Emergence Delirium

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Definition: terms include emergence agitation, delirium, and excitement, and postanesthetic excitement; term emergence delirium (ED) now linked to Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) definition of substance-induced delirium; defined as disturbance of consciousness, changing cognition or perceptual disturbance that develops over short period of time; occurrence fairly common; causes distress and discomfort for patient, family, and caregivers; Sikich and Lerman (2004) — disturbance in child’s awareness of, and attention to, his or her environment with disorientation and perceptual alterations, including hypersensitivity to stimulation and hyperactive motor behavior in immediate postanesthesia period

Characteristics: incidence in literature ranges from 6% to 80%; reasons for broad range may include unclear definition, differences in study modalities, and lack of validated scoring scale; actual incidence likely ≤20%; etiology uncertain; occurs in immediate postoperative period; short-lived; probably associated with postoperative behavioral changes; in children, 7-fold increase in likelihood of temper tantrums, disrupted sleep, and emergence following incident of ED, which may last up to 2 wk postoperatively; drugs — ED associated with inhalation agents, benzodiazepines, atropine, barbiturates, scopolamine, and ketamine (occasionally)

Contributing factors: preschool age (2 to 6 year of age); preexisting difficult temperament; preoperative anxiety; children undergoing ear, nose, throat, or eye surgery; pain possible contributing factor; previous history

ED in adults: incidence less, at 5% to 10%, possibly up to 20%; young, healthy adult males at highest risk; longer duration with no lucid intervals; etiology uncertain; risk factors — preoperative benzodiazepines; lengthy and invasive surgery (particularly breast and abdominal surgery); patients >60 yr of age more prone to postoperative delirium and cognitive dysfunction (separate entities but associated with ED); older adults who develop ED more likely to develop postoperative delirium and cognitive dysfunction; postoperative delirium — usually occurs 1 to 3 days following surgery; often associated with long-term increase in cognitive decline and mortality

Limited knowledge about ED: for many years, no clear definition or validated rating scale; can be difficult to differentiate delirium from pain; possible lack of interest about significance of ED in pediatric patients; Bajwa study — compared Pediatric Anesthesia Emergence Delirium (PAED), Cravero, and Watcha scales; PAED scale probably most used in research, but Watcha scale may be easier to use in clinical practice

Possible etiologies: inadequate preoperative sedation; high level of anxiety; postoperative pain, rapid emergence in unfamiliar surroundings; misperception of environmental stimuli; differing central nervous system (CNS) effects (balance of neuronal synaptic excitation vs inhibition); sympathetic activation; psychomotor side effect

Studies: Oh study — looked at effect of rapid awakening in patients 1 to 7 yr of age; all induced with same medications and received sevoflurane for maintenance; patients randomized to immediate shut-off of sevoflurane had 35% ED, vs 33% in gradual shut-off group (evaluation by blinded observers, validated scale not used); concluded no difference between rapid and slow emergence in development of ED; Constant study — found difference between electroencephalographic (EEG) patterns of children treated with sevoflurane vs halothane; sevoflurane produced greater withdrawal of parasympathetic activity compared to halothane; Kuratani meta-analysis — looked at ED in patients treated with sevoflurane vs halothane; all patients <12 yr of age; incidence of ED was increased in all 4 subgroups in children treated with sevoflurane; Uzono study — looked at children treated with sevoflurane vs propofol; 38% of children receiving sevoflurane for maintenance anesthesia developed ED; none receiving propofol maintenance developed ED

Management strategies: provide quiet, low-stimulation perioperative environment for induction and emergence; consider premedication (eg, oral midazolam [Versed]); selective use of inhalation anesthetics; use of propofol, fentanyl, clonidine, dexmedetomidine, local anesthetics, and melatonin; all have potentially positive effects; optimize analgesia; avoid drugs with known association with ED; no clinical evidence to suggest that switching from sevoflurane to desflurane during procedure lessens likelihood of ED; no positive studies indicating parental presence helpful; rule out other causes

Algorithm: ensure adequate analgesia; consider total intravenous anesthesia (TIVA) or dexmedetomidine because of low association with ED; smooth emergence usually indicates uneventful postoperative course; if agitation develops, rule out causes other than ED (treat as needed); true ED — propofol, fentanyl, and dexmedetomidine helpful for severe cases; mild ED may be treatable with time and parental presence; other causes of agitation — hypoxia, hypercarbia, hypotension, hypoglycemia, pain, increased intracranial pressure (ICP), bladder distention

Preventing ED: Abu-Shahwan study — looked at children 2 to 7 yr of age undergoing general anesthesia; patients randomized to propofol vs saline intravenously (IV); 5. Select appropriate anesthesia drugs to minimize the risk of elevated ICP during neurosurgery.

