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Practice Guidelines for the Prevention, Detection, and Management of Respiratory Depression Associated with Neuraxial Opioid Administration

AQ:2 *An Updated Report by the American Society of Anesthesiologists Task Force on Neuraxial Opioids**

AQ:3 *PRACTICE guidelines* are systematically developed recommendations that assist the practitioner and patient in making decisions about health care. These recommendations may be adopted, modified, or rejected according to clinical needs and constraints, and are not intended to replace local institutional policies. In addition, practice guidelines developed by the American Society of Anesthesiologists (ASA) are not intended as standards or absolute requirements, and their use cannot guarantee any specific outcome. Practice guidelines are subject to revision as warranted by the evolution of medical knowledge, technology, and practice. They provide basic recommendations that are supported by a synthesis and analysis of the current literature, expert and practitioner opinion, open forum commentary, and clinical feasibility data.

This document updates the "Practice Guidelines for the Prevention, Detection and Management of Respiratory Depression Associated with Neuraxial Opioid Administration" adopted by ASA in 2007, and includes new survey data and recommendations pertaining to monitoring for respiratory depression.

 Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org).

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Address reprint requests to the American Society of Anesthesiologists: 520 North Northwest Highway, Park Ridge, Illinois 60068-2573. This Practice Guideline, as well as all American Society of Anesthesiologists Practice Parameters, may be obtained at no cost through the Journal Web site, www.anesthesiology.org.

Methodology

A. Definitions of Neuraxial Opioid Analgesia and Respiratory Depression

Neuraxial opioid analgesia refers to the epidural or spinal administration of opioids, including single-injection, continuous- or intermittent-infusion, and patient-controlled analgesia. For these Guidelines, respiratory depression may be indicated by (1) reduced respiratory rate (e.g., to < 10–12 breaths per minute), (2) reduced oxygen saturation (e.g., arterial oxygen saturation < 90–92%), or (3) hypercapnia/hypercarbia (e.g., arterial carbon dioxide tension > 50 mmHg). Other measures of respiratory function (e.g., tidal volume) or clinical signs (e.g., drowsiness, sedation, periodic apnea, cyanosis) may also provide indications of respiratory depression.

B. Purposes of the Guidelines

The purposes of these Guidelines are to improve patient safety and enhance the quality of anesthetic care by reducing the incidence and severity of neuraxial opioid-related respiratory depression or hypoxemia. In addition, these Guidelines are intended to reduce the incidence and severity of adverse outcomes related to reduced respiratory rate or oxygen levels (e.g., cardiac arrest, brain damage, death).

C. Focus

These Guidelines focus on the treatment of all patients receiving epidural or spinal opioids in inpatient (e.g., operating rooms, intensive care units, labor and delivery suites, postoperative surgical floors, hospital wards) or ambulatory (e.g., stand-alone outpatient facilities) settings. The Guidelines do not apply to patients with chronic or cancer pain (except those with acute postoperative pain), patients with preexisting implantable drug delivery systems, or patients with contraindications to spinal or epidural opioids (e.g., coagulopathy, sepsis).

D. Application

These Guidelines are intended for use by anesthesiologists. They also may serve as a resource for other

physicians administering neuraxial opioids and other healthcare providers involved in the treatment of patients receiving neuraxial opioids.

E. Task Force Members and Consultants

The ASA appointed a Task Force of 11 members, including anesthesiologists in both private and academic practice from various geographic areas of the United States and two consulting methodologists from the ASA Committee on Standards and Practice Parameters.

The Task Force developed the Guidelines by means of a seven-step process. First, they reached consensus on the criteria for evidence. Second, original published research studies from peer-reviewed journals relevant to neuraxial opioid administration were reviewed and evaluated. Third, expert consultants were asked to (1) participate in opinion surveys on the effectiveness of various neuraxial opioid management strategies and (2) review and comment on a draft of the Guidelines developed by the Task Force. Fourth, opinions about the Guideline recommendations were solicited from a random sample of active members of the ASA. Fifth, the Task Force held open forums at two major national meetings† to solicit input on its draft recommendations. Sixth, the consultants were surveyed to assess their opinions on the feasibility of implementing the Guidelines. Seventh, all available information was used to build consensus within the Task Force to finalize the Guidelines (appendix 1).

F. Availability and Strength of Evidence

Preparation of these Guidelines followed a rigorous methodologic process (appendix 2). Evidence was obtained from two principal sources: scientific evidence and opinion-based evidence.

Scientific Evidence. Study findings from published scientific literature were aggregated and are reported in summary form by evidence category, as described herein. All literature (e.g., randomized controlled trials, observational studies, case reports) relevant to each topic was considered when evaluating the findings. However, for reporting purposes in this document, only the highest level of evidence (i.e., level 1, 2, or 3 identified herein) within each category (i.e., A, B, or C) is included in the summary.

Category A: Supportive Literature. Randomized controlled trials report statistically significant ($P < 0.01$)

differences among clinical interventions for a specified clinical outcome.

Level 1: The literature contains multiple randomized controlled trials, and the aggregated findings are supported by meta-analysis.‡

Level 2: The literature contains multiple randomized controlled trials, but there is an insufficient number of studies to conduct a viable meta-analysis for the purpose of these Guidelines.

Level 3: The literature contains a single randomized controlled trial.

Category B: Suggestive Literature. Information from observational studies permits inference of beneficial or harmful relations among clinical interventions and clinical outcomes.

Level 1: The literature contains observational comparisons (e.g., cohort, case-control research designs) of two or more clinical interventions or conditions and indicates statistically significant differences between clinical interventions for a specified clinical outcome.

Level 2: The literature contains noncomparative observational studies with associative (e.g., relative risk, correlation) or descriptive statistics.

Level 3: The literature contains case reports.

Category C: Equivocal Literature. The literature cannot determine whether there are beneficial or harmful relations among clinical interventions and clinical outcomes.

Level 1: Meta-analysis did not find significant differences among groups or conditions.

Level 2: There is an insufficient number of studies to conduct meta-analysis and (1) randomized controlled trials have not found significant differences among groups or conditions or (2) randomized controlled trials report inconsistent findings.

Level 3: Observational studies report inconsistent findings or do not permit inference of beneficial or harmful relations.

Category D: Insufficient Evidence from Literature. The lack of scientific evidence in the literature is described by the following terms.

Silent: No identified studies address the specified relations among interventions and outcomes.

Inadequate: The available literature cannot be used to assess relations among clinical interventions and clinical outcomes. The literature either does not meet the criteria for content as defined in the "Focus" section of the Guidelines or does not permit a clear interpretation of findings because of methodologic concerns (e.g., confounding in study design or implementation).

Opinion-based Evidence. All opinion-based evidence relevant to each topic (e.g., survey data, open forum testimony, Internet-based comments, letters, editorials) is considered in the development of these Guidelines. However, only the findings obtained from formal surveys are reported.

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† International Anesthesia Research Society, 81st Clinical and Scientific Congress, Orlando, Florida, March 25, 2007; and the American Society of Regional Anesthesia and Pain Medicine 32nd Annual Meeting, Vancouver, British Columbia, Canada, April 19, 2007.

‡ All meta-analyses are conducted by the ASA methodology group. Meta-analyses from other sources are reviewed but not included as evidence in this document.

