scales (NRS)</td>
<td>verbal or visual</td>
<td>rheumatic disease</td>
<td>Detects treatment effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>chronic pain</td>
<td>Decreased reliability at extremes of ages, pre-verbal, visual, auditory or cognitive dysfunction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>trauma</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>cancer</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>illiterate</td>
<td></td>
</tr>
<tr>
<td>Verbal description scales (VDS)</td>
<td>verbal or visual</td>
<td>chronic pain</td>
<td>4 or 5 point scales</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Preferred by some patients to VIS or NRS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dependent on literacy and language</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Less sensitive for changes in pain</td>
</tr>
<tr>
<td>Facial pain scales (FPS)</td>
<td>visual</td>
<td>Bieri: adults</td>
<td>Felt easier than NRS or VAS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bieri: children</td>
<td>No influence on culture, gender or ethnicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wong &amp; Baker: children</td>
<td></td>
</tr>
<tr>
<td>Brief Pain Inventory (BPI)</td>
<td>verbal</td>
<td>cancer</td>
<td>Assess location, intensity, pattern</td>
</tr>
<tr>
<td></td>
<td></td>
<td>arthritis</td>
<td>Reports meds, pain relief, patient beliefs, interference in quality of life</td>
</tr>
<tr>
<td></td>
<td></td>
<td>English, Italian and Norwegian</td>
<td></td>
</tr>
<tr>
<td>McGill Pain Questionnaire (MPQ)</td>
<td>verbal</td>
<td>English, French, Norwegian</td>
<td>Long form can take 30 minutes; short form, 2-5 minutes. Measures intensity, location, affective effects, pattern and other miscellaneous</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 2. Assessment Tools for Children

<table>
<thead>
<tr>
<th>Measure</th>
<th>Description</th>
<th>Indications for Use</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-Report Measures</td>
<td>Child is asked re: intensity, rhythm and variations in pain</td>
<td>Adequate cognitive and communicative abilities</td>
<td>Simple and effective, can be administered easily</td>
<td>Subject to bias (e.g., demand characteristics, inaccurate or selective memory)</td>
</tr>
<tr>
<td>Poker Chip Tool (Hester, 1979)</td>
<td>Child chooses 1 to 4 chips (&quot;pieces of hurt&quot;)</td>
<td>4 to 8 years</td>
<td>Correlates with overt behaviors in injections, adequate convergent validity, partial support for discriminate validity</td>
<td>May be childish for older children</td>
</tr>
<tr>
<td>Faces Scale (Bieri, et al., 1990)</td>
<td>Faces indicating intensity were derived from children’s drawings</td>
<td>6 to 8 years</td>
<td>Strong agreement among children re: pain severity of faces and consistency of intervals, adequate test-retest reliability</td>
<td>Validity studies are not yet completed</td>
</tr>
<tr>
<td>Visual analog scale</td>
<td>Vertical or horizontal line with verbal, facial or numerical anchors on a continuum of pain intensity</td>
<td>5 years and over</td>
<td>Reliable and valid (e.g., child report correlates with behavioral measures and with parent, nurse, physician ratings), versatile (can rate different dimensions – pain &amp; effect – on same scale)</td>
<td>Must understand proportionality, intervals on numerical scales may not be equal from a child’s perspective</td>
</tr>
<tr>
<td>Oucher Scale (Beyer, Wells, 1989)</td>
<td>6 photos of children’s faces indicating intensity; 100-point corresponding vertical scale</td>
<td>3 to 12 years</td>
<td>Reliable; adequate content validity; correlates with other VAS scales, presentation of both pictorial and numerical scales is applicable for broader age range</td>
<td>See VAS</td>
</tr>
<tr>
<td>Pain diary</td>
<td>Numerical ratings are repeated along with recording of other relevant information (e.g., time, activity, medication)</td>
<td>Older child/adolescent</td>
<td>Adequate interrater reliability between parent and child, useful in determining patterns of pain and in teaching self-management strategies (thereby providing a sense of mastery)</td>
<td>Require commitment to record regularly and accurately, require effort and prompting if moving from one situation to another (memory over time is rarely accurate)</td>
</tr>
<tr>
<td>Childrens Hospital of Eastern Ontario pain scale (CHEOPS) (McGrath et al., 1985)</td>
<td>6 observed behaviors: crying, facial expression, verbal expression, torso position and leg position</td>
<td>Originally used for post-operative pain and needle pain</td>
<td>Easy to learn and use, interrater reliability = .80, concurrent validity</td>
<td>Insensitive to long-term pain</td>
</tr>
<tr>
<td>CRIES (Krechel, 1995)</td>
<td>0-2 points on 5 variables</td>
<td>Neonatal post-op pain</td>
<td>Interobserver reliability = 94%, useful for requested bedside observation, validated against CHEOPS</td>
<td></td>
</tr>
<tr>
<td>MBPS (Taddio, 1995)</td>
<td>3 items: facial expression, cry and movements</td>
<td>0-6 months</td>
<td>Excellent validity and interobserver reliability (95%)</td>
<td>Studied only as a research tool thusfar</td>
</tr>
<tr>
<td>Postanaesthetic Recovery Score</td>
<td>0-2 points on 6 variables</td>
<td>Originally developed for use in post-operative pain assessment</td>
<td>Simple and efficient, can be administered easily.</td>
<td>Specific to post-anesthesia pain assessment</td>
</tr>
</tbody>
</table>

*The first 7 rows of the above table are reprinted with permission from Pain in Infants, Children and Adolescents, Schecter NI, Bearde CB, Yaster M, eds. Baltimore: Williams and Wilkins, 1992: Table 8.1, page 99.*
Algorithm Annotations (cont)  

6. Determine Mechanism of Pain (Patient May Experience More Than One Type of Pain)  
By identifying the type of pain, the provider can more efficiently treat pain by selecting the intervention most appropriate. The clinician should be aware the patient may experience a combination of pain types. See Annotation Appendix A for an assistive tool in determining mechanism of pain.  
Evidence supporting this recommendation is of classes: D, R.  

7. Arrange Diagnostic Work-Up and Treat Pain as Appropriate per Information Available  
The algorithm acknowledges that in most clinical situations the initial treatment of pain and the diagnostic work-up occur concurrently. In other situations, e.g. CNS injury, it may be important to delay treating a patient’s pain until the underlying diagnosis is established. These initial efforts to treat pain are based on the clinician’s initial hypothesis of the etiology of the patient’s pain.  
See the clinical pearls section in Annotation #17, "Prevention/Intervention."

8. Patient Reports Localized Pin Prick, Sharp or Stabbing Pain  
9. Somatic Pain  
Somatic pain results from tissue damage that causes the release of chemicals from injured cells that mediate pain and inflammation via abundant nociceptors found in the skin and body wall.  
Somatic pain is typically of recent onset, well-localized, and is described as sharp, aching, stabbing, or throbbing in character. Its cause is usually apparent as the pain follows the distribution of a peripheral nerve or nerve root. Traumatic injury results in somatic pain. Typical examples include lacerations, sprains, fractures, and dislocations.  

10. Treatment Choices for Somatic Pain  
Treatment of somatic pain includes the use of topical therapies, non-steroidal anti-inflammatory drugs, acetaminophen, opioids, and local anesthetics.  

11. Patient Reports Generalized Ache or Pressure?  
12. Visceral Pain  
Visceral pain nociceptors are similar to those found in the skin and body wall. However, visceral nociceptors are fewer in number, and when stimulated, result in poorly localized, diffuse, and vague complaints (generalized ache/pressure) that may be referred to sites remote from the primary injury. Visceral afferent fibers converge on the same dorsal horn neurons as somatic afferent fibers resulting in referred pain to the cutaneous area innervated at that level.  
The cause of visceral pain may include ischemia/necrosis, inflammation, ligamentous stretching, smooth muscle spasm, and distension of a hollow viscous or organ capsule. For example, rhythmic contractions of smooth muscles may result in a cramping type of visceral discomfort. Reflex skeletal abdominal muscle contraction results from an inflamed peritoneum resulting in a rigid abdomen.  
Primary visceral pain afferents usually course along with autonomic nerve fibers. For example, abdominal and thoracic visceral pain fibers travel with sympathetic nervous system fibers; esophageal and pharyngeal pain fibers travel with vagal and glossopharyngeal afferents; and deep pelvic struc-
ture pain fibers travel with the sacral parasympathetics. Thus, a hallmark of visceral pain will include autonomic symptoms such as nausea/vomiting, hypotension, bradycardia, and sweating.

The goal in the treatment of visceral pain is to identify and then reduce or eliminate the causative factors. In general, visceral pain is treated not unlike somatic pain and may respond best to opioid therapy.

13. Treatment Choices for Visceral Pain

Treatment choices for visceral pain include NSAIDs, opioids (via any route), and intraspinal local anesthetic agents.

14. Patient Reports Radiating or Specific Burning, Tingling, or Lancinating Pain

15. Neuropathic Pain

Neuropathic pain infers an injury to a neural structure leading to aberrant processing in the peripheral and/or central nervous system. Neuropathic pain is distinguished from nociceptive (somatic and visceral) pain. Nociceptive pain results from activation of nociceptors from a defined noxious stimulus, whereas neuropathic pain results from damage to a nerve. However, the presence of nociceptive and neuropathic pain frequently coexists.

Patients who experience neuropathic pain often complain of dysesthesias (abnormal pain complaints) which are typically not like any previous pain experience. Frequently, pain is described as burning, tingling, electrical-like, or shooting. Examination may reveal allostynia (pain on light touch), hypalgnesia or hyperalgnesia (relatively decreased or increased perception of a noxious stimulus), or hyperpathia (exaggerated pain response). In neuropathic pain, symptoms are initially experienced distal to the site of injury, whereas in nociceptive pain, symptoms are initially apparent at the site of injury.

Neuropathic pain is commonly experienced by patients with conditions such as diabetes, shingles, multiple sclerosis, herniated discs, and Acquired Immunodeficiency Syndrome (AIDS). Neuropathic pain may also result from treatment with radiation or chemotherapy.

See Annotation Appendix F, "Dermatome Map."

16. Treatment Choices for Neuropathic Pain

Neuropathic pain may be resistant to standard opioid therapies or other nociceptive pain treatment strategies. Anticonvulsants and antidepressants are mainstays of therapy. Complaints of continuous burning may best respond to antidepressants, whereas lancinating complaints may best respond to anticonvulsants. Failure to adequately relieve neuropathic pain with one anticonvulsant does not imply that alternative therapies will not work. Please refer to Annotation Appendix E "Pharmacologic Treatment of Neuropathic Pain" for more information.

17. Prevention/Intervention

Annotation #17 includes information on:
- Prevention/Intervention Overview
- Key Patient Education Steps And Messages
- Pharmacological Therapy: Non-opioids, Opioids, Adjuvants
Prevention/Intervention Overview

The ability to influence a patient’s pain experience may be approached in multiple ways. Choices for intervention are varied and frequently involve multiple disciplines. Medications and interventions are selected based on symptomatology and mechanism of pain. Choosing the profile that is the most responsive to the pain complaint and has the least potential for side effects should be done initially. Visceral, somatic and neuropathic pain complaints respond most effectively to different treatments. (See Annotation Appendix A, "Determining Mechanism of Pain"). The route of administration often affects patient compliance and dosing requirements.

Preemptive analgesia may reduce the severity of postoperative pain. This consists of the application of local anesthetics or opioids near the spinal cord, usually by an anesthesiologist, in order to prevent sensitization of the central nervous system.

With proper education and training of patients (see Key Patient Education Steps and Messages) prior to a painful experience, the ability to cope and the outcome of pain treatment may be enhanced.

See Table 3, "Acute Pain Interventions", for summary of interventions.

Evidence supporting the use of preemptive analgesia is of class: A
KEY PATIENT EDUCATION STEPS AND MESSAGES

- Describe the expected type of pain and how long it will last. (Preparatory Sensory Information - decrease uncertainty and fear of unknown. “Knowledge is power.”)

- Individualize the information for the patient.

- Discuss goals of pain management and how these goals help the patient: comfort, quicker recovery, and avoid complications.

- Preventing pain is important to manage pain well. “Stay ahead of the pain.”

- Many drug and non-drug treatments can be helpful in preventing and managing pain.

- Inform the patient of when and how to contact health care providers about his/her pain.

- Patients, parents of children with pain, and the health care providers will decide as a team which treatments are best to manage the pain.
• Discuss treatment choices and plan, including schedule of medications, which are most appropriate for the patient.

• Addiction to opioids used in the treatment of acute pain is rare. There are differences among physical addiction, tolerance, and psychological dependence.

**PHARMACOLOGICAL THERAPY**

The use of pharmacological agents is considered to be the mainstay of therapy for acute pain. There are three broad categories of medications to consider when treating the patient with acute pain: non-opioid analgesics (NSAIDs), opioid analgesics and analgesic adjuvants. They are used in this manner:

1) **Non-opioid analgesics (NSAIDs):**
   - Should be considered initially. Often adequate for *mild* or *moderate* pain.
   - NSAIDS have significant opioid dose-sparing properties and in turn reduce opioid-related side effects.
   - Use with caution in patients with coagulopathies or thrombocytopenia and those who are at risk for bleeding.
   - Watch for GI effects, especially with these risk factors: age greater than 60 years, previous gastrointestinal events and concomitant corticosteroid use.
   - Ketorolac, either parenteral or oral, should be used for no more than 5 days; dose reduction is indicated in the elderly and in those with renal impairment. *[Conclusion Grade III: See Discussion Appendix B, Conclusion Grading Worksheet - Annotation # 17 (Ketorolac).]*
   - See Annotations Appendix C, "Non-Opioid Analgesics."

   Evidence supporting these recommendations is of classes: A, B, D

2) **Opioid Analgesics:**
   - If pain is not adequately controlled with an NSAID or is expected to be *moderate* to *severe*, an appropriate opioid should be added to the NSAID.
   - In patients with absolute or strong relative contraindications to NSAIDs, a weak opioid for mild to moderate pain should be considered.
   - Morphine is considered to be the standard opioid analgesic.
   - Meperidine is a commonly used opioid. Due to the risk of adverse central nervous system effects, meperidine should be reserved for very brief use only in the treatment of acute pain. *[Conclusion Grade III: See Discussion Appendix C, Conclusion Grading Worksheet - Annotation #17 (Meperidine).]*
   - See Annotation Appendix D, “Opioid Analgesics,” also “Recognizing Substance Abuse” in Discussion #17.
   - See Annotation Appendix B, “Equianalgesic Table,” for parenteral and oral equivalency comparisons.