Educational Objectives

The goal of this program is to improve the management of emergence delirium and the care of patients undergoing neuroanesthesia. After hearing and assimilating this program, the clinician will be better able to:

1. Define emergence delirium (ED) and recognize similarities and differences in ED in children and adults.
2. Use an algorithm to diagnose and manage ED.
3. Recognize how cerebral blood flow can affect cerebral blood volume and intracranial pressure (ICP).
4. Evaluate how patients with normal brains and those with brain injury may respond differently to volatile anesthetics.

Facility Disclosure

In adherence to ACCME Standards for Commercial Support, Audio Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, members of the faculty and the planning committee reported nothing to disclose.
patients evaluated with PAED on awakening and at 30 min; 2 children (≈5%) in propofol group experienced ED, compared to ≈26% in saline; no difference in discharge time between groups; Dahmani study — meta-analysis of studies on prevention of ED; propofol single dose or continuous infusion, IV or intranasal fentanyl; oral or IV ketamine, clonidine, dexmedetomidine, and local anesthetics found effective; midazolam and 5HT3 inhibitors found ineffective

**Pharmacologic options for treatment:** give 1 mg of propofol IV if able; 0.5 to 1 μg/kg of fentanyl IV; 0.25 mg/kg of ketamine; dexametomidine 0.1 to 0.3 μg/kg; midazolam — associated with agitation in some children; flumazenil helpful in these cases

**Potential adverse effects:** patient, family, and staff at risk for injury during episodes; patients may pull out IV or disrupt suture lines, drains, or dressings; hypertension and tachycardia may develop; one-on-one supervision needed but not always available; may delay discharge from unit; produces postoperative maladaptive behaviors; results in low patient and family satisfaction

**Neuroanesthesia:** Pharmacology That Really Matters

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**Background:** during surgery, ICP may be elevated, surgical field may become difficult to enter, or cranium difficult to close; four-compartment model includes cells, interstitial fluid, cerebral spinal fluid (CSF), and blood (arterial and venous); changes in cerebral blood flow (CBF) affect cerebral blood volume (CBV) and ICP

**Effect of IV drugs on ICP:** studies of human subjects not anesthetized at baseline show that parallel reductions in blood flow and metabolism occur with almost all IV sedative/hypnotic drugs; with exception of ketamine bolus (which increases CBF without increasing metabolism), bolus induction doses of all anesthetic drugs have reasonable or favorable effect on ICP; coupling phenomenon — possible cause of effect; drugs reduce electro-physiologic and functional activity of neurons, resulting in coupled reduction of CBF; IV agents probably do not have direct effect on cerebral vasculature; ≈60% of utilization functional and can be suppressed by drugs, but 40% not affected; hence, anesthetic drugs “disappointment” as cerebral protective agents

**Metabolic rate and cerebral blood flow:** seizures associated with high metabolic rate and CBF; “barbiturate coma” at lowest end of CBF and cerebral metabolic rate (CMR); barbiturates achieve maximal suppression of functional/electrophysiologic component of oxygen utilization; clinically, monitoring with EEG would show patient in deep burst suppression, with very small residual EEG activity (medication beyond this level causes problems with hemodynamics and wake-up time); may use average dose needed for suppression if EEG not available

**Pentobarbital:** speaker prefers because sustained period of control of ICP usually needed; used in all ICP studies involving head injury; causes fewer hemodynamic difficulties than propofol; slightly slower onset allows better monitoring of vascular filling; 10 mg/kg dose causes complete suppression of burst activity; start with 100 mg increments with fluids; decrease to 50 mg increments to reach 10 mg/kg, then give 1 mg/kg/hr by intermittent bolus to sustain effect; tolerance develops after ≈12 hr

**Propofol:** burst suppression achieved with induction dose of ≈2.5 mg/kg, then infusion of 250 μg/kg/min; propofol can be changed (backed off), whereas pentobarbital requires 12 to 18 hr of ventilation