Opinion surveys were developed by the Task Force to address each clinical intervention identified in the document. Identical surveys were distributed to two groups of respondents: expert consultants and ASA members.

Category A: Expert Opinion. Survey responses from Task Force-appointed expert consultants are reported in summary form in the text. A complete listing of consultant survey responses is reported in a table in appendix 2.

Category B: Membership Opinion. Survey responses from a random sample of members of the ASA are reported in summary form in the text. A complete listing of ASA member survey responses is reported in a table in appendix 2.

Survey responses are recorded using a 5-point scale and are summarized based on median values. §

Strongly agree: median score of 5 (at least 50% of the responses are 5)

Agree: median score of 4 (at least 50% of the responses are 4 or 4 and 5)

Equivocal: median score of 3 (at least 50% of the responses are 3, or no other response category or combination of similar categories contain at least 50% of the responses)

Disagree: median score of 2 (at least 50% of responses are 2 or 1 and 2)

Strongly disagree: median score of 1 (at least 50% of responses are 1)

Category C: Informal Opinion. Open-forum testimony, Internet-based comments, letters, and editorials are all informally evaluated and discussed during the development of Guideline recommendations. When warranted, the Task Force may add educational information or cautionary notes based on this information.

Guidelines

I. Identification of Patients at Increased Risk of Respiratory Depression

History and Physical Examination. Although comparative studies are insufficient to evaluate the impact of conducting a focused history (e.g., reviewing medical records) or a physical examination, the literature suggests that certain patient or clinical characteristics (e.g., obesity, obstructive sleep apnea, coexisting disease) may be associated with respiratory depression when neuraxial opioids are used. [Category B2 evidence].

The consultants and ASA members agree that a directed history and physical exam will identify patients at increased risk of respiratory depression.

Recommendations: The anesthesiologist should conduct a focused history and physical examination before administering neuraxial opioids. Particular attention

should be directed toward signs, symptoms, or a history of sleep apnea, coexisting diseases or conditions (e.g., diabetes, obesity), current medications (including preoperative opioids), and adverse effects after opioid administration. A physical examination should include, but is not limited to, baseline vital signs, airway, heart, lung, and cognitive function.

II. Prevention of Respiratory Depression after Neuraxial Opioid Administration

Noninvasive Positive-pressure Ventilation. The literature is insufficient to assess the efficacy of noninvasive positive-pressure ventilation to prevent respiratory depression in patients who have been given neuraxial opioids. [Category D evidence].

The consultants are uncertain and the ASA members disagree that noninvasive positive-pressure ventilation is effective in preventing respiratory depression in patients who have received neuraxial opioids.

Recommendations: Patients with a history of sleep apnea treated with noninvasive positive airway pressure should be encouraged to bring their own equipment to the hospital.

Drug Selection.

Single-injection Neuraxial Opioids Compared with Parenteral Opioids. Observational studies report a range in the occurrence of respiratory depression from 0.01% to 3.0% of patients who are given single-injection neuraxial opioids. [Category B2 evidence]. When single-injection neuraxial opioids are compared with parenteral (i.e., intravenous, intramuscular, or intravenous patient-controlled) opioids, meta-analysis indicates no difference in the frequency of respiratory depression [Category C1 evidence] and less somnolence or sedation. [Category A1 evidence]. No literature was found comparing single-injection neuraxial opioids with other systemic routes of administration (e.g., oral, transdermal, rectal, nasal). [Category D evidence].

The consultants and ASA members disagree that single-injection neuraxial opioids increase the occurrence of respiratory depression compared with parenteral opioids.

Extended-release Epidural Morphine. A single randomized controlled trial reports no significant difference in the frequency of respiratory depression when extended-release epidural morphine is compared with intravenous opioids. [Category C2 evidence]. In addition, the literature reports no significant difference in the frequency of respiratory depression when extended-release epidural morphine is compared with conventional (i.e., immediate-release) epidural morphine. [Category C2 evidence].

The consultants and ASA members are equivocal regarding whether extended-release epidural morphine increases the occurrence of respiratory depression compared with either parenteral opioids or conventional (immediate-release) epidural morphine.

§ When an equal number of categorically distinct responses are obtained, the median value is determined by calculating the arithmetic mean of the two middle values. Ties are calculated by a predetermined formula.

Continuous Epidural Opioids Compared with Parenteral Opioids. Meta-analysis of the literature indicates less respiratory depression when continuous epidural opioids are compared with parenteral opioids. [Category A1 evidence] The literature is equivocal regarding differences in the frequency of somnolence or sedation. [Category C1 evidence].

Both the consultants and the ASA members disagree that continuous epidural opioids *increase* the occurrence of respiratory depression compared with parenteral opioids.

Neuraxial Morphine-Hydromorphone Compared with Neuraxial Fentanyl-Sufentanil. The literature reports no differences in the frequency of respiratory depression, ventilatory response to carbon dioxide, somnolence, or sedation when single-injection morphine is compared with single-injection fentanyl or sufentanil, administered by either an epidural or an intrathecal route. [Category C2 evidence]. Observational studies report that the frequency of respiratory depression ranges from 0.01% to 7% when single-injection intrathecal morphine is administered and from 0.08% to 3% when single-injection epidural morphine is administered. [Category B2 evidence]. No literature was found that reports rates of respiratory depression for single-injection epidural or intrathecal fentanyl or sufentanil. [Category D evidence].

When continuous epidural administration of morphine is compared with fentanyl, the literature reports no difference in respiratory depression [Category C2 evidence] or hypoxemia. [Category C2 evidence]. The consultants and ASA members agree that the occurrence of respiratory depression is increased after single-injection *epidural* morphine or hydromorphone compared with single-injection epidural fentanyl or sufentanil. The consultants and ASA members agree that the occurrence of respiratory depression is increased after single-injection *intrathecal* morphine or hydromorphone compared with single-injection intrathecal fentanyl or sufentanil. The ASA members agree that the occurrence of respiratory depression after *continuous epidural* morphine or hydromorphone is increased when compared with continuous epidural fentanyl or sufentanil; the consultants are equivocal regarding this issue.

Recommendations for Drug Selection: Single-injection neuraxial opioids may be safely used in place of parenteral opioids without altering the risk of respiratory depression or hypoxemia. Single-injection neuraxial fentanyl or sufentanil may be safe alternatives to single-injection neuraxial morphine. When clinically suitable, extended-release epidural morphine may be used in place of intravenous or conventional (*i.e.*, immediate-release) epidural morphine, although extended monitoring may be required.

Continuous epidural opioids are preferred to parenteral opioids for anesthesia and analgesia for reducing the risk of respiratory depression. When clinically suitable, appropriate doses of continuous epidural in-

fusion of fentanyl or sufentanil may be used in place of continuous infusion of morphine or hydromorphone without increasing the risk of respiratory depression.

Given the unique pharmacokinetic effect of the various neuraxially administered opioids, appropriate duration of monitoring should be matched with the drug. Based on the duration of action of hydrophilic opioids, neuraxial morphine or hydromorphone should not be given to outpatient surgical patients.

Dose Selection.

