The agitated child in the recovery room is distressing, not only for the staff, but also for the parents. This often creates a false impression of the “quality” of the anaesthesia. Before attributing this distress to emergence delirium, other more serious causes should be excluded.

The two most common causes for agitation in the recovery room are pain and drug-induced emergence delirium. Below is a list of some possible causes for agitation in recovery:

- Hypoxia
- Hypercarbia
- Airway obstruction
- Hypoglycemia
- Seizures
- Raised intracranial pressure
- Temperature abnormalities
- Pain
- Drugs
  - Emergence delirium (ED)
  - Extrapyramidal effects, especially from some antiemetics
  - Inadequate reversal of muscle relaxants
- Full bladder
- Fear/anxiety
- Child’s temperament

Most of the causes for recovery room agitation are familiar and can be managed, except for ED. This is now more common in children as less soluble volatile anaesthetic agents are frequently used. ED was identified in the 1960s and is not a new phenomenon. This lecture will focus solely on ED in children.

**Definition and incidence**

Delirium manifests as “perceptual disturbances, hallucinations and psychomotor agitation”, in other words, inconsolable crying, restlessness and agitation unrelated to pain. The term agitation describes a milder condition with less behavioural changes. The two are often used interchangeably when discussing emergence. For the purposes of this talk, ED will be used. ED occurs within the first 30 minutes after anaesthesia. As there are so many variables that can affect it, the incidence varies from 10-50%, with an average of about 15%. Some studies have an incidence as high as 80%. This variation is also a reflection of the difficulty in determining what ED is.

**Assessment**

Sikich and Lerman developed the “Paediatric Anaesthesia Emergence Delirium Scale,” or PAED scale, in an attempt to define ED (Table I). However, they did not give an ED threshold. The scores do correlate well with age, time to awakening and the use of sevoflurane. Numerous other scales have been developed and this makes comparing studies and interpreting outcomes difficult. The fact that there are so many scoring systems shows that ED is not an easily definable condition.

**Aetiology of emergence delirium**

There are many associated causes, but none have been conclusively shown to cause ED. The presence of a combination of aetiologies will most likely increase the risk of ED occurring.

**Rapid awakening**

ED is more common with the newer, less soluble inhalational agents. This has given rise to the theory that too rapid awakening results in ED as the child’s confusion and apprehension about the unfamiliar surroundings is heightened. There is little evidence...
Refresher Course: The agitated child in recovery

Intrinsic characteristics of drugs

All modern inhalational anaesthetic agents can cause ED. The incidence with sevoflurane and desflurane far outstrip those of the older agents. Isoflurane can also cause ED. It is suggested that the newer agents upset the central nervous system (CNS) balance between neuronal synaptic inhibition and excitation. This is not a convulsant effect, as desflurane is not proconvulsant as opposed to sevoflurane. Inhalational agents, in particular sevoflurane and isoflurane, raise noradrenaline (NAdr) levels in adrenergic areas of the brain. This could partly explain the effect of clonidine on ED.

Pain

This is a very difficult factor to exclude, as children who have pain are agitated. Anaesthesia, with both desflurane and sevoflurane for non-painful procedures (such as MRI), is associated with ED. Pre-emptive analgesia has been shown to reduce ED, but these children were also sedated from their analgesic agents (fentanyl and ketamine). Alpha-2 agonists do reduce ED, but patients were likewise also sedated. Caudal analgesia did not reduce the incidence of ED. From these studies, ED seems to be a separate phenomenon from pain. If pain is present, ED seems to be worse.

Site of surgery

Surgery in head and neck areas seems to result in more ED, but especially tonsils, thyroid, teeth, ears and eyes.

Age

Preschoolers (2-5 years) are most at risk. ED may reflect brain immaturity and an inability to cope with a strange environment in the face of CNS control imbalance caused by the inhalational agents. Young brains have less acetylcholone, NAdr, GABA and dopamine.

Preoperative anxiety

Many studies have shown that very anxious children and/or anxious parents will increase the occurrence of ED.

Personality

Certain personality traits will be more likely to produce ED. These include emotional children, those who are very impulsive and those who do not adapt easily to strange environments.

Drugs

Medication that the child may be taking, or pre-medication given, may cause delirium when combined with anaesthesia. Examples of these are phenothiazines (Vallergan®, Stemetil® and Phenergan®), butyrophenones (droperidol), or benzodiazepines (midazolam).