**Recommendations from Brain Trauma Foundation:** level 2 recommendation for use of high-dose barbiturates to control elevated ICP refractory to maximum standard medical and surgical treatment; however, hemodynamic stability essential before and during therapy; propofol — recommended for control of ICP, but not for improvement in mortality or 6 mo outcome; high-dose propofol can produce significant morbidity due to propofol infusion syndrome (etiologically unexplained syndrome of metabolic acidosis, rhabdomyolysis, hyperlipidemia, renal failure, cardiac dysfunction, and often death); use of burst suppression doses of propofol beyond 18 to 24 hr increases risk for adverse effects

**Volatile agents and CBF:** in general, volatile agents do not cause marked change in CBF at less than minimum alveolar concentration (MAC) levels; however, this is simplification, and treatment often more complex in patients with elevated ICP; CBF falls rapidly during early phase of anesthesia with volatile agents in normal patients (blood pressure, temperature, and carbon dioxide tension held constant); CMR likely also falls; nadir reached at ≈1 MAC; CBF then rises with end-tidal concentrations; biphasic response — CMR similarly falls rapidly with volatile agents and possibly coupled reduction in CBF; volatile agents cause direct relaxation of vascular smooth muscle; vasodilatory effect revealed after CMR nadir reached, and CBF begins to rise; at <1 MAC, biphasic effect unlikely to cause difficulties in CBF in normal neurosurgical patients, but many patients not “normal”; biphasic reaction requires that CMR be suppressed; however, if CMR already suppressed (eg, by sedation, pathology) or CMR/CBF coupling impaired (causative pathology unknown), biphasic response may not occur; low levels of volatile agents may cause immediate vasodilation in these cases, and speaker does not recommend use until after cranium opened; use TIVA first and begin combination of IV and inhaled agents when brain visible; additionally, cannot assume lack of adverse effects of sub-MAC concentrations of volatile agents if brain bulging and difficulty in surgery; use of volatile agents not recommended in these situations

**Nitrous oxide (N₂O):** causes average increase of 30% CBF when given alone, and ≈20% increase when added to 1.1 MAC of isoflurane; however, N₂O given with background of barbiturate, benzodiazepines, narcotics, or propofol has minimal to no effect on CBF (reasons unknown); Eng study — propofol plus N₂O resulted in nonsignificant 3% reduction in CBF; N₂O given with fixed agents causes no adverse effects in many cases; however, N₂O potential vasodilator, so avoid use in patients with brain swelling, uncontrolled, or unknown ICP until cranium open or ICP can be measured

**Total intravenous anesthesia:** acceptable method to avoid elevations in ICP in most patients; however, should provide analgesia to patients given large amount of remifentanil; also consider context-dependant half-life of propofol (residual drug may interfere with emergence)

**Muscle relaxants:** available nondepolarizing drugs do not cause significant problems for brain or ICP; succinylcholine — in some situations succinylcholine will cause small rise in ICP; however, will decrease with small increase in dose of induction agent; succinylcholine may affect proprioceptors (Golgi apparatus) and stimulate reticular activating system, producing arousal response and transient ICP increase; Lam study — looked at patients in intensive care unit (ICU) intubated after head injury and subarachnoid hemorrhage; no increase in ICP seen when large dose of succinylcholine given to patients in stable, sedated, nonparalyzed state; likely that reticular activating system unable to produce ICP response in patients with head injuries severe enough to require intubation; reasonable to use succinylcholine to control airway in acutely neurologically injured patients if no contraindications

**Mannitol:** appears to work more rapidly than furosemide (Diaqua-2, Lasix, Lo-Aqua); best osmotic diuretic available, and most commonly used; give dose of 1 gm/kg over 15 min (hypersmolar compounds relax vascular smooth muscle); Marshall study — 0.25 gm/kg achieves same effect on ICP as higher doses (possibly not as durable); should not increase serum osmolality to >320 mOsm/L; however, osmolality rarely
measured (loss of efficacy considered end point); maintenance often in increments of 12.5 gm slow boluses after first gram per kilo given; mannitol draws large amount of fluid into vascular tree; serum sodium will fall transiently (factitious, does not require treatment)

**Hypertonic saline:** studies that compare equiosmolar mannitol and hypertonic saline show no difference in efficacy; some anecdotal reports of success after failure of mannitol; possibly advantageous in ICU, where volume and electrolyte disturbances more likely (hypertonic saline does not produce large diuresis); difficult to recommend a specific regimen for use in operating room, given multiple available concentrations