Low-dose Compared with High-dose Neuraxial Opioids. The literature indicates that respiratory depression is reduced with lower doses (*vs.* higher doses) of single-injection epidural opioids. [Category A1 evidence]. In addition, meta-analysis indicates a reduced frequency of hypoxemia when lower doses (*vs.* higher doses) of single-injection intrathecal opioids are administered. [Category A1 evidence]. The literature reports no differences in respiratory depression or sedation when lower doses of continuous epidural opioids are compared with higher doses. [Category C2 evidence].

The ASA members agree and the consultants strongly agree that the occurrence of respiratory depression is increased when higher (*vs.* lower) doses of epidural or intrathecal opioids are administered. In addition, the consultants and ASA members agree that the occurrence of respiratory depression is increased when higher (*vs.* lower) doses of *continuous epidural* opioids are administered.

Neuraxial Opioids Combined with Parenteral Opioids-Hypnotics. The literature is insufficient to assess whether the addition of parenteral opioids or hypnotics to neuraxial opioids is associated with increased occurrence of respiratory depression or hypoxemia. [Category D evidence].

The consultants and ASA members both strongly agree that the addition of parenteral opioids or hypnotics to neuraxial opioids increases the occurrence of respiratory depression.

Recommendations for Dose Selection: The lowest efficacious dose of neuraxial opioids should be administered to minimize the risk of respiratory depression. Parenteral opioids or hypnotics should be cautiously administered in the presence of neuraxial opioids. The concomitant administration of neuraxial opioids and parenteral opioids, sedatives, hypnotics, or magnesium requires increased monitoring (*e.g.*, intensity, duration, or additional methods of monitoring).

III. Detection of Respiratory Depression

Comparative studies are insufficient to examine the efficacy of pulse oximetry or end-tidal carbon dioxide monitoring to diagnose respiratory depression for patients receiving neuraxial opioids. [Category D evidence]. However, comparative studies report that pulse oximetry is effective in detecting *hypoxemia* in patients

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receiving a variety of anesthetic techniques (*i.e.*, general anesthesia, regional block, or neuraxial block). [Category A2 evidence]. Other literature evaluating end-tidal carbon dioxide monitoring for *parenteral* opioids suggest that such monitoring is effective in detecting hypercapnia/hypercarbia. The literature is silent regarding whether monitoring patients' level of sedation reduces the risk of respiratory depression. [Category D evidence]. The literature is insufficient regarding whether continuous monitoring using pulse oximetry, electrocardiography, or ventilation is associated with improved detection of respiratory depression or hypoxemia for patients given neuraxial opioids. [Category D evidence].

Both the consultants and the ASA members disagree that pulse oximetry monitoring is more likely to detect respiratory depression than are clinical signs. However, the consultants and ASA members both agree that continuous pulse oximetry monitoring is more likely to detect respiratory depression than periodic pulse oximetry monitoring. The consultants and ASA members both agree that end-tidal carbon dioxide monitoring is more likely to detect hypercapnia/hypercarbia and respiratory depression than are clinical signs. Finally, they both agree that checking level of alertness will identify patients at increased risk of respiratory depression.

Both the consultants and the ASA members strongly agree that all patients receiving neuraxial opioids should be monitored for adequacy of ventilation, oxygenation, and level of consciousness.

Monitoring after Administration of Single-injection Neuraxial Lipophilic Opioids (e.g., Fentanyl): Both the consultants and the ASA members agree that monitoring should be performed for a minimum of 2 h after administration, and that continual (*i.e.*, repeated regularly and frequently in steady rapid succession) monitoring should be performed for the first 20 min after administration, followed by monitoring at least once per hour until 2 h has passed. The ASA members agree and the consultants strongly agree that after 2 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

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Monitoring during or after Continuous Infusion or PCEA with Neuraxial Lipophilic Opioids: Both the consultants and the ASA members agree that (1) monitoring should be performed during the entire time the infusion is in use; (2) monitoring should be continual

for the first 20 min after initiation, followed by monitoring at least once per hour until 12 h has passed; (3) from 12 to 24 h, monitoring should be performed at least once every 2 h; (4) after 24 h, monitoring should be performed at least once every 4 h; and (5) after discontinuation of continuous infusion or patient-controlled epidural analgesia (PCEA), frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Monitoring after Administration of Single-injection Neuraxial Hydrophilic Opioids (e.g., Morphine, Not Including Sustained- or Extended- release Epidural Morphine): Both the consultants and the ASA members agree that (1) monitoring should be performed for a minimum of 24 h after administration; (2) monitoring should be performed at least once per hour for the first 12 h after administration, followed by monitoring at least once every 2 h for the next 12 h (*i.e.*, from 12 to 24 h); and (3) after 24 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Monitoring during or after Continuous Infusion or PCEA with Neuraxial Hydrophilic Opioids: Both the consultants and the ASA members strongly agree that monitoring should be performed during the entire time the infusion is in use. Further, both the consultants and the ASA members agree that (1) monitoring at least once every hour should be performed for the first 12 h after initiation, followed by monitoring at least once every 2 h for the next 12 h; (2) after 24 h, monitoring should be performed at least once every 4 h; and (3) after discontinuation of continuous infusion or PCEA, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Monitoring after Administration of Sustained- or Extended-release Epidural Morphine: Both the consultants and the ASA members agree that (1) monitoring at least once every hour should be performed during the first 12 h after administration, and at least once every 2 h for the next 12 h (*i.e.*, from 12 to 24 h); and (2) after 24 h, monitoring should be performed at least once every 4 h for a minimum of 48 h.

Patients at Increased Risk of Respiratory Depression: Both the consultants and the ASA members strongly agree that increased monitoring may be warranted for these patients.

Recommendations: All patients receiving neuraxial opioids should be monitored for adequacy of ventilation (*e.g.*, respiratory rate, depth of respiration [assessed without disturbing a sleeping patient]), oxygenation (*e.g.*, pulse oximetry when appropriate), and level of consciousness.**

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|| American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists: Practice guidelines for sedation and analgesia by non-anesthesiologists: An updated report. *ANESTHESIOLOGY* 2002; 96:1004-17.

* American Society of Anesthesiologists: Standards for basic anesthetic monitoring, Standards, Guidelines and Statements 2006. Available at: <http://www.asahq.org/publicationsAndServices/standards/02.pdf>. Accessed October 9, 2008.

** In cases with other concerning signs, it is acceptable to awaken a sleeping patient to assess level of consciousness.

Single-injection Neuraxial Lipophilic Opioids (e.g., *Fentanyl*): Monitoring should be performed for a *minimum* of 2 h after administration. Continual (i.e., repeated regularly and frequently in steady rapid succession) monitoring should be performed for the first 20 min after administration, followed by monitoring *at least* once per hour until 2 h has passed. After 2 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Continuous Infusion or PCEA with Neuraxial Lipophilic Opioids: Monitoring should be performed during the entire time the infusion is in use. Monitoring should be continual for the first 20 min after initiation, followed by monitoring *at least* once per hour until 12 h has passed. From 12 to 24 h, monitoring should be performed *at least* once every 2 h, and after 24 h, monitoring should be performed *at least* once every 4 h. After discontinuation of continuous infusion or PCEA with neuraxial lipophilic opioids, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Single-injection Neuraxial Hydrophilic Opioids (e.g., *Morphine, Not Including Sustained- or Extended-release Epidural Morphine*): Monitoring should be performed for a *minimum* of 24 h after administration. Monitoring should be performed *at least* once per hour for the first 12 h after administration, followed by monitoring *at least* once every 2 h for the next 12 h (i.e., from 12 to 24 h). After 24 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.