   Evidence supporting these recommendations is of classes: C, D
3) Pharmacological analgesic adjuvants:
   • Used to complement NSAIDs and opioids; not to be used alone in the treatment of acute pain.
   • Some have been shown to enhance the effect of a particular analgesic, such as caffeine when given with aspirin-like drugs; others have analgesic properties themselves, e.g., tricyclic antidepressants and hydroxyzine.
   • See the section in Discussion and References #17 "Prevention/Intervention", Pharmacological Therapy – Pharmacological Analgesics Adjuvants for further discussion of medications used for adjuvant pain management.

Evidence supporting this recommendation is of classes: A, D, R

Further Diagnostic Work-up

Lab studies, x-rays, or other diagnostic tests may be needed, depending on the results of the history and physical examination.

Specialty Consult

General surgical, orthopedic, anesthesiological or other consultation may be deemed necessary.

Procedures

Procedures are used for both diagnostic and therapeutic effects and should be performed by experienced providers.

Policies and Procedures for Safe Medication Use

Policies and procedures regarding safe medication use should be in place.

Adjuvant Therapy

The addition of adjuvant therapies, procedures and pharmaceuticals are frequently helpful in reducing total drug dose requirements and in speeding recovery.

Behavioral/Cognitive Intervention

Behavioral and cognitive interventions can be utilized independently or in conjunction with pharmacological pain therapy. Not all interventions are effective for all patients, and determining the best fit can be very difficult.

The extent of pain and anxiety in response to the same medical procedures or painful event varies widely as does the coping skills. Some patients do better with information about the painful procedure before and during, while others prefer not to be told but rather engage in distracting tasks.
In children, the cognitive stage will also influence the understanding and concept of pain. Behavioral and cognitive interventions are detailed in Table #5.

### Table 5: Behavioral/Cognitive Interventions

<table>
<thead>
<tr>
<th>Type of Treatment</th>
<th>Description</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desensitization</td>
<td>Systematic gradual exposure to feared situations or objects</td>
<td>Decrease anxiety</td>
</tr>
<tr>
<td>Positive reinforcement</td>
<td>Positive statements and tangible rewards after a painful procedure</td>
<td>Transform meaning of pain from a punitive to challenging event</td>
</tr>
<tr>
<td>Relaxation</td>
<td>Progressive relaxation of muscle groups combined with controlled breathing</td>
<td>Decrease anxiety and pain</td>
</tr>
<tr>
<td>Preparation</td>
<td>Explaining the steps of the procedure and providing sensory information about the procedure</td>
<td>Help child to develop realistic expectations about a procedure</td>
</tr>
<tr>
<td>Memory change</td>
<td>Helping child to more positively reframe any negative memories about previous procedures</td>
<td>To reduce anticipatory distress and, over time, procedural distress, through realistic memories</td>
</tr>
<tr>
<td>Hypnosis</td>
<td>Dissociate from painful experience through involvement in imagined fantasy that is fun and safe</td>
<td>Take focus away from procedure and enhance sense of mastery through metaphor in imagined experience</td>
</tr>
<tr>
<td>Thought stopping and positive self-statements</td>
<td>During times of anxiety, the child repeats “Stop!” when anxious thoughts occur, and repeats a set of positive thoughts</td>
<td>Replace catastrophic thinking and reduce anxiety</td>
</tr>
<tr>
<td>Distraction</td>
<td>Techniques include counting, blowing bubbles, or talking about topics unrelated to the procedure</td>
<td>Shift attention away from the procedure and pain onto more enjoyable things</td>
</tr>
<tr>
<td>Modeling and rehearsal</td>
<td>Demonstration of a mock procedure by another child or adult who demonstrates positive coping behaviors; children can then practice procedure using coping techniques</td>
<td>Provide information about the procedure and suggest helpful strategies that can be used during procedure to cope with pain and anxiety</td>
</tr>
</tbody>
</table>
In addition to these, other approaches have included:

1) Verbal preparation and communication with nurses and doctors.
2) Sensorimotor strategies: especially with infants the use of pacifiers, swaddling, rocking and holding.
3) Imaginative involvement: using imaginative stories or “pain switches” or “anesthetic gloves.”
4) Physical strategies: application of heat or cold, massage, immobilization, rest, or exercise.
5) Music, art, and play therapies.

Clinical Pearls

Pediatric

- **Circumcisions**: The March 1999 Task Force Report from the American Academy of Pediatric states, “... data are not sufficient to recommend routine neonatal circumcision. If a decision for circumcision is made, procedural analgesia should be provided.” Dorsal Penile Nerve Block (DPNB), EMLA (Eutectic Mixture of Local Anesthetics), topical lidocaine, and ringblock have all been shown to be efficacious and safe but none completely eliminate the pain of circumcision.

- **Infantile colic**: Colic is characterized by excessive crying in otherwise healthy infants. Uncertainty regarding its etiology has led to multiple treatments. Oral sucrose in high concentrations has been shown to stimulate the opioid pathways in preterm and term infants, and has been demonstrated to have a significant ameliorating effect on the pain of colic. To obtain a 24-25 percent sucrose solution, dilute 1 teaspoon of table sugar (one packet of restaurant sugar) with 10 cc of water.

- **Percutaneous procedures**: Eutectic mixture of local anesthetic (EMLA): Mixture of lidocaine and prilocaine applied under occlusive dressing with onset of action of 60-90 minutes. Has been shown to be useful in venapuncture, intravenous access, circumcision and meatotomy. There have been concerns about methemoglobinemia which thus limits its use in neonates or infants. Recent studies in small populations demonstrate little toxicity.

- **Intramuscular injections** should be avoided if possible; children would rather experience pain.

- **Otalgia**: The ear pain associated with acute middle ear infections has traditionally been ignored or treated with non-opioid analgesics. When compared to olive oil, topical analgesics such as Auralgan Otic Solution (antipyrine, benzocaine, and glycerin) have been shown to provide excellent ear pain reduction. This therapy should never be prescribed if there is a perforation, pressure equalizing tube or otorrhea.

- **Tonsillitis/pharyngitis**: In a study of 231 children ages 6-12 years with tonsillitis/pharyngitis, ibuprofen was shown to be more effective in relieving the sore throat pain in the first 48 hours than acetaminophen or placebo.
Adults

- **Acute ureteral colic**: Parenteral NSAIDs are more effective than meperidine.
- **"As needed" basis**: For optimal treatment of acute pain, avoid the use of intramuscular injections ordered on an "as needed" basis. Acute pain medications should initially be titrated to effect and then given on a scheduled basis.
- **Suturing non-end-artery sites**: Use TAC (Tetracaine, Adrenaline, and Cocaine solution), or LET (Lidocaine, Epinephrine, and Tetracaine solution). See supporting references for solution concentrations.
- **Head injury and stroke**: Avoid strong opioids to allow adequate patient assessment. Strong opioids may also decrease respiration rate, which may adversely affect (increase) intracranial pressure.
- **Medication interaction**: Oxycodone, Hydrocodone, Codeine and Tramadol may not be effective analgesics when given with other agents that strongly inhibit the Cytochrome P4502D6 liver enzymes. Common agents with this characteristic include the selective serotonin reuptake inhibitors Zoloft (doses greater than 150 mg), Paxil, and Prozac.
- **Loading doses** should be utilized for the management of acute pain once the underlying causes are known. See Discussion and References #17 "Prevention/Intervention", for more information on use of loading doses.
- **Meperidine**: In the treatment of acute pain, meperidine should be used only briefly and via a parenteral route.
- **Propoxyphene** is no more effective than acetaminophen in acute pain.
- **“Road rash”**: NSAIDs (any route) or local anesthetic can be used.

Evidence supporting these recommendations is of classes: A, D, R

21. **Intolerable Symptoms Secondary to Analgesia Other than Pain?**

Reassessment should be performed at regular intervals.

Inpatients:
- Within one hour for parenteral administration
- Within two hours for oral therapy

Outpatients: Instruct patient on when and how to contact care provider regarding efficacy of pain therapy.

Intolerable symptoms that could be related to either the pain medication (particularly the opioid) or other causes including:
- decrease in mental status
- confusion or delirium
- nausea and vomiting
- constipation or prolonged ileus
Algorithm Annotations (cont)

Assessment and Management of Acute Pain

- pruritus
- urinary retention

The identification of pain through patient self report, or when that’s not possible through a behavioral rating scale, will dictate the reduction of the opioid dosage or frequency. However, it should not be assumed that the opioid is always the cause.

The differential for decrease in mental status, confusion, or delirium is vast (see Annotation Appendix G, "Side Effects"). Nausea and vomiting may be related to physiologic causes and other medication side effects, as well as pain medications. The cause should be determined. Annotation Appendix G, "Side Effects", presents side effects of pain medications and their management of pain medications.

Accurate documentation of bowel function should be done by the nurses in the postoperative setting. Constipation could be caused by immobility, all types of medications, metabolism dysfunction, etc. and is best treated from a prevention standpoint rather than after the patient complains. It is usually the belief that prolonged ileus is caused by postoperative opioids. Slowing of bowel function may be due to pain itself. The tendency in the surgical setting is to decrease or stop the opioid if an individual has prolonged ileus. If this is a strong opinion, then efforts need to be continued to control the individual’s pain through other means, e.g., local anesthetics, or NSAIDs.

Patient should be given information about possible side effects and other symptoms that should be reported to nurse or provider.

22. Side Effect Management

See Annotation Appendix G, "Side Effects."

Key patient education messages:
- Medications can cause side effects which can be managed or decreased.
- Side effects pertinent to medications and how to manage.

23. Follow-Up Instructions

Reassessment should be continued at regular intervals.

Inpatients:
- Within one hour for parenteral administration
- Within two hours for oral therapy

Outpatients:
- Upon discharge, the discharge plan identifies the patient’s continuing needs
- The discharge plan should be communicated to the patient with regards to appropriate follow-up
### Opioid responsiveness

The following is a visualization of how different types of pain respond to opioids:

<table>
<thead>
<tr>
<th>Location</th>
<th>Somatic Pain</th>
<th>Visceral Pain</th>
<th>Neuropathic Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pin prick, or stabbing, or sharp</td>
<td>Ache, or pressure, or sharp.</td>
<td>Burning, or prickling, or tingling, or electric shock-like, or lancinating</td>
<td></td>
</tr>
<tr>
<td>A-delta fiber activity Located in the periphery(^1)</td>
<td>C Fiber activity Involved deeper innervation(^1)</td>
<td>Dermatomal(^2) (peripheral), or non-dermatomal (central)</td>
<td></td>
</tr>
</tbody>
</table>

\(\text{V}^*\) is most responsive, \(\text{S}\) is responsive, \(\text{N}\) is least responsive.

* Colic and muscle spasms may be less responsive to opioids. Respond best to antispasmodics, NSAIDs, benzodiazepines, baclofen.

---

\(^1\) Most post-operative patients experience A-delta and C fiber pain and respond best to narcotic of any route and NSAIDs.

\(^2\) Segmental distribution follows a dermatome chart. This traces the pathway of sensation to its nerve root. See "Dermatome" in Discussion section.
# Opioid Analgesic Equivalency Comparisons

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Equianalgesic* Dose (mg)</th>
<th>Interval (hours)</th>
<th>Parenteral (IV, IM, SQ)</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10</td>
<td>30**</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Controlled release</td>
<td>10</td>
<td>30</td>
<td>8-12</td>
<td></td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
<td>7.5</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>130</td>
<td>200</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>--</td>
<td>15-30</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Controlled release</td>
<td>--</td>
<td>15-30</td>
<td>12***</td>
<td></td>
</tr>
<tr>
<td>Levorphanol</td>
<td>2.0</td>
<td>4.0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Meperidine****</td>
<td>75</td>
<td>300</td>
<td>2-3</td>
<td></td>
</tr>
<tr>
<td>Methadone****</td>
<td>*****</td>
<td>5</td>
<td>6-8</td>
<td></td>
</tr>
</tbody>
</table>

Transdermal Fentanyl
remember 1 : 2 : 3
25 mg/day IV morphine = 50 mcg/hr q 3 days = 75 mg/day PO morphine

* Equianalgesic ratios:
e.g. for morphine 10 mg IV = 30 mg PO
morphine 30 mg PO = hydromorphone 7.5 mg PO

** Oral to parenteral potency ratio may be as low as 2:1 with chronic administration or as high as 6:1 in the opioid naïve patient

*** Oxycodone controlled release is indicated for dosing every 12 hours. Certain clinical circumstances may require dosing every 8 hours.

**** Meperidine is not preferred for pain management; if used, it should not be administered for more than 3 consecutive days due to CNS toxicity.