Management of ED

The question arises: should one treat ED or not, and are there long-term consequences of an ED episode? There are no clear-cut answers. Children who developed ED tended to be those with higher levels of anxiety and poorer coping mechanisms. Anxious children tend to require more postoperative analgesia, have separation anxiety and other behavioural problems, and have sleep disturbances and nightmares more commonly than less anxious children. These problems usually resolve within three days and seem not to have long term sequelaes. Whether ED and anxiety with postoperative behavioural problems are two separate entities is not known.

Non-pharmacologic management

Some practitioners have opted not to treat ED, as it is self-limiting. Other factors, such as pain, must

---

Table I. The Paediatric Anaesthesia Emergence Delirium (PAED) Scale

| Item | Description | Score |
|------|-------------|-------|
| 1.   | The child makes eye contact with the caregiver. | 0-4 |
| 2.   | The child’s actions are purposeful. | 0-4 |
| 3.   | The child is aware of his/her surroundings | 0-4 |
| 4.   | The child is restless. | 0-4 |
| 5.   | The child is inconsolable. | 0-4 |

Items 1, 2 and 3 are reversed scores as follows: 4 = not at all, 3 = just a little, 2 = quite a bit, 1 = very much, 0 = extremely.

Items 4 and 5 are scored as follows: 0 = not at all, 1 = just a little, 2 = quite a bit, 3 = very much, 4 = extremely.

The scores are summed and the total score correlates positively with the degree of ED.
be excluded. It is important during this period to protect the child from physical injury. The recovery area should be quiet.

Parental presence in the recovery area may or may not help. It is extremely distressing for parents to be in a situation in which they cannot console their child. Parents must be informed about what is happening and be assured that the child has no pain and that the situation will pass.

Pharmacologic management
Treatment strategies evolve largely around drug administration manipulation, or administration of preventative drugs.

Premedication
Children who have had a stormy induction, or who are very frightened, are often restless on awakening. Most studies have used midazolam with varying results. Midazolam in itself can cause agitation. It does not reduce ED after sevoflurane⁶ anaesthesia and causes a ninefold increase in ED in children anaesthetised with halothane or isoflurane.⁷ In Dahmani’s meta-analysis, midazolam had no preventive effect on ED.⁸ Melatonin has been used, but this is not widely available. Ketamine and opiates reduced the incidence of ED, but were associated with a higher incidence of adverse side-effects. Other pre-medicants have been used and most worked in keeping the child sedated in the recovery area.

Manipulation of volatile agents
Higher doses of sevoflurane have been shown to increase ED. Some have advocated changing from sevoflurane to another agent after induction. This has had varying results. Mayer et al showed a significant reduction in ED after changing to desflurane after sevoflurane induction in ENT procedures.⁹ A similar strategy of stopping sevoflurane shortly before surgery and changing to another agent has also not worked. Desflurane in some studies caused more ED than sevoflurane.¹

Analgesic/sedative agents
The use of opiates such as fentanyl (1-2.5 µg/kg) and alfentanil (10 µg/kg)¹⁰ reduced the incidence of ED. The effect was seen in non- or minimally painful procedures as well, such as imaging, and myringotomy and grommets. The efficacy of opiates is probably due to their sedating effects or their potentiation of anaesthesia. Remifentanil has no effect on ED,¹¹,¹² The reduction in ED was also not seen with morphine.

The sedating effects of the alpha-2 receptor agonists clonidine (1 - 3 µg/kg IV over 10 minutes) and dexmeditomidine (0.3-1 µg/kg) also reduced ED.¹³ Administration routes were intravenous or caudal. This reduction was seen even with good analgesia from another source (caudal). As inhalational agents raise NAdr levels in the brain, the alpha-2 receptor agonists may exert their effects centrally by reducing NAdr levels. With clonidine, the number needed to treat (NNT) was 5.2 to prevent one occurrence of ED and 14.4 to prevent one severe episode of ED.⁴ Propofol, either by continuous infusion or as a bolus (1 mg/kg) just before the end of surgery, showed a protective effect against sevoflurane-induced ED.¹⁴,¹⁵ An induction dose only had no effect.⁸ Although ketamine has been used to reduce ED, ketamine itself can result in ED. Low doses seem to be effective, but can still have side-effects. Clonidine can be used to treat these side-effects, as the adverse effects of ketamine may be NAdr induced.¹⁶

Summary
ED is common after inhalation anaesthesia, especially if sevoflurane or desflurane is used. Pre-school children are particularly prone to exhibit ED. It is a self-limiting condition and occurs within the first 30 minutes after anaesthesia. Severe ED should be treated as the child can injure him/herself. It is also extremely distressing for both parents and health care personnel. Currently, there seem to be no long-term sequelae of ED.