Continuous Infusion or PCEA with Neuraxial Hydrophilic Opioids: Monitoring should be performed during the entire time the infusion is in use. Monitoring *at least* once every hour should be performed for the first 12 h after initiation, followed by monitoring *at least* once every 2 h for the next 12 h. After 24 h, monitoring should be performed *at least* once every 4 h. After discontinuation of continuous infusion or PCEA, frequency of monitoring should be dictated by

the patient's overall clinical condition and concurrent medications.

Sustained- or Extended-release Epidural Morphine: Monitoring *at least* once every hour should be performed during the first 12 h after administration, and *at least* once every 2 h for the next 12 h (i.e., from 12 to 24 h). After 24 h, monitoring should be performed *at least* once every 4 h for a minimum of 48 h.

Increased monitoring (e.g., intensity, duration, or additional methods of monitoring) may be warranted in patients at increased risk of respiratory depression (e.g., unstable medical condition, obesity,†† concomitant administration of opioid analgesics or hypnotics by other routes, extremes of age).

IV. Management and Treatment of Respiratory Depression

Supplemental Oxygen. The literature is insufficient to assess whether supplemental oxygen will reduce the frequency or severity of hypoxia or hypoxemia when neuraxial opioids are administered. [Category D evidence]. Other literature supports the use of supplemental oxygen when nonneuraxial anesthetic techniques (e.g., general anesthesia, sedation and analgesia) are administered.‡‡ [Category A1 Evidence].

The consultants and ASA members both agree that, for patients receiving neuraxial opioids, supplemental oxygen should be available. They both strongly agree that, for patients receiving neuraxial opioids, supplemental oxygen should be administered to patients with altered level of consciousness, respiratory depression, or hypoxemia. The consultants and ASA members both strongly agree that, in patients with respiratory depression or hypoxemia after administration of neuraxial opioids, supplemental oxygen should be continued until the patient is alert and no respiratory depression or hypoxemia is present. The consultants and ASA members both agree that the routine use of supplemental oxygen may hinder detection of atelectasis, transient apnea, and hypoventilation.

Recommendations: For patients receiving neuraxial opioids, supplemental oxygen should be available. Supplemental oxygen should be administered to patients with altered level of consciousness, respiratory depression, or hypoxemia and continued until the patient is alert and no respiratory depression or hypoxemia is present. The Task Force cautions that routine use of supplemental oxygen may increase the duration of apneic episodes and may hinder detection of atelectasis, transient apnea, and hypoventilation.

Reversal Agents. Although there are insufficient comparative studies to assess the efficacy of naloxone or naltrexone for patients given neuraxial opioids, case reports suggest an association between the use of naloxone and reversal of opioid-induced respiratory depression. [Category B3 evidence]. Other literature supports

†† "Hospitalized patients who are at increased risk of respiratory compromise from [obstructive sleep apnea] should have continuous pulse oximetry monitoring after discharge from the recovery room. Continuous monitoring may be provided in a critical care or stepdown unit, by telemetry on a hospital ward, or by a dedicated, appropriately trained professional observer in the patient's room. Continuous monitoring should be maintained as long as patients remain at increased risk. Intermittent pulse oximetry or continuous bedside oximetry without continuous observation does not provide the same level of safety." From: American Society of Anesthesiologists Task Force on Perioperative Management of Obstructive Sleep Apnea: Practice guidelines for the perioperative management of obstructive sleep apnea. ANESTHESIOLOGY 2006; 104: 1081-93

‡‡ American Society of Anesthesiologists Task Force on Management of the Difficult Airway: Practice guidelines for management of the difficult airway: An updated report. ANESTHESIOLOGY 2003; 98:1269-77; and American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists: Practice guidelines for sedation and analgesia by nonanesthesiologists: An updated report. ANESTHESIOLOGY 2002; 96:1004-17.

the use of naloxone for respiratory depression when systemic opioids are administered. §§

Fn9 The consultants and ASA members both agree that reversal agents should be administered to all patients experiencing significant respiratory depression after neuraxial opioid administration.

Recommendations: Intravenous access should be maintained if recurring respiratory depression occurs. Reversal agents should be available for administration to all patients experiencing significant respiratory depression after neuraxial opioid administration. In the presence of severe respiratory depression, appropriate resuscitation should be initiated.

Fn10 **Noninvasive Positive-pressure Ventilation.** The literature is insufficient to assess the efficacy of noninvasive positive-pressure ventilation to treat patients who have been given neuraxial opioids. [Category D evidence]. Other literature supports the use of noninvasive positive-pressure ventilation for patients with respiratory compromise. |||

The consultants and ASA members are both equivocal regarding whether noninvasive positive-pressure ventilation will improve ventilatory status in patients with opioid-related respiratory depression.

Recommendations: Noninvasive positive-pressure ventilation may be considered for improving ventilatory status. If frequent or severe airway obstruction or hypoxemia occurs during postoperative monitoring, noninvasive positive-pressure ventilation should be initiated.

Appendix 1: Summary of Recommendations

I. Identification of Patients at Increased Risk of Respiratory Depression

- The anesthesiologist should conduct a focused history and physical examination before administering neuraxial opioids.
 - Particular attention should be directed toward signs, symptoms, or a history of sleep apnea, coexisting diseases or conditions (e.g., diabetes, obesity), current medications (including preoperative opioids), and adverse effects after opioid administration.
 - A physical examination should include, but is not limited to, baseline vital signs, airway, heart, lung, and cognitive function.

II. Prevention of Respiratory Depression after Neuraxial Opioid Administration

- Noninvasive positive-pressure ventilation

§§ American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists: Practice guidelines for sedation and analgesia by nonanesthesiologists: An updated report. *ANESTHESIOLOGY* 2002; 96:1004-17.

||| American Society of Anesthesiologists Task Force on Perioperative Management of Obstructive Sleep Apnea: Practice guidelines for the perioperative management of obstructive sleep apnea. *ANESTHESIOLOGY* 2006; 104:1081-93.

In cases with other concerning signs, it is acceptable to awaken a sleeping patient to assess level of consciousness.

*** American Society of Anesthesiologists: Standards for basic anesthetic monitoring, Standards, Guidelines and Statements 2006. Available at: <http://www.asahq.org/publicationsAndServices/standards/02.pdf>. Accessed October 9, 2008.

- Patients with a history of sleep apnea treated with non-invasive positive airway pressure should be encouraged to bring their own equipment to the hospital.

- Drug selection

- Single-injection neuraxial opioids may be safely used in place of parenteral opioids without altering the risk of respiratory depression or hypoxemia.
- Single-injection neuraxial fentanyl or sufentanil may be safe alternatives to single-injection neuraxial morphine.
- When clinically suitable, extended-release epidural morphine may be used in place of intravenous or conventional (i.e., immediate-release) epidural morphine, although extended monitoring may be required.
- Continuous epidural opioids are preferred to parenteral opioids for anesthesia and analgesia for reducing the risk of respiratory depression.
- When clinically suitable, appropriate doses of continuous epidural infusion of fentanyl or sufentanil may be used in place of continuous infusion of morphine or hydromorphone without increasing the risk of respiratory depression.
- Given the unique pharmacokinetic effect of the various neuraxially administered opioids, appropriate duration of monitoring should be matched with the drug.
- Neuraxial morphine or hydromorphone should not be given to outpatient surgical patients.