***** Methadone: Confer with pain specialist before parenteral use.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Usual Adult Dose</th>
<th>Maximum Adult Dose</th>
<th>Usual Pediatric Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acetaminophen (Tylenol)</strong></td>
<td>650-975 mg PO q 4-6 hr</td>
<td>4000 mg</td>
<td>10-15 mg/kg PO q 4-6 hr</td>
<td>Lacks the peripheral anti-inflammatory activity of other NSAIDS</td>
</tr>
<tr>
<td><strong>Salicylates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>650-975 mg PO q 4-6 hr</td>
<td>4000 mg</td>
<td>10-15 mg/kg PO q 4-6 hr</td>
<td>Inhibits platelet aggregation, may cause postop bleeding</td>
</tr>
<tr>
<td>Choline magnesium trisalicylate (Trilisate)</td>
<td>1000-1500 mg PO q 12 hr</td>
<td>3000 mg</td>
<td>10-25 mg/kg PO q 12 hr</td>
<td>Effectiveness compared to aspirin not clear; onset of analgesia probably slower; less gastropathy and impairment of platelet function</td>
</tr>
<tr>
<td>Diflunisal (Dolobid)</td>
<td>1000 mg PO initial dose followed by 500 mg q 12 hr</td>
<td>1500 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium Salicylate (Doan's Pills)</td>
<td>650 mg PO q 4-6 hr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salicylate (Disalcid)</td>
<td>500 mg PO q 4 hr</td>
<td>3000 mg</td>
<td></td>
<td>Appears to provide anti-inflammatory activity equivalent to aspirin; does not inhibit platelet aggregation</td>
</tr>
<tr>
<td>Sodium Salicylate</td>
<td>325-650 mg PO q 3-4 hr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other NSAIDS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulindac (Clinoril)</td>
<td>200 mg PO q 12 hrs, after satisfactory response is achieved, dose may be decreased accordingly</td>
<td>400 mg</td>
<td></td>
<td>Comparable to aspirin with a lower overall incidence of total adverse effects</td>
</tr>
<tr>
<td>Diclofenac potassium (Voltaren)</td>
<td>50 mg PO q 8 hr</td>
<td>150 mg</td>
<td></td>
<td>Comparable to aspirin with longer duration; available with misoprostol to decrease GI toxicity</td>
</tr>
<tr>
<td>Etodolac (Lodine)</td>
<td>200-400 mg PO q 6-8 hr</td>
<td>1200 mg</td>
<td></td>
<td>200 mg comparable to, and 400 mg possibly superior to 650 mg of aspirin</td>
</tr>
<tr>
<td>Fenoprofen calcium (Nalfon)</td>
<td>200-600 mg PO q 6 hrs</td>
<td>3200 mg</td>
<td></td>
<td>Compared to aspirin; contraindicated in patients with impaired renal function</td>
</tr>
<tr>
<td>Ibuprofen (Advil, Motrin)</td>
<td>400-800 mg PO q 6-8 hrs</td>
<td>2400 mg</td>
<td>10 mg/kg PO q 6-8 hrs</td>
<td>200 mg equal to 650 mg of aspirin and acetylsalicylic acid; 400 mg superior to 650 mg of aspirin and acetylsalicylic acid; 400 mg comparable to acetylsalicylic acid/codeine combination; available as 30 mg suppository</td>
</tr>
<tr>
<td>Indomethacin (Indocin)</td>
<td>25-50 mg PO q 8 hrs</td>
<td>200 mg</td>
<td>0-3 mg/kg or 10 mg PR</td>
<td>Max pediatric dose of 200 mg/day</td>
</tr>
<tr>
<td>Ketoprofen (Orudis)</td>
<td>25-75 mg PO q 6-8 hrs</td>
<td>300 mg</td>
<td></td>
<td>12.5 mg comparable to Ibuprofen 200 mg; 25 mg comparable to Ibuprofen 400 and superior to 650 mg of aspirin; 50 mg superior to acetylsalicylic acid/codeine combination</td>
</tr>
<tr>
<td>Ketorolac (Toradol)</td>
<td>Ps. &lt; 65 yrs of age: 30-60 mg IM initially followed by 15-30 mg q 6 hr. Oral dose following IM dosage: 10 mg q 6-8 hr. IV Dosage: 50 mg IV q 6 hrs. Ps. &gt; 65 yrs of age: 15 mg IV/IM q 6 hrs</td>
<td>Ps. &lt; 65 yrs of age: 120 mg</td>
<td>Ps &gt; 65 yrs of age: 60 mg</td>
<td>IV/IM comparable to 10 mg morphine with longer duration; use should be limited to 5 days</td>
</tr>
<tr>
<td>Meclotenamate sodium (Meclomen)</td>
<td>50-100 mg PO 4-6 hrs</td>
<td>400 mg</td>
<td></td>
<td>Comparable to aspirin; approved for dysmenorrhea</td>
</tr>
<tr>
<td>Mefenamic acid (Ponstel)</td>
<td>500 mg PO initially followed by 250 mg PO q 6 hr</td>
<td>1250 mg</td>
<td></td>
<td>Comparable to aspirin; approved for dysmenorrhea; duration of use not to exceed 1 week</td>
</tr>
<tr>
<td>Naproxen (Naprosyn)</td>
<td>500 mg PO initially followed by 250 mg PO q 6-8 hrs</td>
<td>1250 mg the first day, then 1000 mg</td>
<td>5-10 mg/kg PO q 12 hrs</td>
<td>250 mg probably comparable to 650 mg aspirin with longer duration; 500 mg superior to 650 mg aspirin</td>
</tr>
<tr>
<td>Naproxen sodium (Anaprox)</td>
<td>500 mg PO initially, followed by 275 mg PO q 6-8 hrs</td>
<td>15/3 mg the first day, then 1100 mg</td>
<td>5-10 mg/kg PO q 12 hrs</td>
<td>2/5 mg comparable to 650 mg of aspirin with longer duration; 550 mg superior to 650 mg of aspirin with longer duration</td>
</tr>
</tbody>
</table>

1Drug recommendations are limited to non-opioid analgesics where pediatric dosing information is available.

2Contraindicated in presence of fever or other evidence of a viral illness.

3Cost is relative to the medications identified in this table. This is based off the average wholesale price identified in the "Mosby's Complete Drug Reference. Physicians GenRx." The relative price may vary at the reader’s institution and local pharmacy.

This table was completed using the following resources:
3. AHCPR Clinical Guideline
### Agonists related to Morphine

<table>
<thead>
<tr>
<th>Medication</th>
<th>Recommended starting dose (adults &gt; 50 kg body weight)</th>
<th>Recommended starting dose (children/adults &lt; 50 kg body weight)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>30 mg q 3-4 hrs</td>
<td>10 mg q 3-4 hrs</td>
<td></td>
</tr>
<tr>
<td>Hydrocodone (Dilaudid)</td>
<td>6 mg q 3-4 hrs</td>
<td>1.5 mg q 3-4 hrs</td>
<td>0.75 mg/kg q 3-4 hrs</td>
</tr>
<tr>
<td>Oxymorphone (Numorphan)</td>
<td>Not available</td>
<td>1 mg q 3-4 hrs</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

### Agonists related to Codeine

<table>
<thead>
<tr>
<th>Medication</th>
<th>Recommended starting dose (adults &gt; 50 kg body weight)</th>
<th>Recommended starting dose (children/adults &lt; 50 kg body weight)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>60 mg q 3-4 hrs</td>
<td>60 mg q 3-4 hrs (IM/SQ)</td>
<td>1-2 mg/kg q 3-4 hrs</td>
</tr>
<tr>
<td>Dihydrocodeine</td>
<td>16 mg q 4 hrs</td>
<td>Not available</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Hydrocodone (Hycoan, Vicodin)</td>
<td>10 mg q 3-4 hrs</td>
<td>Not available</td>
<td>0.2 mg/kg q 3-4 hrs</td>
</tr>
<tr>
<td>Oxycodone (Percodan, Tylox)</td>
<td>10 mg q 3-4 hrs</td>
<td>Not available</td>
<td>0.15 mg/kg q 3-4 hrs</td>
</tr>
</tbody>
</table>

### Synthetic opioid agonists

<table>
<thead>
<tr>
<th>Medication</th>
<th>Recommended starting dose (adults &gt; 50 kg body weight)</th>
<th>Recommended starting dose (children/adults &lt; 50 kg body weight)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meperidine (Demerol)</td>
<td>Not available</td>
<td>50-100 mg q 3-4 hrs</td>
<td>1 mg/kg</td>
</tr>
<tr>
<td>Methadone (Dolophine)</td>
<td>5 mg q6-8 hrs</td>
<td>10 mg q 6-8 hrs</td>
<td>0.2 mg/kg q 6-8 hrs</td>
</tr>
<tr>
<td>Propoxyphene (Darvon, Darvocet)</td>
<td>65-100 mg q 4-6 hrs</td>
<td>Not available</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Levorphanol (Levo-Dromuran)</td>
<td>2-4 mg q 6-8 hrs</td>
<td>1.5-2.5 mg q 6-8 hrs</td>
<td>0.04 mg/kg q 6-8 hrs</td>
</tr>
<tr>
<td>Tramadol (Ultram)</td>
<td>25-50 mg q 6 hrs</td>
<td>Not available</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

### Partial agonist and mixed agonist/antagonist

<table>
<thead>
<tr>
<th>Medication</th>
<th>Recommended starting dose (adults &gt; 50 kg body weight)</th>
<th>Recommended starting dose (children/adults &lt; 50 kg body weight)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine (Buprenex)</td>
<td>Not available</td>
<td>0.4 mg q 6-8 hrs</td>
<td>Not available</td>
</tr>
<tr>
<td>Butorphanol (Stadol)</td>
<td>Not available</td>
<td>2 mg q 3-4 hrs</td>
<td>Not available</td>
</tr>
<tr>
<td>Dezocine</td>
<td>Not available</td>
<td>5-10 mg q 3-6 hrs</td>
<td>Not available</td>
</tr>
<tr>
<td>Nalbuphine (Nubain)</td>
<td>Not available</td>
<td>10 mg q 3-4 hrs</td>
<td>Not available</td>
</tr>
<tr>
<td>Pentazocine (Talwin)</td>
<td>50 mg q 4-6 hrs</td>
<td>60 mg q 2-4 hrs</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

---

See notes on next page
The following notes refer to the table on the preceding page:

**Caution:** Recommended doses do not apply to patients with renal or hepatic insufficiency or other illness that may effect drug metabolism and kinetics.

1. **Caution:** Doses listed for patients less than 50 kg body weight cannot be used as initial starting doses in infants less than 6 months of age.
2. **Caution:** Doses of aspirin and acetaminophen in combination preparations with opioid/NSAID must also be adjusted to the patient’s body weight.

This table was completed using the following sources:

3. AHCPR Clinical Guidelines
## Annotation Appendix E – Pharmacologic Treatment of Neuropathic Pain

### Alphabetical Listing of Recommended Medications for Neuropathic Pain

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting dose</th>
<th>Maximum dose</th>
<th>Indications</th>
<th>Contraindications</th>
<th>Most common side effects</th>
<th>Titration</th>
<th>Most common side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine (Tegretol)</td>
<td>100 mg bid</td>
<td></td>
<td>TN*, PN*, central pain</td>
<td>Liver abnormalities, ataxia, confusion, bone marrow suppression, known sensitivity to tricyclic compounds</td>
<td>Sedation, dizziness, ataxia, confusion, nausea, liver toxicity, blood dyscrasia, Stevens-Johnson syndrome</td>
<td>100 mg every 3-7 days</td>
<td></td>
</tr>
<tr>
<td>Gabapentin (Neurontin)</td>
<td>300 mg qhs</td>
<td>6,000 mg/day</td>
<td>Demonstrated hypersensitivity to the drug or its ingredients</td>
<td>Known sensitivity to local anesthetics of amide type</td>
<td>Sedation, dizziness, confusio, peripheral edema, weight gain</td>
<td>300 mg every 3-7 days</td>
<td></td>
</tr>
<tr>
<td>Lidocaine patch 5% (Lidoderm)</td>
<td>Up to 3 patches applied to painful skin area</td>
<td>Up to 3 mg/day</td>
<td>Localized skin irritation</td>
<td>Known sensitivity to local anesthetics of amide type</td>
<td>None needed</td>
<td>None needed</td>
<td></td>
</tr>
<tr>
<td>Mexiletine (Mexitil)</td>
<td>150 mg qd</td>
<td>500 mg 5-7 days</td>
<td>Titrated to toxic serum level</td>
<td>Known sensitivity to local anesthetics of amide type</td>
<td>Nausea, dizziness, anxiety</td>
<td>150 mg 5-7 days</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>2.5 mg bid</td>
<td>25 mg bid</td>
<td>PHN*, PN*, CRPS, TN*</td>
<td>Known hypersensitivity in situations where opioids are contraindicated</td>
<td>Nausea, sedation, constipation, confusion, swelling, itching, depression</td>
<td>25 mg every 5-7 days</td>
<td></td>
</tr>
</tbody>
</table>

### Most common side effects
- Sedation, dizziness, ataxia, confusion, nausea, liver toxicity, blood dyscrasia, Stevens-Johnson syndrome
- Localized skin irritation
- Sedation, dizziness, anxiety
- Nausea, dizziness, anxiety
- Known sensitivity to local anesthetics of amide type

### Contraindications
- Liver abnormalities, ataxia, confusion, bone marrow suppression, known sensitivity to tricyclic compounds
- Known sensitivity to local anesthetics of amide type
- Known hypersensitivity in situations where opioids are contraindicated
# Annotation Appendix E – Pharmacologic Treatment of Neuropathic Pain (cont)

## Alphabetic Listing of Recommended Medications for Neuropathic Pain

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting dose</th>
<th>Maximum dose</th>
<th>Titration</th>
<th>Most common side effects</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenytoin (Dilantin)</td>
<td>100 mg bid</td>
<td>100 mg every 3-7 days</td>
<td>Titrate to intolerable side effects</td>
<td>Sedation, dizziness, confusion, nausea, gingival hyperplasia, peripheral neuropathy, Stevens-Johnson syndrome</td>
<td>Bradycardia ≥2-3° heart block, hypersensitivity</td>
</tr>
<tr>
<td>Tizanidine (Zanaflex)</td>
<td>1 mg qhs</td>
<td>2 mg every 3-7 days (tid)</td>
<td>Titrate to toxic serum level</td>
<td>Sedation, dizziness, hypotension, liver function abnormalities</td>
<td>Liver abnormalities, known hypersensitivity</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>10-25 mg qhs</td>
<td>20 mg every 5-7 days (entire dose qhs)</td>
<td>Titrate to toxic serum level</td>
<td>Dry mouth, sedation, dizziness, constipation, urinary hesitancy, orthostatic hypotension</td>
<td>Narrow-angle glaucoma, urinary retention, 2°-3° heart block, arrhythmia, hypersensitivity</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>10-25 mg qhs</td>
<td>30 mg</td>
<td>20 mg every 5-7 days (entire dose qhs)</td>
<td>Dry mouth, sedation, dizziness, constipation, urinary hesitancy, orthostatic hypotension</td>
<td>Narrow-angle glaucoma, urinary retention, 2°-3° heart block, arrhythmia, hypersensitivity</td>
</tr>
<tr>
<td>Desipramine</td>
<td>10-25 mg qhs</td>
<td>30 mg</td>
<td>20 mg every 5-7 days (entire dose qhs)</td>
<td>Dry mouth, sedation, dizziness, constipation, urinary hesitancy, orthostatic hypotension</td>
<td>Narrow-angle glaucoma, urinary retention, 2°-3° heart block, arrhythmia, hypersensitivity</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>10-25 mg qhs</td>
<td>30 mg</td>
<td>20 mg every 5-7 days (entire dose qhs)</td>
<td>Dry mouth, sedation, dizziness, constipation, urinary hesitancy, orthostatic hypotension</td>
<td>Narrow-angle glaucoma, urinary retention, 2°-3° heart block, arrhythmia, hypersensitivity</td>
</tr>
<tr>
<td>Doxepin</td>
<td>10-25 mg qhs</td>
<td>30 mg</td>
<td>20 mg every 5-7 days (entire dose qhs)</td>
<td>Dry mouth, sedation, dizziness, constipation, urinary hesitancy, orthostatic hypotension</td>
<td>Narrow-angle glaucoma, urinary retention, 2°-3° heart block, arrhythmia, hypersensitivity</td>
</tr>
<tr>
<td>Tramadol (Ultram)</td>
<td>50 mg bid</td>
<td>400 mg</td>
<td>50 mg every 5-7 days (give tid or qd)</td>
<td>Nausea, sedation</td>
<td>Previously demonstrated sensitivity to the drug or opioids</td>
</tr>
</tbody>
</table>

* CRPS, complex regional pain syndrome; PHN, postherpetic neuralgia; PN, peripheral neuropathy; i.e., diabetic neuropathy, human immunodeficiency virus neuropathy, idiopathic neuropathy, mononeuropathy, etc.; SCI, spinal cord injury; TN, trigeminal neuralgia.