Risk factors include the use of iso-, sevo- or desflurane, pre-school age, anxiety (including the parents) and emotional immaturity, and head and neck procedures. Premedication with midazolam has no effect on ED and may aggravate it. However, if the child is very anxious, then premedication may be given. Pain will exacerbate ED, but not cause it. ED can be treated with agents that have a sedative effect, such as propofol, fentanyl, alfentanil and alpha-2 receptor agonists. If there is a high risk for ED, then triggering agents should be avoided and/or the condition treated prophylactically.

References
1. Viljakovic GP, Sindjelic RP. Emergence delirium in children: many questions, few answers. Anesth Analg. 2007; 104: 84-91.
2. Sikich N, Lerman J. Developmental and psychometric evaluation for the paediatric anaesthesia emergence delirium score. Anaesthesiol. 2004; 100: 1138-45.
3. Meyer RR, Münster H et al. Isoflurane is associated with
a similar incidence of emergence agitation/delirium as sevoflurane in young children – a randomised controlled study. Paediatr Anaesth. 2007; 17(1): 56-60.

4. Tesoro S, Mezzetti D et al. Clonidine treatment for agitation in children after sevoflurane anaesthesia. Anesth Analg. 2005; 101: 1619-22.

5. Kain ZN, Mayers LC et al. Pre-operative anxiety, post-operative pain, and behavioural recovery in young children undergoing surgery. Paediatrics. 2006; 118(2): 851-8.

6. Breschan C, Platzer M, Stettner H. Midazolam does not reduce emergence delirium after sevoflurane anaesthesia in children. Pediatr Anaesth. 2007; 17(4): 347-52.

7. Cole JW, Murray DJ et al. Emergence behaviour in children: defining the incidence of excitement and agitation following anaesthesia. Paediatr Anaesth. 2002; 12(5): 442-7.

8. Dahmani S, Stany I et al. Pharmacological prevention of sevoflurane- and desflurane-related emergence agitation in children: a meta-analysis of published studies. BJA. 2010; 104(2): 216-23.

9. Mayer J, Boldt J et al. Desflurane anaesthesia after sevoflurane inhaled induction reduces severity of emergence agitation in children undergoing minor ear-nose–throat surgery compared with sevoflurane induction and maintenance. Anesth Analg. 2006; 102: 400-4.

10. Kim JY, Chang J et al. Post-induction alfentanil reduces sevoflurane-associated emergence agitation in children undergoing an adenotonsillectomy. Acta Anaesth Scand. 2009; 53(5): 678-81.

11. Sfyra E, Soumpasis I et al. Does remifentanil affect emergence agitation after sevoflurane anaesthesia in children? Europ J Anaesth. 2004; 21: 153 A625.

12. Kim HJ, Baik SW et al. The effect of remifentanil on sevoflurane anaesthesia in the paediatric patients. Korean J Anaesthesiol. 2007; (53) 5: 602-8

13. Isik B, Arslam M, et al. Dexmeditomidine decreases emergence agitation in paediatric patients after sevoflurane anaesthesia without surgery. Paediatr Anaesth. 2006; 16(7): 748-53.

14. Abu-Shawaml. Effect of propofol on emergence behaviour in children after sevoflurane anaesthesia. Paediatr Anaesth. 2008; 12 (1): 55-9

15. Aouad MT, Yazbeck-Karam VG et al. A single dose of propofol at the end of surgery for the prevention of emergence agitation in children undergoing strabismus surgery during sevoflurane anaesthesia. Anaesthesiol. 2007; 107 (5): 733-8.

16. Kubota T, Hirota K et al. Inhibitory effect of clonidine on ketamine-induced norepinephrine release from medial prefrontal cortex in rats. BJA. 1999; 83 (6): 945-7.