- Dose selection

- The lowest efficacious dose of neuraxial opioids should be administered to minimize the risk of respiratory depression.
- Parenteral opioids or hypnotics should be cautiously administered in the presence of neuraxial opioids.
- The concomitant administration of neuraxial opioids and parenteral opioids, sedatives, hypnotics, or magnesium requires increased monitoring (e.g., intensity, duration, or additional methods of monitoring).

III. Detection of Respiratory Depression

- All patients receiving neuraxial opioids should be monitored for adequacy of ventilation (e.g., respiratory rate, depth of respiration [assessed without disturbing a sleeping patient]), oxygenation (e.g., pulse oximetry when appropriate), and level of consciousness. ## Fn11
- Single-injection neuraxial lipophilic opioids (e.g., fentanyl)
 - Monitoring should be performed for a minimum of 2 h after administration.
 - Continual (i.e., repeated regularly and frequently in steady rapid succession***) monitoring should be performed for the first 20 min after administration, followed by monitoring at least once per hour until 2 h has passed. Fn12
 - After 2 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.
- Continuous infusion or patient-controlled epidural analgesia (PCEA) with neuraxial lipophilic opioids
 - Monitoring should be performed during the entire time the infusion is in use.
 - Monitoring should be continual for the first 20 min after initiation, followed by monitoring at least once per hour until 12 h has passed.
 - From 12 to 24 h, monitoring should be performed at least once every 2 h.
 - After 24 h, monitoring should be performed at least once every 4 h.

- After discontinuation of continuous infusion or PCEA with neuraxial lipophilic opioids, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.
- Single-injection neuraxial hydrophilic opioids (e.g., morphine, not including sustained- or extended-release epidural morphine)
 - Monitoring should be performed for a minimum of 24 h after administration.
 - Monitoring should be performed at least once per hour for the first 12 h after administration, followed by monitoring at least once every 2 h for the next 12 h (i.e., from 12 to 24 h).
 - After 24 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.
- Continuous infusion or PCEA with neuraxial hydrophilic opioids
 - Monitoring should be performed during the entire time the infusion is in use.
 - Monitoring at least once every hour should be performed for the first 12 h after initiation, followed by monitoring at least once every 2 h for the next 12 h.
 - After 24 h, monitoring should be performed at least once every 4 h.
 - After discontinuation of continuous infusion or PCEA, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.
- Sustained- or extended-release epidural morphine
 - Monitoring at least once every hour should be performed during the first 12 h after administration, and at least once every 2 h for the next 12 h (i.e., from 12 to 24 h).
 - After 24 h, monitoring should be performed at least once every 4 h for a minimum of 48 h.
- Increased monitoring (e.g., intensity, duration, or additional methods of monitoring) may be warranted in patients at increased risk of respiratory depression (e.g., unstable medical condition, obesity, obstructive sleep apnea,††† concomitant administration of opioid analgesics or hypnotics by other routes, extremes of age).

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IV. Management and Treatment

- Supplemental oxygen
 - For patients receiving neuraxial opioids, supplemental oxygen should be available.
 - Supplemental oxygen should be administered to patients with altered level of consciousness, respiratory depression, or hypoxemia and continued until the patient is alert and no respiratory depression or hypoxemia is present.
 - Routine use of supplemental oxygen may increase the duration of apneic episodes and may hinder detection of atelectasis, transient apnea, and hypoventilation.

††† "Hospitalized patients who are at increased risk of respiratory compromise from [obstructive sleep apnea] should have continuous pulse oximetry monitoring after discharge from the recovery room. Continuous monitoring may be provided in a critical care or stepdown unit, by telemetry on a hospital ward, or by a dedicated, appropriately trained professional observer in the patient's room. Continuous monitoring should be maintained as long as patients remain at increased risk. Intermittent pulse oximetry or continuous bedside oximetry without continuous observation does not provide the same level of safety." From American Society of Anesthesiologists Task Force on Perioperative Management of Obstructive Sleep Apnea: Practice guidelines for the perioperative management of obstructive sleep apnea. *ANESTHESIOLOGY* 2006; 104:1081-93.

‡‡‡ Unless otherwise specified, outcomes for the listed interventions refer to the reduction or detection of respiratory depression or hypoxemia.

- Reversal agents
 - Intravenous access should be maintained if recurring respiratory depression occurs.
 - Reversal agents should be available for administration to all patients experiencing significant respiratory depression after neuraxial opioid administration.
 - In the presence of severe respiratory depression, appropriate resuscitation should be initiated.
- Noninvasive positive-pressure ventilation
 - Noninvasive positive-pressure ventilation may be considered for improving ventilatory status.
 - If frequent or severe airway obstruction or hypoxemia occurs during postoperative monitoring, noninvasive positive-pressure ventilation should be initiated.

Appendix 2: Methods and Analyses

A. State of the Literature

For these Guidelines, a literature review was used in combination with opinions obtained from expert consultants and other sources (e.g., American Society of Anesthesiologist [ASA] members, open forums, Internet postings). Both the literature review and the opinion data were based on *evidence linkages*, or statements regarding potential relations between clinical interventions and outcomes. The interventions listed below were examined to assess their impact on a variety of outcomes related to respiratory depression related to neuraxial opioid anesthesia and analgesia.‡‡‡

Fn14

I. Identification of Patients at Increased Risk of Respiratory Depression:

1. History and physical examination: selected patient condition/ characteristics

II. Prevention of Respiratory Depression:

2. Single-injection neuraxial opioids *versus* parenteral opioids
3. Extended-release epidural morphine *versus* parenteral morphine
4. Extended-release epidural morphine *versus* immediate-release epidural morphine
5. Continuous epidural opioids *versus* parenteral opioids
6. Single-injection epidural morphine-hydromorphone *versus* epidural fentanyl-sufentanil
7. Single-injection intrathecal morphine-hydromorphone *versus* single-injection intrathecal fentanyl-sufentanil
8. Continuous epidural morphine-hydromorphone *versus* continuous epidural fentanyl-sufentanil
9. High *versus* low doses of single-injection epidural opioids
10. High *versus* low doses of single-injection intrathecal opioids
11. High *versus* low doses of continuous epidural opioids
12. Dose reduction *versus* cessation of opioids
13. Neuraxial opioids with *versus* without parenteral opioids or hypnotics

III. Detection of Respiratory Depression:

14. Pulse oximetry monitoring *versus* no pulse oximetry monitoring
15. End-tidal carbon dioxide monitoring *versus* no end-tidal carbon dioxide monitoring
16. Monitoring level of sedation monitoring *versus* not monitoring level of sedation
17. Continuous *versus* intermittent monitoring

Table 1. Meta-Analysis Summary

Linkage	n	Fisher Chi-square	P Value	Weighted Stouffer Zc	P Value	Effect Size	Mantel- Haenszel Odds Ratio	Confidence Interval	Heterogeneity	
									Significance	Effect Size
Single-injection neuraxial opioids vs. parenteral opioids										
Respiratory depression	9	—	—	—	—	—	1.40	0.59–3.30	—	NS
Somnolence/sedation	11	—	—	—	—	—	0.43	0.25–0.72	—	NS
Continuous epidural opioids vs. parenteral opioids										
Respiratory depression	6	—	—	—	—	—	0.32	0.12–0.86	—	NS
Somnolence/sedation	7	22.79	0.060	2.67	0.004	0.18	—	—	NS	NS
High-vs. low-dose epidural opioids										
Respiratory depression	7	—	—	—	—	—	3.57	1.22–10.43	—	NS
High vs. low-dose intrathecal opioids										
Hypoxemia	5	—	—	—	—	—	1.75	0.52–5.92	—	NS

NS = not significant.