† Anecdotal evidence

+ Some patients require tid dosing

* FDA-approved indication (with randomized controlled trials)

Randomized controlled trial evidence
Dermatome Map (pertains to neuropathic pain)

Dermatomes are cutaneous sensory paths that are defined by sensation. Each dermatome is the area of skin supplied by the dorsal roots of a given sensory nerve. The levels of the bones of the vertebral column label the dermatome. A dermatome map can be used to determine the origin of pain impulses as well as to determine spread of analgesia when intraspinal medications are used. (NOTE: Not all neuropathic pain is radicular.)
## Annotation Appendix G – Side Effects

**Assessment and Management of Acute Pain**

<table>
<thead>
<tr>
<th>Drug Category</th>
<th>Side Effect</th>
<th>Adult Dose</th>
<th>Pediatric Dose</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioids</strong></td>
<td>Nausea &amp; vomiting</td>
<td>&gt; 10 kg: PO/IV/IM q6-12h</td>
<td>&gt; 10 kg: 0.4mg/kg/day in 3-4 divided doses; IM 0.15mg/kg/dose (usual 0.13-0.16 mg/kg/dose)</td>
<td>Droperidol (Inapsine) 0.625 to 2.5mg IV/IM q2-4hr or PR 0.5mg IV/IM q6h</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-12 years: 5-7.5mg/kg/day in 2-3 divided doses</td>
<td>0.4-0.5mg/kg/day in 4 divided doses</td>
<td>Metoclopramide (Reglan) 10-20mg IV q6h</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 12 years: 2.1-20mg/kg/day in 2-3 divided doses</td>
<td>Not recommended in &lt;3yo</td>
<td>Ondansetron (Zofran) or Dolasetron (Anzemet) Ondansetron: 0.1mg/kg up to 4mg dose Dolasetron: 0.35mg/kg up to 12.5mg</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>Infants: 0.5-1mg/kg/day in 3 divided doses</td>
<td>Infants: 0.5mg PO q4h</td>
<td>Bisacodyl (Dulcolax) 10mg PO/pr qhs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 1mo: 2-4ml/kg/day in divided doses</td>
<td>&gt; 1.5yo: 150-200ml/3-4 divided doses</td>
<td>Milk of Magnesia (MOM) 15-30ml PO qhs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 2yo: 2-4ml/kg/dose; &gt; 5yo: 6-10ml/kg/qid</td>
<td>&gt; 1yo: 15-30 ml/day</td>
<td>Magnesium Citrate (MOM) 150-300 ml/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 5yo: 200-400 ml/day</td>
<td>&gt; 12yo: 15-30ml/day</td>
<td>Lactulose (Cephulac) 15-30ml PO H1D-QID</td>
</tr>
</tbody>
</table>

**Comments**
- Consider changing opioid (e.g., to hydromorphone).
- Non-drug toast/crackers, sherbet, pretzels, oatmeal, soft & bland fruits and vegetables.
### Annotation Appendix G – Side Effects (cont)

#### Opioids (cont.)

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Management</th>
<th>Pediatric Dose</th>
<th>Adult Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Constipation</strong></td>
<td>Sorbitol</td>
<td><strong>No recommendations</strong></td>
<td>15-30mL TID-QID</td>
<td>Good hydration; if necessary, prune juice, prune juice, smooth move tea (1 tea bag = 2.5 senna tablets); mobility</td>
</tr>
<tr>
<td></td>
<td><strong>Non-drug</strong></td>
<td></td>
<td></td>
<td>Consider changing opioid (i.e., to hydromorphone)</td>
</tr>
<tr>
<td></td>
<td><strong>Sorbitol</strong></td>
<td></td>
<td></td>
<td>For epidural and intrathecal morphine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>For epidural and intrathecal morphine</td>
</tr>
<tr>
<td><strong>Pruritus</strong></td>
<td>Diphenhydramine (Benadryl)</td>
<td>20-50mg q6h ATC if opioid continues, then prn</td>
<td>5mg/kg/day divided in 2-3 doses</td>
<td>Consider changing opioid (i.e., to hydromorphone)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>For epidural and intrathecal morphine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>For epidural and intrathecal morphine</td>
</tr>
<tr>
<td><strong>Respiratory Depression</strong></td>
<td>Naloxone (Narcan)</td>
<td></td>
<td></td>
<td>Dilute 0.4mg (1ml.) Naloxone with 9ml of normal saline (total volume 10ml). Administer 0.02mg (0.5ml) bolus every minute until the patient’s respiratory rate increases. Repeat as necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>May consider changing to NAID</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Infants and children: Limit dose to 25mg/kg/day</td>
</tr>
<tr>
<td><strong>Hepatotoxicity</strong></td>
<td>Acetaminophen</td>
<td></td>
<td></td>
<td>May consider lower total daily dose in patients with pre-existing liver disease</td>
</tr>
<tr>
<td><strong>Hyperglycemia</strong></td>
<td>Corticosteroids</td>
<td></td>
<td></td>
<td>Appropriate mgmt</td>
</tr>
</tbody>
</table>

#### Drug Category

**Opioids (cont.)**
<table>
<thead>
<tr>
<th>Drug Category</th>
<th>Side Effect</th>
<th>Management</th>
<th>Adult Dose</th>
<th>Pediatric Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td>GI upset</td>
<td>Misoprostil (Cytotec)</td>
<td>200µg PO BID-TID</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bleeding tendency</td>
<td></td>
<td></td>
<td></td>
<td>Use Trilisate, Disalcid, or Celcoxib: no effect on platelet aggregation</td>
</tr>
<tr>
<td></td>
<td>Nephrotoxicity</td>
<td></td>
<td></td>
<td></td>
<td>Alternatives: Sulindac or Celcoxib (celcoxib has shown no benefit in post-op surgical pain)</td>
</tr>
<tr>
<td>Anticonvulsant Drugs</td>
<td>Somnolence</td>
<td>Decrease dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cerebellar symptoms</td>
<td>Decrease dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamzepine (Tegretol)</td>
<td>Myelosuppression</td>
<td>Change to another antiepileptic drug</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Adjust drugs based on SE profile</td>
</tr>
</tbody>
</table>

### Tricyclic Antidepressants

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Brand Names</th>
<th>Anticholinergic</th>
<th>Sedation</th>
<th>Orthostatic Hypotension</th>
<th>Consider switching drugs based on side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>Elavil</td>
<td>+++</td>
<td>++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doxepin</td>
<td>Adapin, Sinequan</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Imipramine</td>
<td>Tofranil</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Desipramine</td>
<td>Norpramin</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>Aventyl, Pamelor</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

References:

**DEFINITION OF TERMS USED IN THIS GUIDELINE:**

*Addiction*: Addiction is a neurobehavioral syndrome with genetic and environmental influences that results in psychological dependence on the use of substances for their psychic effects and is characterized by compulsive use despite harm. Addiction may also be referred to by terms such as “drug dependence” and “psychological dependence.” Physical dependence and tolerance are normal physiological consequences of extended opioid therapy for pain and should not be considered addiction.

*Analgesic Tolerance*: Analgesic tolerance is the need to increase the dose of opioid to achieve the same level of analgesia. Analgesic tolerance may or may not be evidenced during opioid treatment and does not equate with addiction.

*DPNB*: Dorsal Penile Nerve Block.

*EMLA*: Eutectic Mixture of Local Anesthetics.

*LET*: Anesthetic solution comprised of Lidocaine, Epinephrine, and Tetracaine.

*Neuropathic*: A pathological change in the peripheral nervous system.

*Nociception*: The process of detection and signaling the presence of a noxious stimulus.

*Pain*: An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

*Physical Dependence*: Physical dependence on a controlled substance is a physiologic state of neuroadaptation which is characterized by the emergence of a withdrawal syndrome if drug use is stopped or decreased abruptly, or if an antagonist is administered. Physical dependence is an expected result of opioid use. Physical dependence, by itself, does not equate with addiction.

*Pseudoaddiction*: Pattern of drug-seeking behavior of pain patients who are receiving inadequate pain management that can be mistaken for addiction.

*Radicular*: Pertaining to a nerve root.

*Somatic*: Pertaining to the body wall in contrast to the viscera.

*Substance Abuse*: Substance abuse is the use of any substance(s) for non-therapeutic purposes; or use of medication for purposes other than those for which it is prescribed.

*TAC*: Anesthetic solution comprised of Tetracaine, Adrenaline (Epinephrine), and Cocaine.

*Tolerance*: Tolerance is a physiologic state resulting from regular use of a drug in which an increased dosage is needed to produce the same effect or a reduced effect is observed with a constant dose.

*Visceral*: Pertaining to a bodily organ.

*From "Model Guidelines for the Use of Controlled Substances for the Treatment of Pain"* (5/98), Federation of State Medical Boards of the United States.
### Discussion and References:
#### Assessment and Management of Acute Pain

<table>
<thead>
<tr>
<th>Event</th>
<th>Date Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Document Drafted</td>
<td>Jan – Jun 1999</td>
</tr>
<tr>
<td>Critical Review</td>
<td>July – Aug 1999</td>
</tr>
<tr>
<td>Revision/Approval</td>
<td>Sept – Nov 1999</td>
</tr>
<tr>
<td>Revision/Approval</td>
<td>Jul – Sep 2000</td>
</tr>
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<td>Jun – Sep 2001</td>
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<td>Second Cycle General Implementation</td>
<td>Oct 2001 – May 2002</td>
</tr>
<tr>
<td>Revision/Approval</td>
<td>Jun – Sep 2002</td>
</tr>
<tr>
<td>Third Cycle General Implementation</td>
<td>Begins Oct 2002</td>
</tr>
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</table>

Released in October 2002 for General Implementation. *The next scheduled revision will occur within the next 18 months.*

Contact ICSI at:

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All work group members: none declared.
I. CLASSES OF RESEARCH REPORTS

A. Primary Reports of New Data Collection:

Class A: Randomized, controlled trial
Class B: Cohort study
Class C: Non-randomized trial with concurrent or historical controls
Case-control study
Study of sensitivity and specificity of a diagnostic test
Population-based descriptive study
Class D: Cross-sectional study
Case series
Case report

B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

Class M: Meta-analysis
Systematic review
Decision analysis
Cost-benefit analysis
Cost-effectiveness study
Class R: Narrative review
Consensus statement
Consensus report
Class X: Medical opinion

II. CONCLUSION GRADES

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system defined in Section I, above, and are assigned a designator of +, -, or ø to reflect the study quality. Conclusion grades are determined by the work group based on the following definitions:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is uncertainty attached to the conclusion because of inconsistencies among the results from different studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results from different studies or because of serious doubts about
Discussion and References –
Evidence Grading (cont)

...generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

**Grade IV:** The support for the conclusion consists solely of the statements of informed medical commentators based on their clinical experience, unsubstantiated by the results of any research studies.

The symbols +, −, ø, and N/A found on the conclusion grading worksheets are used to designate the quality of the primary research reports:

+ indicates that the report has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis;

− indicates that these issues have not been adequately addressed;

ø indicates that the report is neither exceptionally strong or exceptionally weak;

N/A indicates that the report is not a primary reference and therefore the quality has not been assessed.
1. Patient Has Pain or is Likely to Have Pain

There are many statements in the medical literature decrying the inadequate treatment of pain. Reasons for under-treatment of pain range from educational, cultural, social and legal, to moral and financial. The benefits of properly treating or preventing pain are numerous and include reduced hospital stays, quicker return to work, decreased disability, and decreased postoperative complications like atelectasis, pneumonia, DVT and suppression of immune system. Also included in the benefits of treating pain are the prevention of "pain memories." This is manifested by studies demonstrating that boys given adequate circumcision analgesia have a decreased pain response to infant immunizations compared to boys without adequate circumcision pain control. Likewise, it has been shown that adults given adequate acute pain control have a reduced tendency to develop chronic pain syndromes. There are also reports that when given certain types of anesthesia and analgesia some patients undergoing amputations may be less likely to develop "phantom limb pain."


Doctor wins round against board on pain medication: pain management licensure decision; physician wins appeal.” Am Med News March: 14, 1999. (Class not assignable)


Hayes CH, Molloy AR. “Neuropathic pain in the perioperative period.” Int Anesthesiol Clin 35:67-81, 1997. (Class R)


2. Critical First Steps

Observer/Caregiver Ratings of Pain and Pain Relief

Often in clinical situations, the health care team is confronted with patients who are cognitively impaired, heavily medicated, ventilated, or non-English speaking. At these times it is necessary to form clinical judgments regarding the patient’s potential level of discomfort. Observer or caregiver ratings of pain and of the relief of pain with medical therapy are efficient in these clinical settings.

There are many other behaviors that can be observed when someone is experiencing pain. Humans are able to control behavior to a degree, which will individually depend on conditioning, personality, past experience and present circumstances. Moreover, pain-related behavior may change with time for the patient. For instance, Lim and Guzman reported that when pain was inflicted on volunteers, 81% reported feeling pain, 52% displayed facial features of pain and only 31% continued the same patterns of pain behavior with repeated stimuli.

Facial expressions have historically been viewed as especially reliable indicators of the intensity of pain. In a very laborious process of observing patients experiencing various types of pain, Prkachin has determined a few facial movements that are consistently related to different types of pain. The four actions which comprise the basic pain signal are brow lowering, orbit tightening, levator contraction, and eyelid closing. Other clinical indicators are a result of an adrenergic response to severe and acute pain. Tachycardia, hypertension, diaphoresis, restlessness and other signs will dissipate with duration of pain and as a result are less reliable over time.

Caution should be used in this type of pain since only the sufferer knows severity of pain. A caregiver’s assessment of a patient’s current level of pain can be influenced by stereotypes, interactions with the patient, other patients, and other interactions on the health care team. Nurses and physicians have been reported to underestimate patients’ pain levels. For those who are cognitively impaired, prevalence rates or pain have been found to be lower than those of same age who can relay information about pain themselves. A conscious awareness of potential bias will allow for clinical data gathering; however, this should never be the means of collecting scientific data.