**Alpha agonists:** *phenylephrine*—studies have shown that patients had no change in CBF when infused with norepinephrine by carotid (blood pressure increased by ≈22 mm Hg), when infused peripherally (pressure increased ≈50 mm Hg), and when given phenylephrine during cardiopulmonary bypass surgery; alpha agonists do not cause vasoconstriction in normal patients; *Kim study*—patients given phenylephrine in amounts to raise blood pressure by 30 mm Hg; CBF increased from mid-teens to lower 30s mm Hg; no decline in CBF seen in normal or abnormal areas

**Adverse effects in compartments:** *venous compartment*—high jugular and/or airway pressure; *arterial*—hypercapnia, hypoxia, increased CMR, seizures, hypertension, vasodilators; *CSF space*—hydrocephalus, trapping of ventricle; *interstitial fluid*—edema; *abnormal cells*—tumor mass, bleeding elsewhere in intracranial space; *treatment*—ensure no constriction of neck; manage ventilation; eliminate inhaled agents; lower CO2 tension; decrease CMR; drain CSF; give diuretics and steroids to treat fluid

**Suggested Reading**


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**Estimated time to complete the educational process:**

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<td>Review Educational Objectives on page 1</td>
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<td>Take pretest</td>
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<td>Listen to audio program</td>
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1. Which of the following statements are true about emergence delirium (ED) in children?
   1. Incidence is probably ≤20%
   2. Studies have clearly shown etiology
   3. Associated with an increased incidence of postoperative behavioral changes
   4. Incidence is independent of preexisting difficult temperament or preoperative anxiety
   5. Associated with use of inhalation agents
      (A) 1,2 (B) 3,4 (C) 1,3,5 ** (D) 2,4,5

2. Which of the following statements about ED in adult patients is correct?
   (A) Patients >60 yr of age are at highest risk
   (B) Associated with preoperative benzodiazepines **
   (C) Same entity as postoperative delirium
   (D) Seen equally with highly invasive and less invasive surgeries

3. In studies of children undergoing anesthesia, halothane has been associated with a _______ risk of ED compared to sevoflurane; rapid emergence from sevoflurane anesthesia _______ the incidence of ED compared to gradual emergence.
   (A) Higher; increased (C) Higher; did not increase
   (B) Lower; increased (D) Lower; did not increase

4. If a young patient shows signs of agitation upon emergence from anesthesia, the first step in management is to:
   (A) Request parental presence
   (B) Rule out or treat other potential causes of agitation **
   (C) Give 1 mg of intravenous (IV) propofol
   (D) Give oral melatonin

5. According to a meta-analysis, which of the following is not effective in the treatment of ED?
   (A) 5HT3 inhibitors ** (C) Local anesthetics
   (B) IV ketamine (D) Clonidine

6. Which of the following statements about the favorable effect of intravenous (IV) anesthetics on intracranial pressure (ICP) is true?
   (A) Induction bolus of ketamine increases cerebral metabolic rate (CMR) but not cerebral blood flow (CBF)
   (B) IV anesthetics have a direct effect on cerebral vasculature
   (C) Anesthetics reduce the functional activity of neurons
   (D) IV anesthetics are good protective agents for the brain

7. Choose the correct statement about the use of propofol in patients undergoing neurosurgery.
   (A) Unable to produce burst suppression
   (B) Studies show reduction in 6 mo mortality when used to control ICP
   (C) Propofol-associated adverse effects such as metabolic acidosis and cardiac dysfunction have a clear etiology
   (D) Use beyond 18 to 24 hr (eg, in the intensive care unit) increases the risk for adverse effects

8. In patients undergoing neurosurgery who have severe pathology or brain injury, it is prudent to assume that:
   (A) Cerebral metabolic rate (CMR) is already suppressed
   (B) CMR remains coupled to CBR
   (C) Low levels of volatile anesthetics will not cause vasodilatation
   (D) Combination of IV and volatile agents can be started before the cranium is opened

9. Inhaled nitrous oxide can increase CBR and intracranial pressure (ICP) when it is:
   1. Administered alone
   2. Combined with barbiturates
   3. Combined with propofol
   4. Combined with isoflurane
      (A) 1,2 (B) 2,3 (C) 3,4 (D) 1,4

10. Use of mannitol for treatment of elevated ICP should include all of the following, except:
    (A) Keeping serum osmolality <320 mOsm/L
    (B) Treating the resulting hyponatremia
    (C) Administering 1 mg/K over 15 minutes
    (D) Giving maintenance doses in slow boluses of 12.5 gm