IV. Management and Treatment of Respiratory Depression:

- 18. Supplemental oxygen may reduce the frequency of hypoxia or hypoxemia
- 19. Naloxone *versus* no naloxone
- 20. Naltrexone *versus* no naltrexone
- 21. Positive-pressure ventilation improves respiratory rate and reduces adverse outcomes related to respiratory depression

For the literature review, potentially relevant clinical studies were identified *via* electronic and manual searches of the literature. The electronic and manual searches covered a 41-yr period from 1967 through 2007. More than 1,200 citations were initially identified, yielding a total of 371 nonoverlapping articles that addressed topics related to the evidence linkages. After review of the articles, 212 studies did not provide direct evidence and were subsequently eliminated. A total of 159 articles contained direct linkage-related evidence (see Bibliography, Supplemental Digital Content 1, which shows a complete list of references for these Practice Guidelines, <http://links.lww.com/A595>).

Initially, each pertinent outcome reported in a study was classified as supporting an evidence linkage, refuting a linkage, or equivocal. The results were then summarized to obtain a directional assessment for each evidence linkage before conducting a formal meta-analysis. Literature pertaining to four evidence linkages contained enough studies with well-defined experimental designs and statistical information sufficient for meta-analyses. These linkages were (1) single-injection neuraxial opioids *versus* parenteral opioids, (2) continuous epidural opioids *versus* parenteral opioids, (3) high *versus* low doses of single-injection epidural opioids, and (4) high *versus* low doses of single-injection intrathecal opioids.

General variance-based effect size estimates or combined probability tests were obtained for continuous outcome measures, and Mantel-Haenszel odds ratios were obtained for dichotomous outcome measures. Two combined probability tests were used as follows: (1) the Fisher combined test, producing chi-square values based on logarithmic transformations of the reported *P* values from the independent studies; and (2) the Stouffer combined test, providing weighted representation of the studies by weighting each of the standard normal deviates by the size of the sample. An odds ratio procedure based on the Mantel-Haenszel method for combining study results using 2 × 2 tables was used with outcome frequency information. An acceptable significance level was set at *P* < 0.01 (one-tailed). Tests for heterogeneity of the independent studies were conducted to assure consistency among the study results. DerSimonian-Laird random-effects odds ratios

were obtained when significant heterogeneity was found (*P* < 0.01). To control for potential publishing bias, a “fail-safe *n*” value was calculated. No search for unpublished studies was conducted, and no reliability tests for locating research results were done.

Meta-analytic results are reported in table 1. To be accepted as significant findings, Mantel-Haenszel odds ratios must agree with combined test results whenever both types of data are assessed. In the absence of Mantel-Haenszel odds ratios, findings from both the Fisher and the weighted Stouffer combined tests must agree with each other to be acceptable as significant.

Interobserver agreement among Task Force members and two methodologists was established by interrater reliability testing. Agreement levels using a κ statistic for two-rater agreement pairs were as follows: (1) type of study design, κ = 0.78–0.90; (2) type of analysis, κ = 0.74–1.00; (3) evidence linkage assignment, κ = 0.79–1.00; and (4) literature inclusion for database, κ = 0.70–1.00. Three-rater chance-corrected agreement values were (1) study design, *Sav* = 0.86, *Var* (*Sav*) = 0.009; (2) type of analysis, *Sav* = 0.82, *Var* (*Sav*) = 0.017; (3) linkage assignment, *Sav* = 0.85, *Var* (*Sav*) = 0.004; and (4) literature database inclusion, *Sav* = 0.79, *Var* (*Sav*) = 0.310. These values represent moderate to high levels of agreement.

B. Consensus-based Evidence

Consensus was obtained from multiple sources, including (1) survey opinion from consultants who were selected based on their knowledge or expertise in neuraxial opioid administration, (2) survey opinions solicited from active members of the ASA, (3) testimony from attendees of publicly held open forums at two national anesthesia meetings, (4) Internet commentary, and (5) Task Force opinion and interpretation. An initial survey was sent to consultants and ASA members in 2007 covering all evidence linkages. The rate of return among consultants for the initial survey was 63% (*n* = 77 of 123), and 150 surveys were received from active ASA members. A second survey focusing on specifically on monitoring was sent in 2008 to consultants and a second random sample of ASA members. The rate of return among consultants for the second survey was 30% (*n* = 37 of 123), and 178 surveys were received from the second sample of ASA members. Results of these four surveys are reported in tables 2–5 and in the text of the Guidelines.

The consultants were asked to indicate which, if any, of the evidence linkages would change their clinical practices if the Guidelines were instituted. The rate of return was 14% (*n* = 17 of 123). The percent of responding consultants expecting *no change* associated with each linkage were as follows: (1) history and physical examination, 94%; (2) single-injection neuraxial opioid administration, 88%; (3) continuous epidural