3. Pain Assessment

Discussion # 3 is organized as follows:

- Pain Assessment Overview
- Pain Assessment in the Elderly
- Pain Assessment in Children

Pain Assessment Overview

The National Institutes for Health has stated that patient self-reporting is the “most reliable indicator of the existence and intensity of pain.” There are multiple pain assessment tools available for determining the quantity and quality of a patient’s pain experience. Proper use of these tools mandates that the assessment occur not only at the time of presentation, but also throughout the course of the clinical encounter and after institution of therapy. In an acute care setting, pain intensity should be reassessed within one hour for parenteral administration of medication and two hours after oral therapy is begun. In an outpatient setting, patients should be instructed to contact their care provider with feedback on the efficacy of the therapy prescribed. Dosing adjustments should be made on the basis of the patient’s self-report, pattern of pain response to therapy and other clinical indicators available to the clinician for evaluation.

In the assessment of pain, it is useful to recruit the active involvement of the patient or caretakers. The patient or caretaker should be taught how to use the pain scale with an emphasis placed on encouraging self-report of pain intensity or change in quality. Patients may need to understand that although complete relief is the ultimate goal, it is not always possible. They should determine for themselves what level of discomfort is acceptable and will allow for maximal function with activities of daily living.

Pain Scales: Pain scales are classified as single or multidimensional and self-report or observational. No one scale is consistently associated with more administration- or response-related problems. Several scales are depicted in Annotation #3 (Table 1, "Assessment Tools for Adults").

The single dimensional scales measure only pain intensity and by their nature are self-report. They are reasonable for use in acute pain when the etiology is clear (i.e., trauma, pancreatitis, otitis media). The assessment tools in this classification were initially developed for research trials. One concern is that measuring intensity alone may be an oversimplification of the pain experience.

The multidimensional scales measure not only the intensity but also the nature and location of the pain and in some cases the impact the pain is having on activity or mood. These are excellent tools in the setting of persisting acute or chronic pain when intensity as well as social support, interference with ADL’s and relationship to depression may need to be assessed. Each of these was developed as a self-report but may be completed with the assistance of an interviewer or health care provider.


Validation studies (single dimensional):

Visual analog scale (VAS)


Numeric rating scales (NRS)


Paice JA, Cohen FL. “Validity of a verbally administered numeric rating scale to measure cancer pain intensity.” Cancer Nurs 2:88-93, 1997. (Class C)

Verbal description scales (VDS)


Facial pain scales (FPS)


Validation studies (multi-dimensional):

**Brief Pain Inventory**


Daut RL, Cleeland CS, Flanery RC. “Development of Wisconsin Brief Pain Questionnaire to assess pain in cancer and other diseases.” Pain 17:197-210, 1983. (Class C)

**McGill Pain Questionnaire**


**Pain Assessment in the Elderly**

**Overview**

Both acute and chronic types of pain are very common in the elderly. Effective pain management in this population allows for effective mobilization and functional independence, with resultant decreased morbidity. This in turn results in decreases in health care expenditures. In spite of the obvious benefits resulting from adequate pain relief there are many challenges contributing to the significant risk of uncontrolled discomfort.

The multiple medical comorbidities and impaired functional status in this population presents significant challenge in the treatment of pain. Positive correlations have been reported between the number of medications, ratings of depression and amount of pain experienced by this population. Unfortunately, the very medications used to control pain can have intolerable side effects in the elderly; yet, baseline functional impairment may worsen with significant pain. The specifics of these challenges are beyond the scope of this guideline. The American Geriatrics Society Panel on Chronic Pain in Older Persons is an excellent clinical resource.

In addition to the challenges of treating, the assessment and reporting of pain present the most problematic area in this population. One contributing factor is their own under reporting of discomfort. Some feel it is an expected part of the aging process and they “don’t want to bother anyone,” and hence do not complain. Likewise, others may use pain to mask other newly developing physical or cognitive disabilities. In addition, those with cognitive impairment present the difficulties of observer-related pain assessment mentioned in Discussion #2. Even in nondemented patients, a correlation of only 0.38 was demonstrated between the elderly patient’s report of pain and the RN’s assessment of the severity of pain.

There is a paucity of data available on the validity of any of the pain assessment tools in the sick or institutionalized elderly. Psychometrics for the NRS, VDS, VAS, FPS have all been tested in groups of patients older than 65, but for the most part the patients have been cognitively intact and not institutionalized. The assessment of pain in the aged is complicated by decreases in hearing and visual acuity. Tools that require a lot of explanation or visualization to perform will be more difficult and possibly less reliable.

The VAS may be an example of these hindrances to pain assessment in the elderly. It has a reported twenty-five percent failure rate along with other reports of concern with the difficulty of the VAS for the elderly population. In comparisons with other tools, the VAS has been least preferred by elderly
patients. Facial pain scales have been thought to be easier to administer in this population. Theoretically, the Bieri FPS should be good with elderly patients because it does not appear child-like, avoids a happy face and tears. The latter two are significant to prevent bias introduced by personal beliefs and reflections of current health state. The Bieri FPS has been validated for use in cognitively intact, community-dwelling elderly. The VDS is felt to be the easiest tool for the elderly to use and in one population was the tool most preferred for pain intensity assessment. Specifically the VDS allows patients to describe what they are feeling with common words rather than having to go through the abstract process of converting how they feel to a number, facial representation or a point somewhere on a straight line. Several authors have suggested the importance of allowing the elderly patient to choose their preferred tool of pain intensity assessment in order to facilitate the best communication.

One of the most sensitive assessments of pain in the elderly population may actually be the effect the pain is having on their life, rather than the intensity of the pain itself. Many can maintain necessary activities of daily living in spite of severe pain. However, advanced ADL’s or elective activities such as social functions or even walking may correlate better with severity of pain. One may also suppose that as with cognitive ability, any baseline impairment in activity may also worsen with significant pain.

Ferrell BA, Ferrell BR, Osterweil D. "Pain in the nursing home." JAGS 38:409-14, 1990. (Class D)
Herr KA, Mobily PR. "Comparison of selected pain assessment tools for use with the elderly." Appl Nurs Res 6:39-46, 1993. (Class D)

Pain Assessment in Children

Overview

Infants cannot verbalize their pain sensations and therefore are entirely dependent on their caregivers to assess their pain and to determine the effectiveness of management efforts.

Pre-term infants as young as 20-24 weeks postconception have the anatomic and functional capacity to mount a response to noxious stimuli. Descending pathways from the CNS that inhibit transmission of
pain signals may not be developed and therefore the preterm may be more rather than less sensitive to pain.

The consequences of pain are often minimized by health professionals because they are believed to be transient, inconsequential, and not remembered. Infants have been shown though to have the capacity for pain memory. Neonates experiencing a painful procedure (circumcision) showed a stronger pain response to subsequent immunizations. Anesthesia for the initial procedure attenuated the subsequent response. The pain itself may not be recalled, but the stress may mediate pain responses later in life.

Although physiological indicators (e.g., increased heart rate, respiratory rate, blood pressure, palmar sweating, intracranial pressure, cortisol levels, decreased oxygen saturation, vagal tone, CO₂ levels) provide precise objective information reflecting the neonate’s response to a noxious stimulus, they are more indicative of stress rather than pain.

The lack of association between physiological and behavioral measures suggests that they may be providing different information about the mechanisms responsible for pain.

The most frequently studied behavioral responses to pain in neonates are the facial activity, crying, and body movements.

In infants, a limited number of facial actions have been studied, but they have been found to be consistent across ages and situations. The most widely used measure is the Neonatal Facial Coding System. Predominantly a research tool due to the need for experienced coders and length of time to administer, it has been shown to be sensitive to pain intensity and most helpful in the evaluation of pain management. Both reliability and validity are good and it has been used at bedside.

An infant’s cry has been the most obvious index, but the interpretation has been difficult. A significant proportion of preterm infants do not cry or may be influenced by drugs or mechanical ventilation. The spectral analysis of the cry is occasionally used in research studies, but is not practical at the bedside.

Changes in body activity or the withdrawal of a limb in response to a painful stimulus, may also be difficult to interpret in the small premature who is mechanically and/or pharmacologically restrained.


**Multivariable Measurement Tools for Infants**

Two tools using a combination of behavioral and physiological measurements have been shown to be the most practical.
**CRIES** is a neonatal postoperative pain scale assessing 5 variables (C-crying; R-Requires oxygen; I-Increased vital signs; E-expression; S-sleeplessness) on a 0-2 point scale (much like an APGAR score). This scale has been validated against the nonverbal components of the Children's Hospital of Eastern Ontario Pain Scale (CHEOPS). The interobserver reliability was found to be 94% and it has been useful for repeated bedside observations.

*Modified Behavioral Pain Scale (MBPS)* utilizes three items (facial expression, cry, movements) from the original CHEOPS scoring. This scale has been validated for 2- to 6-month-olds. It has excellent validity and interobserver agreement (95%). It has been studied only as a research tool but holds promise for bedside use.

Two other pain scales for neonates, The Neonatal Infant Pain Scale (NIPS) and the Premature Infant Pain Scale (PIPP), suffer from poor interrater reliability and content validity.


**Pain Assessment in Young Children**

In children, pain measures may be influenced by limited cognitive or language skills or by the positive or negative consequences their pain reports or behaviors produce. The caregiver must be aware of the developmental stage of the child to best determine the assessment tool to utilize.

Behavioral observations must be interpreted cautiously. For example, a child who is sleeping all the time may be in significant pain without crying or whimpering. One must be culturally sensitive regarding the families’ beliefs about pain and medical care.

Self-report measures are best used in children above the age of 3-4 years. Children may underreport their pain to avoid future injections or other “painful” procedures aimed at alleviating the pain.


**6. Determine Mechanism of Pain (Patient May Experience More Than One Type of Pain)**

The physiology of pain guides the practitioner to more effectively and efficiently control pain. An understanding of the physiology of pain entails familiarity with transmission of the painful experience.

Nociception is the detection of painful stimuli; this initiates the chain of events of pain transmission. The site of the injury gives rise to a release of prostaglandin that is the precursor to impel the painful impulse through the peripheral nervous system to the spinal cord where Substance P (a neurotransmitter) is released, facilitating the impulse through the spinal cord to the brain, in particular the cerebral cortex. Nonsteroidal antiinflammatory drugs inhibit the synthesis of prostaglandin (PGE2). PGE2 are potent vasodilators producing pain and edema and are quite active in arthritis, musculoskeletal injuries and bone disorders.
At the periphery there is generation of an “action potential” which allows for the transmission of pain through the peripheral nerve. The action potential is the result of an exchange of ions along the inner and outer neural membrane. Anticonvulsants and local anesthetics block this influx and efflux of ions, preventing the generation of the action potential.

Within the spinal cord there is a release of many substances responsible for transmitting pain. They are Substance P, cholecystokinin, calcitonin gene-related peptide, and excitatory amino acids. These are released by the primary afferent neurons and stimulate the ascending fibers towards the brain. Opioids bind to the opiate receptors within the spinal cord at the substantia gelatinosa where there are two actions: 1) blocking the pain transmission, and 2) inhibiting the release of the above neurotransmitters.

Within the brain, the ascending tract enters by way of the periaqueductal grey, the reticular formation, and the thalamus, where it continues to travel along to various areas of the limbic system (the emotional center) and cerebral cortex. Experts believe awareness of pain occurs in the somatosensory cortex. Opiate receptors in the brain are located in the periaqueductal grey and this is where systemic narcotics bind to create analgesia.

The diminishing of the painful response occurs in the descending tract which originates in the higher centers of the brain and descends to the dorsal horn of the spinal cord. This is where there is a release of endogenous opiates (enkephalin and dynorphin), serotonin, and norepinephrine. It is at this level that the tricyclic antidepressants work by preventing the reuptake of serotonin and norepinephrine and thereby facilitating analgesia.


Yaksh TL. “Spinal opiate analgesia: characteristics and principles of action.” Pain 11:293-346, 1981. (Class R)

8. Patient Reports Localized Pin Prick, Sharp or Stabbing Pain

9. Somatic Pain

10. Treatment Choices for Somatic Pain


11. Patient Reports Generalized Ache or Pressure
12. Visceral Pain
13. Treatment Choices for Visceral Pain


14. Patient Reports Radiating or Specific Burning, Tingling, or Lancinating Pain
15. Neuropathic Pain
16. Treatment Choices for Neuropathic Pain


17. Prevention/Intervention

The discussion material for Step #17 is organized as follows:

- Prevention/Intervention Overview: Preemptive Analgesia
- Pharmacological Therapy: Non-opioids, Opioids, Recognizing Substance Abuse, Adjuvants
- Behavioral/Cognitive Intervention
- Clinical Pearls

**Prevention/Intervention Overview**

**Preemptive Analgesia**

Clinical studies have indicated that painful stimuli may produce changes in the spinal cord that in turn influence the response to further stimuli. The concept of preemptive analgesia is that, by preventing the sensitization of the central nervous system which would normally amplify subsequent nociceptive input, one may reduce the severity of postoperative pain. The neuroplastic response may be prevented by appropriate administration of analgesics before the stimulus in order to block painful nerve transmission. A nerve conduction block is required, either by infiltration of local anesthetics near the site of expected injury, or by neuraxis blockade in the epidural or intrathecal spaces, also with
local anesthetic. The use of neuraxial opioids may also play a role. Application of local anesthetics or opioids near the spinal cord is usually performed by an anesthesiologist.


**PHARMACOLOGICAL THERAPY**

*Overview of Pharmacological Management*

The use of pharmacological agents is considered to be the mainstay of therapy for acute pain. There are three broad categories of medications to consider when treating the patient with acute pain: non-opioid analgesics (NSAIDs), opioid analgesics and analgesic adjuvants.

**Non-Opioid Analgesics**

NSAIDs are useful in the treatment of acute pain due to a variety of etiologies, including trauma, postoperative pain and arthritis. Mild to moderate acute pain can often be adequately controlled with the use of an appropriate NSAID. Even when used in the treatment of moderate to severe pain secondary to surgery, NSAIDs have a significant opioid dose-sparing effect and can therefore reduce opioid-related side effects.

Before using NSAIDs, the hematological gastrointestinal and renal effects should be taken into consideration. All but two NSAIDs, choline magnesium and salicylate, have been shown to inhibit platelet aggregation by inhibiting prostaglandin synthetase. Therefore, care must be used when prescribing NSAIDs in patients with coagulopathies or thrombocytopenia and in those who are at risk for bleeding.