T1

T2-5, AQ:4

Table 2. Consultant Survey Responses

	n	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
Identification of patients at increased risk of respiratory depression						
1. A directed history and physical examination will identify patients at increased risk of respiratory depression.	77	23.4	48.0*	13.0	14.3	1.3
Prevention of respiratory depression						
<i>Noninvasive positive-pressure ventilation</i>						
2. Noninvasive positive-pressure ventilation is effective in preventing respiratory depression in patients who have received neuraxial opioids.	77	1.3	11.7	42.8*	36.4	7.8
<i>Drug selection</i>						
3a. Single-injection neuraxial opioids <i>increase</i> the occurrence of respiratory depression compared with parenteral opioids.	77	1.3	15.6	14.3	57.1*	11.7
3b. Extended-release epidural morphine <i>increases</i> the occurrence of respiratory depression compared with parenteral opioids.	77	11.7	27.3	36.4*	23.4	1.3
3c. Extended-release epidural morphine <i>increases</i> the occurrence of respiratory depression compared with conventional (immediate-release) epidural morphine.	77	11.7	23.4	45.4*	19.5	0.0
4. Continuous epidural opioids <i>increase</i> the occurrence of respiratory depression compared with parenteral opioids.	77	1.3	20.8	11.7	58.4*	7.8
5a. The occurrence of respiratory depression after single-injection epidural morphine or hydromorphone is <i>increased</i> compared with single-injection epidural fentanyl or sufentanil.	77	10.4	50.6*	14.3	22.1	2.6
5b. The occurrence of respiratory depression after single-injection intrathecal morphine or hydromorphone is <i>increased</i> compared with single-injection intrathecal fentanyl or sufentanil.	77	9.1	58.4*	10.4	19.5	2.6
5c. The occurrence of respiratory depression after continuous epidural morphine or hydromorphone is <i>increased</i> compared with continuous epidural fentanyl or sufentanil.	77	6.5	32.4	31.2*	27.3	2.6
<i>Dose selection</i>						
6a. The occurrence of respiratory depression is <i>increased</i> when higher (vs. lower) doses of epidural opioids are administered.	77	54.5*	44.2	0.0	1.3	0.0
6b. The occurrence of respiratory depression is <i>increased</i> when higher (vs. lower) doses of intrathecal opioids are administered.	77	57.1*	41.6	0.0	1.3	0.0
6c. The occurrence of respiratory depression is <i>increased</i> when higher (vs. lower) doses of continuous epidural opioids are administered.	77	49.3	45.5*	1.3	3.9	0.0
7. The addition of parenteral opioids or hypnotics to neuraxial opioids <i>increases</i> the occurrence of respiratory depression.	77	55.8*	33.8	5.2	5.2	0.0
Detection of respiratory depression†						
8a. Pulse oximetry monitoring is more likely to detect respiratory depression than clinical signs.	77	2.6	26.0	18.2	46.7*	6.5
8b. Continuous pulse oximetry monitoring is more likely to detect respiratory depression than periodic pulse oximetry monitoring.	77	29.9	50.6*	9.1	7.8	2.6
8c. End-tidal carbon dioxide monitoring is more likely to detect respiratory depression than clinical signs.	77	20.8	41.5*	20.8	15.6	1.3
8d. Checking level of alertness will identify patients at increased risk of respiratory depression.	77	24.7	62.3*	9.1	2.6	1.3
Management and treatment of respiratory depression						
9a. For patients receiving neuraxial opioids, supplemental oxygen should be available.	77	39.0	41.5*	7.8	11.7	0.0
9b. For patients receiving neuraxial opioids, supplemental oxygen should be administered to patients with altered level of consciousness, respiratory depression, or hypoxemia.	77	62.3*	31.2	5.2	1.3	0.0
9c. In patients with respiratory depression or hypoxemia after administration of neuraxial opioids, supplemental oxygen should be continued until the patient is alert and no respiratory depression or hypoxemia is present.	77	51.9*	42.9	2.6	2.6	0.0
9d. Routine use of supplemental oxygen may hinder detection of atelectasis, transient apnea, and hypoventilation by pulse oximetry.	77	18.2	50.6*	16.9	13.0	1.3
10. Reversal agents should be administered to all patients experiencing significant respiratory depression after neuraxial opioid administration.	77	35.1	44.1*	7.8	13.0	0.0
11. Noninvasive positive-pressure ventilation will improve ventilatory status in patients with opioid-related respiratory depression.	77	1.3	11.7	61.0*	19.5	6.5

* Median. † Refer to table 4 for updated survey findings for the "Detection of respiratory depression" section.

n = number of consultants who responded to each item.

Table 3. American Society of Anesthesiologists Membership Survey Responses

	n	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
Identification of patients at increased risk of respiratory depression						
1. A directed history and physical examination will identify patients at increased risk of respiratory depression.	150	28.7	52.0*	6.6	12.7	0.0
Prevention of respiratory depression						
<i>Noninvasive positive-pressure ventilation</i>						
2. Noninvasive positive-pressure ventilation is effective in preventing respiratory depression in patients who have received neuraxial opioids.	150	4.0	14.7	31.3	44.0*	6.0
<i>Drug selection</i>						
3a. Single-injection neuraxial opioids <i>increase</i> the occurrence of respiratory depression compared with parenteral opioids.	150	3.3	23.3	15.3	52.0*	6.0
3b. Extended-release epidural morphine <i>increases</i> the occurrence of respiratory depression compared with parenteral opioids.	150	9.3	30.7	36.0*	21.3	2.7
3c. Extended-release epidural morphine <i>increases</i> the occurrence of respiratory depression compared with conventional (immediate-release) epidural morphine.	150	6.0	30.7	47.3*	14.7	1.3
4. Continuous epidural opioids <i>increase</i> the occurrence of respiratory depression compared with parenteral opioids.	150	4.7	22.0	10.0	58.0*	5.3
5a. The occurrence of respiratory depression after single-injection epidural morphine or hydromorphone is <i>increased</i> compared with single-injection epidural fentanyl or sufentanil.	150	12.0	53.3*	12.0	21.3	1.3
5b. The occurrence of respiratory depression after single-injection intrathecal morphine or hydromorphone is <i>increased</i> compared with single-injection intrathecal fentanyl or sufentanil.	150	12.0	62.0*	9.3	14.7	2.0
5c. The occurrence of respiratory depression after continuous epidural morphine or hydromorphone is <i>increased</i> compared with continuous epidural fentanyl or sufentanil.	150	9.3	46.0*	21.3	21.3	2.0
<i>Dose selection</i>						
6a. The occurrence of respiratory depression is <i>increased</i> when higher (vs. lower) doses of epidural opioids are administered.	150	46.7	49.3*	0.7	3.3	0.0
6b. The occurrence of respiratory depression is <i>increased</i> when higher (vs. lower) doses of intrathecal opioids are administered.	150	48.0	48.7*	0.6	2.7	0.0
6c. The occurrence of respiratory depression is <i>increased</i> when higher (vs. lower) doses of continuous epidural opioids are administered.	150	38.7	56.0*	3.3	2.0	0.0
7. The addition of parenteral opioids or hypnotics to neuraxial opioids increases the occurrence of respiratory depression.	150	53.3*	42.0	2.7	1.3	0.7
Detection of respiratory depression†						
8a. Pulse oximetry monitoring is more likely to detect respiratory depression than clinical signs.	150	6.7	23.3	8.7	51.3*	10.0
8b. Continuous pulse oximetry monitoring is more likely to detect respiratory depression than periodic pulse oximetry monitoring.	150	28.0	56.6*	10.0	4.7	0.7
8c. End-tidal carbon dioxide monitoring is more likely to detect respiratory depression than clinical signs.	150	30.7	40.6*	13.3	14.7	0.7
8d. Checking level of alertness will identify patients at increased risk of respiratory depression.	150	26.0	56.7*	5.3	12.0	0.0
Management and treatment of respiratory depression						
9a. For patients receiving neuraxial opioids, supplemental oxygen should be available.	150	47.3	42.7*	5.3	4.7	0.0
9b. For patients receiving neuraxial opioids, supplemental oxygen should be administered to patients with altered level of consciousness, respiratory depression, or hypoxemia.	150	64.7*	30.0	3.3	2.0	0.0
9c. In patients with respiratory depression or hypoxemia after administration of neuraxial opioids, supplemental oxygen should be continued until the patient is alert and no respiratory depression or hypoxemia is present.	150	61.3*	33.3	3.3	1.3	0.7
9d. Routine use of supplemental oxygen may hinder detection of atelectasis, transient apnea, and hypoventilation by pulse oximetry.	150	18.0	52.7*	16.0	11.3	2.0
10. Reversal agents should be administered to all patients experiencing significant respiratory depression after neuraxial opioid administration.	150	34.0	46.0*	8.7	10.0	1.3
11. Noninvasive positive-pressure ventilation will improve ventilatory status in patients with opioid-related respiratory depression.	150	4.0	27.3	35.3*	30.7	2.7

* Median. † Refer to table 5 for updated survey findings for the "Detection of respiratory depression" section.

n = number of members who responded to each item.

Table 4. Updated Consultant Survey Responses

	n	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
Detection of respiratory depression						
1. All patients receiving neuraxial opioids should be monitored for adequacy of ventilation, oxygenation, and level of consciousness.	37	56.8*	37.8	0.0	5.4	0.0
Single-injection neuraxial lipophilic opioids (e.g., fentanyl)						
2a. Monitoring should be performed for a minimum of 2 h after administration.	37	32.4	59.5*	2.7	2.7	2.7
2b. Continual (defined as "repeated regularly and frequently in steady rapid succession") monitoring should be performed for the first 20 min after administration, followed by monitoring at least once per hour until 2 h has passed.	37	35.1	46.0*	10.8	5.4	2.7
2c. After 2 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.	37	51.3*	46.0	0.0	2.7	0.0
Continuous infusion or PCEA with neuraxial lipophilic opioids						
3a. Monitoring should be performed during the entire time the infusion is in use.	37	44.4	44.4*	5.6	5.6	0.0
3b. Monitoring should be continual for the first 20 min after initiation, followed by monitoring at least once per hour until 12 h has passed.	37	29.7	43.3*	13.5	13.5	0.0
3c. From 12 to 24 h, monitoring should be performed at least once every 2 h.	37	24.3	46.0*	12.2	8.1	5.4
3d. After 24 h, monitoring should be performed at least once every 4 h.	37	18.9	43.2*	24.3	8.1	5.4
3e. After discontinuation of continuous infusion or PCEA, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.	37	48.6	46.0*	0.0	5.4	0.0
Single-injection neuraxial hydrophilic opioids (e.g., morphine, not including sustained-or extended-release epidural morphine)						
4a. Monitoring should be performed for a minimum of 24 h after administration.	37	48.7	43.2*	2.7	2.7	2.7
4b. Monitoring should be performed at least once per hour for the first 12 h after administration, followed by monitoring at least once every 2 h for the next 12 h (i.e., from 12 to 24 h).	37	21.6	43.3*	16.2	13.5	5.4
4c. After 24 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.	37	48.7	48.7*	0.0	2.7	0.0
Continuous infusion or PCEA with neuraxial hydrophilic opioids						
5a. Monitoring should be performed during the entire time the infusion is in use.	37	64.9*	27.0	5.4	2.7	0.0
5b. Monitoring at least once every hour should be performed for the first 12 h after initiation, followed by monitoring at least once every 2 h for the next 12 h.	36	27.8	36.1*	22.2	11.1	2.8
5c. After 24 h, monitoring should be performed at least once every 4 h.	37	32.4	40.5*	16.2	5.4	5.4
5d. After discontinuation of continuous infusion or PCEA, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.	37	43.3	37.8*	8.1	10.8	0.0
Sustained- or extended-release epidural morphine						
6a. Monitoring at least once every hour should be performed during the first 12 h after administration, and at least once every 2 h for the next 12 h (i.e., from 12 to 24 h).	36	41.6	27.8*	16.7	11.1	2.8
6b. After 24 h, monitoring should be performed at least once every 4 h for a minimum of 48 h.	35	37.1	28.6*	17.2	11.4	5.7
Patients at increased risk of respiratory depression						
7. Increased monitoring may be warranted in patients at increased risk of respiratory depression.	36	82.9*	17.1	0.0	0.0	0.0

* Median.

n = number of consultants who responded to each item; PCEA = patient-controlled epidural analgesia.

opioid administration, 88%; (4) extended-release epidural opioid administration, 71%; (5) monitoring for adequacy of ventilation, oxygenation, and level of consciousness, 59%; (6) supplemental oxygen administration, 88%; and (7) use of noninvasive positive-pressure ventilation, 100%. Fifty-

nine percent of the respondents indicated that the Guidelines would have *no effect* on the amount of time spent on a typical case, and 41% indicated that there would be an *increase* of the amount of time spent on a typical case with the implementation of these Guidelines.

Table 5. Updated American Society of Anesthesiologists Members Survey Responses

	n	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
Detection of respiratory depression						
1. All patients receiving neuraxial opioids should be monitored for adequacy of ventilation, oxygenation, and level of consciousness.	178	65.7*	30.3	1.7	1.7	0.6
Single-injection neuraxial lipophilic opioids (e.g., fentanyl)						
2a. Monitoring should be performed for a minimum of 2 h after administration.	178	44.9	42.1*	5.1	6.2	1.7
2b. Continual (defined as "repeated regularly and frequently in steady rapid succession") monitoring should be performed for the first 20 min after administration, followed by monitoring at least once per hour until 2 h has passed.	177	40.1	40.7*	8.5	10.2	0.5
2c. After 2 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.	178	31.4	56.2*	4.5	7.3	0.6
Continuous infusion or PCEA with neuraxial lipophilic opioids						
3a. Monitoring should be performed during the entire time the infusion is in use.	177	45.7	43.5*	7.9	2.3	0.6
3b. Monitoring should be continual for the first 20 min after initiation, followed by monitoring at least once per hour until 12 h has passed.	177	30.5	45.8*	9.6	11.3	2.8
3c. From 12 to 24 h, monitoring should be performed at least once every 2 h.	177	28.7	44.9*	11.2	13.5	1.7
3d. After 24 h, monitoring should be performed at least once every 4 h.	178	23.0	38.8*	18.5	15.2	4.5
3e. After discontinuation of continuous infusion or PCEA, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.	176	39.8	54.0*	2.8	3.4	0.0
Single-injection neuraxial hydrophilic opioids (e.g., morphine, not including sustained- or extended-release epidural morphine)						
4a. Monitoring should be performed for a minimum of 24 h after administration.	178	43.3	42.1*	5.6	7.9	1.1
4b. Monitoring should be performed at least once per hour for the first 12 h after administration, followed by monitoring at least once every 2 h for the next 12 h (i.e., from 12 to 24 h).	178	29.8	46.6*	9.6	12.3	1.7
4c. After 24 h, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.	178	41.0	54.5*	2.8	1.1	0.6
Continuous infusion or PCEA with neuraxial hydrophilic opioids						
5a. Monitoring should be performed during the entire time the infusion is in use.	177	54.8*	37.3	6.8	0.6	0.6
5b. Monitoring at least once every hour should be performed for the first 12 h after initiation, followed by monitoring at least once every 2 h for the next 12 h.	176	36.4	47.7*	6.2	9.1	0.6
5c. After 24 h, monitoring should be performed at least once every 4 h.	176	26.2	47.7*	10.2	14.2	1.7
5d. After discontinuation of continuous infusion or PCEA, frequency of monitoring should be dictated by the patient's overall clinical condition and concurrent medications.	175	42.8	49.7*	2.9	4.6	0.0
Sustained- or extended-release epidural morphine						
6a. Monitoring at least once every hour should be performed during the first 12 h after administration, and at least once every 2 h for the next 12 h (i.e., from 12 to 24 h).	172	36.6	36.6*	24.4	2.3	0.0
6b. After 24 h, monitoring should be performed at least once every 4 h for a minimum of 48 h.	172	24.4	33.7*	32.0	8.7	1.2
Patients at increased risk of respiratory depression						
7. Increased monitoring may be warranted in patients at increased risk of respiratory depression.	174	81.6*	16.7	1.7	0.0	0.0

* Median.

n = number of American Society of Anesthesiology members responding to each item; PCEA = patient-controlled epidural analgesia.