The use of NSAIDs can also cause various gastrointestinal effects ranging from mild dyspepsia to more serious reactions such as bleeding and perforation. In a meta-analysis of the relative risk for serious gastrointestinal complications, users of NSAIDs were at approximately three times greater risk of developing serious gastrointestinal side effects than of non-users. Additional factors that appear to make an individual at a greater risk for gastrointestinal side effects are age greater than 60 years, previous gastrointestinal events and concomitant corticosteroid use.


Segal ES. Personal communication from Syntex Laboratories. November 25, 1991. (Class not assign-able)

Steinberg RB, Tessier EG. “Gastrointestinal bleeding after administration of ketorolac.” Anesthesiology 79:1146, 1993. (Class D)


Two NSAIDs that serve as a Cox-2 inhibitors have recently been introduced. NSAIDS produce their anti-inflammatory response by inhibiting cyclooxygenase, thereby inhibiting prostaglandin synthesis. Cyclooxygenase is present in the body in two forms: type 1, which produces prostaglandins that are beneficial to renal and gastric function, and type 2, which produces prostaglandins related to the inflammatory process. The Cox-2 inhibitors selectively inhibit cyclooxygenase type 2, thereby reducing inflammation. The advantage of this medication is that the type 1 cyclooxygenase is preserved and the side effects of NSAID-induced gastritis and gastric ulceration are decreased. Celecoxib was approved in December 1998 for the treatment of signs and symptoms related to osteoarthritis and adult rheumatoid arthritis. Rofecoxib (Vioxx) has been approved for management of acute pain.

Opioid Analgesics

Opioids are used for the treatment of moderate to severe pain from various etiologies. If not contrain- dicated, the management of acute pain should begin with the use of an appropriate NSAID. If the pain is not controlled with an NSAID, or moderate to severe pain is expected, an opioid should be added in combination therapy. When opioids are used appropriately to treat acute pain in the nonchemically dependent patient, physiological dependence or tolerance to the opioid is quite un- common. Also, these same patients are unlikely to develop psychological dependence or addiction when opioids are used appropriately in the short-term management of acute pain. There are many opioid agents to select from and the practitioner should become familiar and comfortable with their pharmacological kinetics and their appropriate indications. The standard opioid agent is morphine sulfate. However, due to several ill-defined reasons, meperidine has often been the opioid of choice for the management of acute pain in both the inpatient and outpatient setting.


Meperidine is an opioid analgesic that is commonly used for the relief of acute pain due to numerous etiologies, such as trauma, acute abdomen, migraine therapy and postoperative pain. Meperidine has multiple actions similar to morphine, principally analgesia and sedation.
Unfortunately, meperidine is commonly given in doses too small and too infrequent to obtain adequate analgesia. As discussed in the AHCPR Acute Pain Management Guideline, meperidine produces analgesia for approximately 2.5 to 3.5 hours, and a dose of 75 mg every 4 hours produces an equivalent analgesic effect of 5-7.5 mg of morphine. To obtain an equianalgesia of 10 mg of morphine, meperidine should be dosed at 100-150 mg every 3 hours.

However, the metabolism of meperidine can lead to serious side effects. Meperidine is metabolized to a toxic metabolite called normeperidine. Normeperidine is a CNS irritant and appears to cause tremors, muscle twitches, dilated pupils, hyperactive reflexes and convulsions. The half-life of normeperidine is 15-20 hours compared to the 3-hour half-life of meperidine. Since the kidney and liver eliminate normeperidine, patients with decreased renal or hepatic function are at an increased likelihood of suffering from the toxic effect of normeperidine.

Due to the risk of adverse central nervous system effects, meperidine should be reserved for only very brief use in the treatment of acute pain. [Conclusion Grade III: See Discussion Appendix C, Conclusion Grading Worksheet - Annotation #17 (Meperidine).]


Austin KL, Stapleton JV, Mather LE. “Rate of formation of norpethidine from pethidine.” J Anaesth 53:255-58, 1981. (Class D)


Mauro VF, Bonfiglio MF, Spunt AL. “Meperidine-induced seizure in a patient without renal dysfunction or sickle cell anemia.” Clin Pharm 5:837-39, 1986. (Class D)


Recognizing Substance Abuse

Chemically dependent patients are undertreated with opioids when they have surgery. Nurses and doctors are typically unaware of the amount of medication it takes to actually achieve analgesia in a chemically dependent patient. When providers have to administer large doses of opioid to control pain, they may be afraid of causing respiratory depression and potentially enhancing the addiction.

This problem is not novel, but it has been and continues to be a neglected problem. There are guidelines that help identify potential problems. However, the issues surrounding pain as well as chemical dependency are complex and the plan of care needs to be individualized. As pain management experts and addiction medicine experts continue to work together, more will be known in the future about how these two issues intertwine. In 1980 a report was published by Porter and Jick indicating that addiction is rare in patients treated with opioids for acute pain. Nevertheless there is an overwhelming concern about causing addiction in someone with acute pain. This overestimation of the
risk of addiction originates from an inadequate understanding of the characteristics that define this syndrome, and inappropriate extrapolation of information derived from the addict population.

Some guidelines for recognizing substance abusers are available, e.g. those prepared by the Hennepin County Medical Society. The DSM-IV defines substance dependency. (See Discussion and References Appendix A, “DMS-IV Diagnostic Criteria for Substance Dependence.”)


**Pharmacological Analgesic Adjuvants**

The use of adjuvant therapies and pharmaceuticals is frequently helpful in reducing total drug dose requirements (opioids and NSAIDs) and speeding recovery. Some of the medications have been shown to enhance the effect of a particular analgesic, such as caffeine when given with aspirin-like drugs, whereas other medications have been shown to have analgesic properties themselves (e.g., tricyclic antidepressants and hydroxyzine). This group of medicines is not intended to treat acute pain alone, but rather to be used as a complement to the primary analgesias.

The following material about analgesic adjuvants (#1-10b) has been reprinted from Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain, Fourth Edition with permission of the American Pain Society, 4700 W. Lake Avenue, Glenview, IL 60025-1485. Copyright ©1999. (Reference is Class R)

A number of other classes of drugs may either enhance the effects of opioids or aspirin-like drugs, have independent analgesic activity in certain situations, or counteract the side effects of analgesics. All classes of medications listed below (according to usual doses in a 70 kg adult) can be used in children with cancer-related pain, adjusting the dose for weight.

1. **Tricyclic antidepressants** (amitriptyline, imipramine, nortriptyline, desipramine). Tricyclic antidepressants are relatively contraindicated for patients with coronary disease, in whom they can worsen ventricular arrhythmias (Roose et al., 1998). Controlled trials show that these agents relieve pain related to diabetic neuropathy and postherpetic neuralgia, regardless of whether patients are depressed (Max et al., 1992; Watson et al., 1982). They are frequently used to treat neuropathic pain that has been caused by surgical trauma, radiation therapy, chemotherapy, or malignant nerve infiltration, but no controlled studies have been done in these conditions. Amitriptyline (e.g., Elavil, Endep) has the best documented analgesia but also is tolerated least well because of its potent anticholinergic effects (e.g., dry mouth, urinary retention, constipation, delirium). Sedation and orthostatic hypotension are also frequent and may limit the concomitant use of opioid analgesics. A baseline ECG is necessary to exclude patients with conduction abnormalities, which may be worsened by tricyclic antidepressants; this may be a particular risk in patients on anthracycline antitumor agents. Administration of the entire amitriptyline dose at bedtime promotes sleep and minimizes daytime side effects, although the patient should be cautioned about nocturnal orthostatic hypotension. Many clinicians prefer nortriptyline (Aventyl, Pamelor [Watson et al., 1998], or desipramine (Norpramin, Pertofrane) to amitriptyline because it causes less sedation and anticholinergic effects; nortriptyline can also cause somewhat less orthostatic hypotension than other tricyclics. Desipramine and nortriptyline can produce insomnia and therefore should be administered during the day. Desipramine is not recommended for children, however, because there are anecdotal reports of sudden death possibly associated with its use.

The analgesic effects of tricyclics begin at lower doses (typically 25-150 mg/day for amitriptyline) than the commonly recommended antidepressant doses. We suggest starting doses of 10-20 mg for patients who weigh more than 50 kg, and 0.3 mg/kg in patients weighing less than 40
kg. The dose is slowly increased until the desired effect is obtained, up to a maximum of 150 mg in adults and 3 mg/kg in children. For patients unable to take tablets, nortriptyline is commercially available in liquid form, and amitriptyline tablets can readily be dissolved in water or juice. Fluoxetine and paroxetine and, to a lesser degree, other serotonin specific reuptake inhibitors block the metabolism of tricyclic antidepressants and may increase their blood levels as much as seven-fold (Virani et al., 1997).

In animal studies, the tricyclics potentiate opiate analgesia, possibly by blocking the reuptake of serotonin and norepinephrine at CNS synapses, but it is not known whether these effects are clinically relevant. There are no data to support the use of tricyclics in acute pain syndromes.

2. **Antihistamines.** Hydroxyzine (Vistaril, Atarax) has analgesic, antiemetic, and mild sedative activity in addition to its antihistamine effects. The usual dose is 25-50 mg PO or IM q4-6 hours prn (0.5-1 mg/kg for children). Analgesia has been demonstrated only after IM administration, however. It is not clear that oral administration provides significant pain relief. For this reason, oral hydroxyzine is given primarily to counteract nausea or anxiety in patients with chronic cancer pain.

3. **Benzodiazepines** (e.g., diazepam [Valium], lorazepam [Ativan]). Benzodiazepines are effective for treatment of acute anxiety or muscle spasm associated with acute pain. They are also of some benefit to cancer patients in whom recurrent anxiety is apparent and antidepressants are not indicated, or for treatment of terminal dyspnea. Except for pain related to muscle spasm, these agents are not effective analgesics, and because of their sedative and respiratory depressant effects, they may limit the amount of opioid the physician can give. In anxious patients with pain, therefore, opioid titration should precede treatment with benzodiazepines.

4. **Caffeine.** Doses of at least 65 mg have been shown to increase analgesia when given with aspirin-like drugs for uterine cramping, episiotomy pain, dental pain, headaches, and other pain syndromes (Laska et al., 1984). The optimal daily dose of caffeine has not been established, but 65-200 mg/day appears to be well tolerated by most patients. Single doses of 1.0-1.5 mg/kg can be used in children with chronic cancer pain.

5. **Dextroamphetamine.** Dextroamphetamine may produce additive analgesia when combined with opioids in the postoperative period (Forrest et al., 1977). The analgesic effects of amphetamines for chronic cancer pain have not been well studied; the usual indication is to counteract opioid sedation.

6. **Steroids.** Steroids have specific and nonspecific effects in managing acute and chronic cancer pain (Ettinger & Portenoy, 1988). They may directly lyse some tumors (e.g., lymphoma) and ameliorate painful nerve or spinal cord compression by reducing edema in tumor and nervous tissue. Their use is standard emergency practice in the treatment of suspected malignant spinal cord compression (dexamethasone, 16 -96 mg/day or its equivalent). Steroid treatment (dexamethasone, 16 mg/day or its equivalent) may be useful in managing pain caused by malignant lesions of the brachial or lumbosacral plexus in patients for whom large doses of opioids are ineffective. In the moribund patient, steroids may provide euphoria and increase appetite as well as relieve tumor-related pain; chronic side effects are not to be feared in this situation. Chronic use produces weight gain, Cushing’s syndrome, proximal myopathy, and psychosis (rarely) and increases the risk of GI bleeding, especially when used in combination with NSAIDs. Rapid withdrawal of steroids may exacerbate pain.

7. **Phenothiazines** (methotrimeprazine, chlorpromazine, promethazine, prochlorperazine). Except for methotrimeprazine (Levoprome 10-20 mg, available in parenteral formulation only), phenothiazines neither relieve pain nor potentiate opioid analgesia. Methotrimeprazine lacks the
constipating and respiratory depressant effects of opioids and may be useful as an analgesic in opioid-tolerant cancer patients. Sedation and orthostatic hypotension may be pronounced, so one should start with small doses. Starting doses are 5 mg IM or 10 mg PO q6hr (0.2 mg/kg PO in children). Many experts administer methotrimeprazine by IV drip (starting dose 0.05-0.1 mg/kg IV over 20 minutes). If side effects are tolerable, doses can be increased gradually to 5-10 times these starting doses. Intravenous doses as frequent as every hour may be helpful in patients with terminal agitation. Prolonged use of phenothiazines can lead to tardive dyskinesia. Extrapyramidal manifestations can occur, particularly in children, and can be treated with diphenhydramine.

8. **Anticonvulsants** (gabapentin, phenytoin, carbamazepine, sodium valproate, clonazepam) may relieve brief lancinating pains arising from peripheral nerve syndromes such as trigeminal neuralgia, postherpetic neuralgia, glossopharyngeal neuralgia, and posttraumatic neuralgia. In the United States, approximately 5% of all anticonvulsant medications are prescribed for the management of pain. Nerve injury caused by cancer or cancer therapy sometimes gives rise to such tic-like pains. Controlled clinical trials in diabetic neuropathy (Backonja et al., 1998) and postherpetic neuralgia (Rowbotham et al., 1998) show that gabapentin at 2,400-3,600 mg/day has an efficacy similar to the tricyclic antidepressants. Gabapentin doses must be reduced considerably for patients with renal insufficiency. Carbamazepine (Tegretol), clonazepam (Klonopin), and baclofen (Lioresal) are also used. A recent meta-analysis evaluated 20 randomized trials of the following four anticonvulsants: carbamazepine, phenytoin, clonazepam, and sodium valproate (McQuay, et al., 1995). Most of the trials involved chronic nonmalignant pain; only one trial evaluated cancer pain, and one involved postoperative pain. This meta-analysis concluded that anticonvulsants were effective for trigeminal neuralgia, diabetic neuropathy, and migraine prophylaxis.

9. **Clonidine** has been approved recently by the FDA for the treatment of pain. This alpha receptor agonist is available for epidural administration in a 100 mg/ml concentration. A recent controlled trial involving selected patients with cancer pain indicated the effectiveness of a 30 mg/hr epidural infusion, particularly for neuropathic pain (Eisenach, et al., 1995). Hypotension and bradycardia are possible side effects, but these are uncommon at low doses.

The following additional references also describe the effectiveness of pharmacological adjuvants in reducing total drug dose requirements:


**Behavioral/Cognitive Intervention**


CLINICAL PEARLS

Pediatric

- **Circumcisions**: The March 1999 Task Force Report from the American Academy of Pediatrics states, “... data are not sufficient to recommend routine neonatal circumcision. If a decision for circumcision is made, procedural analgesia should be provided.” Dorsal Penile Nerve Block (DPNB), EMLA (Eutectic Mixture of Local Anesthetics), topical lidocaine, and ringblock have all been shown to be efficacious and safe but none completely eliminate the pain of circumcision.

- **Infantile colic**: Colic is characterized by excessive crying in otherwise healthy infants. Uncertainty regarding its etiology has led to multiple treatments. Oral sucrose in high concentrations has been shown to stimulate the opioid pathways in preterm and term infants, and has been demonstrated to have a significant ameliorating effect on the pain of colic. To obtain a 24-25 percent sucrose solution, dilute 1 teaspoon of table sugar (one packet of restaurant sugar) with 10 cc of water.

- **Percutaneous procedures**: Eutectic mixture of local anesthetic (EMLA): Mixture of lidocaine and prilocaine applied under occlusive dressing with onset of action of 60-90 minutes. Has been shown to be useful in venapuncture, intravenous access, circumcision and meatotomy. There have been concerns about methemoglobinemia which thus limits its use in neonates or infants. Recent studies in small populations demonstrate little toxicity.

- **Intramuscular injections** should be avoided if possible; children would rather experience pain.

- **Otalgia**: The ear pain associated with acute middle ear infections has traditionally been ignored or treated with non-opioid analgesics. When compared to olive oil, topical analgesics such as Auralgan Otic Solution (antipyrine, benzocaine, and glycerin) has been shown to provide excellent ear pain reduction. This therapy should never be prescribed if there is a perforation, pressure equalizing tube or otorhea.

- **Tonsillitis/Pharyngitis**: In a study of 231 children ages 6-12 years with tonsillitis/pharyngitis, ibuprofen was shown to be more effective in relieving the sore throat pain in the first 48 hours than acetaminophen or placebo.


**Adults**

**Acute ureteral colic:** Parenteral NSAIDS are more effective than meperidine.

**“As needed” basis:** For optimal treatment of acute pain avoid the use of intramuscular injections ordered on an “as needed” basis. Acute pain medications should initially be titrated to effect and then given on a scheduled basis.

**Head injury and stroke:** Avoid potent narcotics.

**Medication interaction:** Codeine and Tramadol may not be effective analgesics when given with other agents that strongly inhibit the Cytochrome P4502D6 liver enzymes. Common agents with this characteristic include the selective serotonin reuptake inhibitors Zoloft (> 150 mg), Paxil, and Prozac.
Loading doses should be utilized for the management of acute pain once the underlying causes are known. Based on principles of pharmacokinetics, a loading will help achieve a steady state concentration faster than a maintenance dose. Although there is no defined concentration-response relationship for opioids, as there is for other drugs such as theophylline, adequate opioid concentrations for analgesia can be achieved more quickly. Refer to the diagrams below.

No loading dose

Log Concentration

Correct loading dose

Log Concentration
Meperidine: In the treatment of acute pain, meperidine should be used only briefly and via a parenteral route due to the following reasons: 1) after oral administration, a hepatic first-pass results in only approximately 50% of meperidine reaching the systemic circulation unchanged and 2) with repeated use, potential adverse effects of CNS stimulation may occur secondarily to the accumulation of the toxic metabolite, normeperidine (See Discussion Appendix C).

Propoxyphene is no more effective than acetaminophen on acute pain. In addition, it has a higher incidence of drug-induced delirium in the elderly.

“Road rash”: NSAIDs (any route) or local anesthetic can be used.

Suturing non-end-artery sites: Use TAC (Tetracaine, Adrenaline, and Cocaine solution), TAL (Tetracaine, Adrenaline, and Lidocaine solution), and LET (Lidocaine, Epinephrine, and Tetracaine solution). See supporting references for solution concentrations.


DMS-IV Diagnostic Criteria for Substance Dependence

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:

1) Tolerance, as defined by either of the following:
   (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect
   (b) markedly diminished effect with continued use of the same amount of the substance
2) Withdrawal, as manifested by either of the following:
   (a) the characteristic withdrawal syndrome for the substance
   (b) the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms
3) The substance is often taken in larger amounts over a longer period than was intended
4) There is a persistent desire or unsuccessful efforts to cut down or control substance use
5) A great deal of time is spent in activities necessary to obtain the substance (e.g., chain-smoking), to recover from its effects
6) Important social, occupational, or recreational activities are given up or reduced because of substance use
7) The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption)

### Conclusion Grading Worksheet – Annotation #17 (Ketorolac)

**Work Group's Conclusion:** Ketorolac, either parenteral or oral, should be used for no more than 5 days; dose reduction is indicated in the elderly and in those with renal impairment.

**Conclusion Grade:** III

<table>
<thead>
<tr>
<th>Author/Year</th>
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</thead>
</table>
| Pearce et al. (1993) | Case Reports | D     | N/A     | -3 cases that occurred within 1 week at 2 hospitals in the community                                                                 | -Case 1 – 58 year old patient given ketorolac (60 mg intramuscularly followed by 30 mg every 6 hours for 6 days, total dose of 750 mg) for pain following cholecystectomy; developed fever and confusion on day 6; died on day 9  
-Case 2 – 46 year old patient given ketorolac (total dose of 1350 mg) for pain associated with chest tube; potassium levels were elevated at 11 days; at 16 days ketorolac was discontinued and potassium levels normalized  
-Case 3 – 53 year old patient given ketorolac (total dose 1140 mg) for pain associated with simple mastectomy; renal insufficiency with hyperkalemia at 10 days; electrolytes returned to baseline within 24 hours after discontinuing ketorolac; creatinine and serum urea nitrogen levels improved to normal range within 9 days | -Clinical conditions pre-existed in each patient that rendered them susceptible to the renal complications of NSAID use. Caution should be observed while using NSAIDs (including ketorolac) in patients whose renal function may be preserved through prostaglandin-mediated vasodilatory effects. The potent effect of ketorolac on prostaglandin synthesis must be emphasized. |
| Corelli & Gericke (1993) | Case Reports | D     | N/A     | -6 reports of possible ketorolac-induced renal insufficiency (defined as >30% increase in serum creatinine over baseline)  
-Included patients with renal insufficiency temporarily related to ketorolac administration, resolution of insufficiency after discontinuation of ketorolac, no other cause of insufficiency identified                                                                 | -4 men, 2 women with mean age of 58 years  
-3 patients had major surgical procedure within 5 days of start of ketorolac therapy  
-Mean duration of therapy was 3 days (excluding one patient whose creatinine values were not monitored for 9 days)  
-Mean total dosage was 153 mg  
-One case of acute oliguric renal failure within 2 hours after single dose  
-Renal function returned to normal after an average of 2.3 days following the maximum measured creatinine value  
-All patients experienced a decrease in urine output; serum potassium values stayed within normal limits | -Although ketorolac may be advantageous for the short-term management of pain in patients intolerant of narcotic analgesics, it shares the adverse-effect profile of other NSAIDs including gastrointestinal ulceration, inhibition of platelet aggregation, alterations in hepatic function, and nephrotoxicity.  
-Short-term administration of ketorolac can be associated with reversible oliguric renal insufficiency; risk factors identified in this study include increased age, recent major surgery, underlying cardiovascular disease. |
## Conclusion Grading Worksheet – Annotation #17 (Ketorolac) (cont)

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<tbody>
<tr>
<td>Murray &amp; Watson (1993)</td>
<td>Case Report</td>
<td>D</td>
<td>N/A</td>
<td>-1 patient</td>
<td>46 year old patient given ketorolac (60 mg intramuscular loading dose followed by 30 mg every 5 hours, total dose of 180 mg) for pain following uncomplicated shoulder surgery; ketorolac was discontinued on day 2 because of nausea; patient experienced complete transient renal failure (within 2 days) and subsequent serious gastrointestinal bleeding requiring transfusion (13 days post-operatively and 2 days after discharge); patient had also received vancomycin (1 gm intravenously every 12 hours – 2 doses total)</td>
<td>-Vancomycin in association with ketorolac may have an additive toxic effect. Ketorolac can cause acute oliguric renal failure in young, previously healthy patients when used in association with nephrotoxic agents. NOTE: patient was given Feldene pre-operatively which may have initiated gastric alteration</td>
</tr>
<tr>
<td>Steinberg &amp; Tessier (1993)</td>
<td>Case Reports</td>
<td>D</td>
<td>N/A</td>
<td>-3 patients from 1 institution</td>
<td>Case 1 – 76 year old given ketorolac (60 mg intramuscular loading dose then 30 mg every 6 hours for 5 days) for pain associated with rib fractures and pneumothorax; ketorolac was stopped due to hemepositive stools and decreasing hematocrit; duodenal ulcer identified with endoscopy Case 2 – 83 year old patient given ketorolac (same dose as above for 3 days) for pain associated with hemicolecotomy; gastrointestinal bleeding (source not defined) developed several days later Case 3 – 63 year old patient with renal failure and occlusive vascular disease that resulted in above-knee amputation; given ketorolac (30 mg every 6 hours intramuscularly for 10 days) for stump pain; stopped ketorolac after gastrointestinal bleeding required transfusion of 3 units of packed cells; numerous gastric erosions observed with endoscopy</td>
<td>-Common factor was the use of relatively large doses of ketorolac (in view of patient weights of 60 kg, 55 kg, and 65 kg, respectively). -Gastrointestinal bleeding can occur with parenteral administration of NSAIDs.</td>
</tr>
</tbody>
</table>
### Conclusion Grading Worksheet – Annotation #17 (Ketorolac) (cont)

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</thead>
<tbody>
<tr>
<td>Strom et al. (1996)</td>
<td>Cohort</td>
<td>B</td>
<td>ø</td>
<td>- Patients who received intra-muscular or intravenous ketorolac at one of 35 hospitals; unexposed group received parenteral opiates; patients were matched by hospital, admitting service (medical vs surgical), and date of initiation of therapy - Course of treatment was from first dose through 3rd day after final dose (patients may have had &gt;1 course – only one course of opiates was studied) - Data abstracted from medical records: demographics, previous illnesses, doses and duration of treatment, aspects of the hospital course, adverse events (classified as clinically serious if caused death, residual disability, prolonged hospitalization, or was life threatening)</td>
<td>-9,900 patients received 10,272 courses of ketorolac - 10,247 patients received 10,247 courses of opiates - Gastrointestinal (GI) bleeding occurred in 4% of all ketorolac courses and 3.6% of all opiate courses (for clinically important GI bleeding the values were 2.1% and 1.9%, respectively; for clinically serious GI bleeding the values were 1.3% and 1.0%, respectively); the adjusted ORs were 1.3 (1.11-1.52) for all GI bleeding, 1.17 (0.95-1.44) for clinically important GI bleeding, and 1.44 (1.09-1.98) for clinically serious GI bleeding; fatal GI bleeding was rare with no difference between groups - Operative site bleeding occurred in 29.6% of ketorolac courses and 38.6% of opiate courses (OR=1.02; 0.95-1.10); clinically serious operative site bleeding occurred in 1.5% of ketorolac group and 1.8% of opiate group - Risk of GI or operative site bleeding increased with age in both groups (significant for ketorolac group p&lt;0.02) - More GI bleeding in patients receiving higher doses of ketorolac; effect of dose was greater for clinically important or clinically serious GI bleeding - More operative site bleeding in patients receiving higher doses of ketorolac - Increased risk of GI bleeding as therapy was prolonged beyond 5 days; relationship not observed for operative site bleeding.</td>
<td>- Compared to use of opiates, use of ketorolac was associated with a small increased risk of GI bleeding. The risk was notably increased in the elderly, with use &gt;5 days, and with higher dose. Use of ketorolac was also associated with a small increased risk of overall operative site bleeding but only in elderly patients or with higher-dose therapy</td>
</tr>
</tbody>
</table>

**NOTES:** patients who received ketorolac may also have received opiates; patients who received opiates did not receive ketorolac; there were differences between groups in gender, age, and past medical history; ketorolac was more likely to be used in orthopedic surgery patients; opiates were more likely used in other types of surgery; ketorolac was more likely initiated in operating room, recovery room, or emergency department; opiates more likely initiated in ICU, procedure unit, or general medicine, surgical, or pediatric floor; ketorolac was more likely used intraoperatively or for chronic pain; opiates were more likely used preoperatively, for addiction relief, for relief of anxiety with dyspnea, and for obstetrical analgesia.
### Conclusion Grading Worksheet – Annotation #17 (Ketorolac) (cont)

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<tr>
<td>Feldman et al. (1997)</td>
<td>Cohort</td>
<td>B</td>
<td>ø</td>
<td>-Patients – same as above except excluded long-term dialysis patients</td>
<td>-9,850 patients received 10,219 courses of ketorolac -10,145 patients received 10,145 courses of opiates -Greater history of chronic renal failures (p=0.001), papillary necrosis (p=0.002), and nephrotic syndrome (p=0.02) in opiate group -Acute renal failure occurred during 109 courses of ketorolac (1.07%) and 113 courses of opiates alone (1.11%) -Acute renal failure occurred more often in the presence of hypertension, chronic renal disease, cirrhosis, admission to ICU, cancer, concomitant use of aminoglycoside antibiotics, and medical admission (all p&lt;0.01) -Risk for acute renal failure increased with age (p&lt;0.01) -Ketorolac was not associated with acute renal failure except when analysis was focused on duration of therapy of greater than 5 days (p=0.03 compared to opiates)</td>
<td>-Overall incidence of acute renal failure after a course of analgesics was low, even in ill, hospitalized patients. -Overall incidence of renal failure among patients receiving parenteral ketorolac was similar to that among patients receiving opiates. With therapy lasting longer than 5 days, ketorolac may be associated with a higher incidence of acute renal failure than opiates. -No clinically distinct subgroup was identified to be a particular risk for ketorolac nephrotoxicity.</td>
</tr>
</tbody>
</table>
**Conclusion Grading Worksheet – Annotation #17 (Meperidine)**

**Work Group's Conclusion:** Due to the risk of adverse central nervous system effects, meperidine should be reserved for only very brief use in the treatment of acute pain.

**Conclusion Grade:** III

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</table>
| Szeto et al. (1977) | Case Reports | D     | N/A     | - 7 patients with end-stage renal disease (post-transplant)  
- 7 cancer patients (no evidence of renal dysfunction)  
- All patients received either 50 or 75 mg of meperidine intramuscularly as needed for pain  
- Case reports from two additional patients who experienced CNS excitation | - 2 cases of CNS excitation  
  a. 42 yr old male with osteogenic sarcoma of sacrum; gradually became agitated and confused; 2 episodes of seizures; total of 63 doses of meperidine; meperidine level was 0.14 µg/ml and normeperidine level was 0.67 µg/ml (ratio=4.8) after 2nd seizure  
  b. 25 yr old female with chronic renal failure in a transplanted kidney; became irritable after 2 wks of meperidine therapy and developed twitches; meperidine level was 0.28 µg/ml and normeperidine level was 1.8 µg/ml (ratio=6.4)  
  - For the 7 cancer patients, the normeperidine/meperidine ratio (measured at 1 hour after last dose of meperidine) ranged from 0.25-0.90  
  - For the 7 renal failure patients the ratio ranged from 1.00-3.00  
  - Meperidine levels were lower (p=0.01) and normeperidine levels were higher (p=0.03) in the renal failure patients (cancer patients received more doses of meperidine) | - The excitatory signs that developed in 2 patients during chronic administration of meperidine disappeared when meperidine administration was discontinued.  
- High levels of normeperidine may contribute to the excitatory effects seen after meperidine administration. This is especially important in renal failure patients who accumulate normeperidine rapidly. |
## Conclusion Grading Worksheet – Annotation #17 (Meperidine) (cont)

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<tbody>
<tr>
<td>Miller &amp; Jick (1978)</td>
<td>Case Series</td>
<td>D</td>
<td>ø</td>
<td>26,294 hospitalized medical patients (Boston Collaborative Drug Surveillance Program); 22 sites (U.S. &amp; abroad)</td>
<td>-366 patients (1.4%) received meperidine orally and 3263 (12.4%) received meperidine parenterally; 43% of the oral recipients had neoplastic disease; 23% of parenteral recipients had neoplastic disease and 23% had cardiovascular disease.</td>
<td>-Adverse reactions to meperidine occur in about 4% of oral recipients and 3% of parenteral recipients in hospital and occur more often at higher doses; nearly all of the reactions to oral meperidine were minor whereas parenteral administration causes serious adverse effects in a small number of patients.</td>
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<td>Adverse Reactions:</td>
<td>No relationship between blood concentrations of norpethidine and either analgesic activity or toxic effects has been established. Further studies are needed.</td>
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<td>Oral Gastrointestinal 2.7% Parenteral Gastrointestinal 1.0% CNS* 1.6% Parenteral CNS* 1.2% Cardiovascular 0% Parenteral Cardiovascular 0.003% Other 0% Parenteral Other 0.006%</td>
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<td>Frequency of all adverse reactions increased as dose increased and as duration of hospitalization increased; may also be related to receipt of other analgesics.</td>
<td>-Reported CNS effects included disorientation, bizarre feelings, hallucinations, or psychosis; drowsiness or malaise; vertigo; respiratory depression; coma, headache, convulsions or tremor; hyperactivity or agitation; and depression.</td>
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<td>-IM group: norpethidine (normeperidine) concentrations increased steadily after first injection; at 32 hrs after first injection mean level was 0.37 µg/ml (still increasing); maximum level (in any patient) was 1.13 µg/ml; rate of increase was 0.013 µg/ml/hr -IV group: pattern was similar to IM group; rate was same as IM group.</td>
<td>-No adverse effects (other than occasional nausea and vomiting) were reported.</td>
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*Reported CNS effects included disorientation, bizarre feelings, hallucinations, or psychosis; drowsiness or malaise; vertigo; respiratory depression; coma, headache, convulsions or tremor; hyperactivity or agitation; and depression.
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| Kaiko et al. (1983) | Case Series and Non-Random | C - | Two studies:  
a. 65 adults and 2 children receiving meperidine for either acute post-op pain (n=48) or chronic pain (n=19) associated with advanced cancer; patients with objective neurological signs had complete medical and neurological evaluation; patients were grouped in to 4 categories based on intensity of signs and symptoms of CNS excitation: I= asymptomatic (n=19), II= shaky feelings (n=20), III= tremors (n=9) or twitches (n=9), and IV= multifocal myoclonus (n=8) or grand mal seizures (n=2)  
b. 47 patients receiving meperidine as post-op analgesic and 29 patients receiving other narcotic analgesics; the 47 patients were part of a cross-over study of heroin vs. morphine (given on alternate days); meperidine or other drugs given before and after study drugs for routine management of pain; mood was assessed before administration of study drugs (day 1 and day 2) using contrast phrase-pairs | -For the first study, patients with symptoms of CNS excitation received meperidine for a longer period (p<0.001) and at a higher rate (p<0.001) than asymptomatic patients (no differences among symptomatic patients – groups II, III, & IV); symptomatic patients had higher normeperidine plasma level and higher ratio of normeperidine to meperidine in plasma (both p<0.001); no differences in meperidine plasma levels; in symptomatic patients the normeperidine plasma levels (p<0.01) and the ratio of normeperidine to meperidine in plasma (p<0.05) were higher as a function of intensity of CNS excitation  
-All the asymptomatic patients had post-operative pain while 19 of the 48 symptomatic patients had chronic pain related to advanced stages of disease; none of the asymptomatic patients had renal involvement with their disease while 11 of the symptomatic patients had genitourinary cancers and 14 had elevated BUN levels  
-For study of mood the mean change from day 1 to day 2 of the study was determined; for the 47 patients receiving meperidine there were changes toward feelings of being angry (p<0.01), “blue” (p<0.001), sad (p<0.02), pessimistic (p<0.02), apprehensive (p<0.05), restless (p<0.05), and shaky (p<0.05); 12 of 15 phrase-pairs were more negative on day 2; in the group taking other narcotics there were no significant changes in mood scores and 13 phrase-pairs were more positive on day 2 | -The routine use of meperidine for post-op pain does not appear to correlate with objective signs of CNS excitation but is associated with mild negative alterations in various elements of mood while chronic use results in the accumulation of normeperidine and may be associated with the appearance of adverse objective effects. The intensity of CNS excitation is highly associated with the accumulation of normeperidine.  
NOTES: many of the patients were also receiving sedative or anxiolytic medications, or both (evenly distributed among all categories of symptoms)  
Work Group’s Comments:  
-Days of meperidine administration ranged from 1 to 30 and rate of administration (mg/day) ranged from 46 to 1,100. |
| Armstrong & Bersten (1986) | Case Reports | D N/A | -2 cases of apparent normeperidine toxicity | -Case 1: 40 yr old female with disseminated carcinoma of colon (admitted with subacute intestinal obstruction - bypass surgery performed); had received long-term epidural opioids for upper abdominal pain; following surgery meperidine was added; grand mal convulsion at 24 hr post-operatively (after receiving 2800 mg meperidine); meperidine concentration was 2.9 µg/ml, normeperidine was 4.3 µg/ml  
-Case 2: 38 yr old female after 3 surgeries related to morbid obesity; given 1000 mg/day of IM meperidine for 2 wks; became agitated with worsening pain and myoclonic jerks; 1 hr after last dose meperidine concentration was 0.692 µg/ml, normeperidine was 1.562 µg/ml | -CNS excitability associated with normeperidine toxicity, though not frequently recognized, deserves consideration in patients receiving large doses of meperidine. Toxicity may be prevented by avoiding prolonged administration of meperidine, especially to patients with impaired renal function. |
## Conclusion Grading Worksheet – Annotation #17 (Meperidine) (cont)

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| Mauro et al. (1986)       | Case Report | D     | N/A     | -1 case of apparent normeperidine toxicity | -26 yr old female with complaints of abdominal pain, nausea, and vomiting (surgery 4 months earlier for peptic ulcer disease); also complained of migraine headaches; required increasing amounts of meperidine for relief; on day 10 of hospitalization experienced transient bilateral twitching of upper extremities followed by involuntary tremors of all extremities and a 1 minute tonic-clonic seizure; concentrations of meperidine and normeperidine (2 hrs before seizure) were 590 ng/mL and 930 ng/mL, respectively | -Patients with normal renal function who receive frequent doses of meperidine appear to be susceptible to drug-induced neuroexcitement; seizures probably result from accumulation of normeperidine, but an elevated normeperidine-to-meperidine concentration ratio may be a contributing factor.

NOTE: patient had received prochlorperazine 30 minutes before the seizure (but had received larger doses previously with no adverse effects). |

| Hagmeyer et al. (1993)    | Case Reports| D     | N/A     | -3 cases of meperidine-related seizures when the drug was received via a patient-controlled analgesia pump (PCAP) | -Case 1: 35 yr old female with painful sickle cell crisis; received 175 mg iv meperidine in emergency department; on admission given 150 mg/hr of meperidine via PCAP with patient-administered boluses of 25 mg q15 min pm; on day 7 (after approximately 135 hrs of meperidine – accumulated dosage of at least 21g) patient experienced 2 generalized, tonic-clonic seizures; within 6 hrs of seizure meperidine concentration was 300 ng/mL, normeperidine was 7450 ng/mL, normeperidine-to-meperidine concentration ratio was 24:1

-Case 2: 33 yr old female with worsening pelvic pain (ovarian cyst discovered); on post-op day 1 given meperidine 10 mg q15 min administered by PCAP; titrated up to 30 mg q15min over next 24 hrs; experienced seizure on day 2; became diaphoretic, tachycardic, and combative; cumulative dose was 2.7 g; 8 hrs after seizure meperidine concentration was 1300 ng/mL, normeperidine was 1000 ng/mL, and ratio was 0.77:1

-Case 3: 22 yr old male with painful sickle cell crisis; given meperidine 100mg/hr with PCAP (boluses of 25 mg q15 min); on day 3 dosage was lowered to 75 mg/hr with 25 mg boluses allowed every 30 min; on day 5 there were 2 episodes of myoclonic jerks; meperidine concentration was 620 ng/mL, normeperidine was 1130 ng/mL, ratio was 1.8:1 | -Meperidine administered by PCAP systems increases the risk of normeperidine-induced seizures, meperidine doses delivered by this route of administration as well as traditional routes should be monitored closely and titrated down as quickly as possible. |
### Conclusion Grading Worksheet – Annotation #17 (Meperidine) (cont)

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<tr>
<td>Adair &amp; Gilmore (1994)</td>
<td>Case Report</td>
<td>D</td>
<td>N/A</td>
<td>-1 case of recurrent convulsions, myoclonus, and asterixis in a renal-pancreas transplant patient</td>
<td>-40 yr old male who had a combined pancreas and renal transplant; 6 months later developed severe abdominal discomfort and refractory emesis; diagnosed with acute pancreatitis; treated with parenteral nutrition and meperidine (dose not reported); on day 10 of hospitalization nurses observed involuntary movements including tremor, myoclonus; also experienced 3 separate generalized convulsions; meperidine concentration was 0.18 ( \mu g/mL ), normeperidine was 0.70 ( \mu g/mL ).</td>
<td>-Seizures following renal transplantation frequently develop from circumstances unique to these patients. Neurotoxicity from medications must be considered since drug interaction, deranged drug metabolism, or impaired drug elimination might be reasonably expected to regularly co-occur in transplant recipients.</td>
</tr>
</tbody>
</table>
This document provides resources, strategies and measurement specifications for use in closing the gap between current clinical practice and the recommendations set forth in the guideline.
Support for Implementation – Priority Aims and Suggested Measures

OVERVIEW

The following aims were identified by the guideline work group as key areas for which medical groups may receive benefits in implementing this guideline.

The measures associated with these aims are presented as possible measures. Measures of aim help medical groups determine progress in achieving a particular aim. However, additional approaches may be customized by individual medical groups to ferret out improvement information important to the medical group’s individual practice.

PRIORITY AIMS FOR MEDICAL GROUPS WHEN USING THIS GUIDELINE

1. Improve pain management through assessment of all patients throughout hospitalization including on admission, ongoing assessment and at discharge or during an outpatient visit.
   Possible measures of accomplishing this aim:
   a. Percentage of patients with initial assessment for pain using a formal assessment tool.
   b. Percentage of patients with documentation of pain rating on the vital sign sheet (5th vital sign).
   c. Percentage of patients with discharge plan identifying patient’s continuing needs for pain management and orders to meet these needs.

2. Improve the appropriate selection and dosing of pain management treatment.
   Possible measures of accomplishing this aim:
   a. Percentage of patients taking NSAID with continued pain (> 4/10 on pain scale or exceeding patient’s pain goal), who are prescribed an opioid.
   b. Percentage of all patients who receive meperidine.
   c. After 48 hours, the percentage of patients reporting pain at either a level > 4 or at unacceptable level to patient.
   d. Percentage of patients reporting good or very good satisfaction with the approach to pain control.
   e. Percentage of patients with a diagnosis consistent with neuropathic pain (see Appendix A for clinical examples) who given a trial of either anticonvulsants or tricyclic antidepressants.
3. Increase the involvement of patients in pain management.

   Possible measure of accomplishing this aim:
   
a. Percentage of patients with acute pain with documentation of patient-reported pain, intensity, and degree of relief after intervention.

b. Percentage of patients reporting an understanding of the need to communicate unrelieved pain.

c. Percentage of inpatients prescribed an opioid who are assessed within one hour for parenteral administration or within two hours for oral therapy for symptoms secondary to analgesia (e.g., decreased mental status, confusion, delirium, nausea, vomiting).

d. Percentage of patients with documentation of an intervention to reduce pain, of those patients who have a pain level > 4/10 or at unacceptable level to patient.

e. Percentage of inpatients with documentation of patient’s goal for pain control on admission.

f. Percentage of patients with documentation of receiving education on the pain assessment scale and on goals of pain management.
Possible Success Measurement #2c

After 48 hours, the percentage of patients who rate pain greater than 4 (on a 10-point scale) or at an unacceptable level to patient.

Population Definition

All adult patients.

Data of Interest

\[
\frac{\text{# of patients with documented pain scores greater than 4 within 48 hours of procedure, or admission}}{\text{Total # of patients reviewed}}
\]

Numerator/Denominator Definitions

Numerator: Documentation must include within 48 hours of procedure or admission:

- numerical score documented as greater than 4 (on a 10-point scale)

OR

- narrative descriptions of "pain unrelieved", "pain uncontrolled"

Denominator: Adult patients reviewed.

Method/Source of Data Collection

Patients within the preceding month can be randomly sampled to produce a list of at least 20 records for review. Selected records are audited to see if an assessment of pain was completed and documented within 48 hours of the procedure or admission and if the last score was rated greater than four on a ten point scale.

Time Frame Pertaining to Data Collection

Data can be collected monthly.
SYSTEMS APPROACHES TO IMPLEMENTATION FOR THIS GUIDELINE

1. All patients presenting with a complaint of acute pain are assessed for origin of pain through physical examination and detailed history.

2. An individualized care plan is developed for each patient to ensure adequate pain control while monitoring for signs of psychological and/or physical dependence.