Obstetrical and Pediatric Anesthesia

# The ankle clonus test is not a clinically useful measure of spinal cord integrity in children

## *[Le test du clonus du pied n'est pas une mesure cliniquement utile de l'intégrité de la moelle épinière chez les enfants]*

Alastair Ewen MB CHB FRCA FRCPC, Robin G. Cox MB BS MRCP(UK) FRCA FRCPC, Sîon A. Davies MB BS FANZCA, Jeremy B. Luntley MB BS FRCA, Yair Rubin MD FRCPC, Gordon H. Fick BSc MSc PhD, Bevin B. Bart MD FRCPC

**Purpose:** Bilateral flexion-induced ankle clonus has been proposed as a test of spinal cord integrity during anesthesia for scoliosis surgery. The purpose of this study was to establish the reliability of this test in normal children emerging from volatile anesthesia. A secondary objective was to determine if there was a difference in the validity of this test with either sevoflurane or isoflurane anesthesia.

**Methods:** In a randomized, prospective blinded clinical trial, 32 healthy children aged three to 13 yr, were randomized to receive either isoflurane (Group I, $n = 15$) or sevoflurane (Group S, $n = 17$) for maintenance of anesthesia during dental restorative surgery. During emergence, an observer, blinded to group allocation, recorded ankle clonus scores (number of beats to a maximum of 5 on each side) at 60-sec intervals until tracheal extubation. End-tidal anesthetic concentration was measured contemporaneously.

**Results:** Non-sustained ankle clonus was elicited in a majority of children during emergence: 13 (87%) patients in Group I and 15 (88%) in Group S demonstrated at least non-sustained or unilateral clonus. However, bilateral sustained ($> 5$ beats·min$^{-1}$) ankle clonus occurred in only four (27%) patients in Group I and four (24%) patients in Group S ($P = 0.83$).

**Conclusion:** We conclude that the specificity of the ankle clonus test is too low to be clinically useful as a measure of spinal cord integrity in children, both when isoflurane and sevoflurane are used as the primary anesthetic agent.

***Objectif :*** *Le clonus du pied bilatéral induit par la flexion a été proposé comme test de l'intégrité de la moelle épinière pendant l'anesthésie pour une opération de scoliose. Le but de notre étude était d'établir la fiabilité de ce test chez des enfants normaux au réveil d'une anesthésie avec agent volatil. Un objectif secondaire était de déterminer s'il y avait une différence de validité du test avec l'anesthésie au sévoflurane ou à l'isoflurane.*

***Méthode :*** *Dans une étude clinique randomisée, prospective aveugle, 32 enfants de 3 à 13 ans ont été répartis au hasard et ont reçu de l'isoflurane (Groupe I, n = 15) ou du sévoflurane (Groupe S, n = 17) pour le maintien de l'anesthésie pendant une restauration dentaire chirurgicale. Pendant le retour à la conscience, un observateur impartial a enregistré les scores de clonus du pied (nombre de battements jusqu'à un maximum de 5 de chaque côté) à intervalles de 60 s jusqu'à l'extubation endotrachéale. La concentration télé-expiratoire d'anesthésique a été mesurée aux mêmes moments.*

***Résultats :*** *Un clonus non soutenu a été obtenu chez la majorité des enfants pendant le retour à la conscience : 13 (87 %) patients du Groupe I et 15 (88 %) du Groupe S ont présenté au moins un clonus non soutenu ou unilatéral. Cependant, un clonus bilatéral soutenu (> 5 battements·min$^{-1}$) est survenu chez seulement 4 (27 %) patients du Groupe I et 4 (24 %) du Groupe S (P= 0,83).*

***Conclusion :*** *La spécificité du test de clonus du pied est trop faible pour être cliniquement significative comme mesure de l'intégrité de la moelle épinière chez les enfants, autant avec l'isoflurane qu'avec le sévoflurane comme anesthésique principal.*

From the Division of Pediatric Anesthesia, Alberta Children's Hospital at the University of Calgary, Calgary, Alberta, Canada.

*Address correspondence to*: Dr. Robin Cox, Division of Pediatric Anesthesia, Alberta Children's Hospital at the University of Calgary, 1820 Richmond Road SW, Calgary, Alberta T2T 5C7, Canada. Phone: 403-943 7260; Fax: 403-943 7606; E-mail: robin.cox@calgaryhealthregion.ca

*Accepted for publication October 28, 2004.*

*Revision accepted February 16, 2005.*

SPINAL cord injury is a feared complication of surgery for scoliosis correction. Hoppenfeld *et al.*[1] have suggested that the absence of ankle clonus under "light anesthesia" may indicate spinal cord injury during spinal surgery. In this study, 958 adolescents with idiopathic scoliosis undergoing spinal instrumentation had their inspired concentration of volatile anesthetic agent deliberately reduced during spinal distraction. Bilateral ankle clonus could then be elicited in all but nine patients, and six of those nine awoke with a neurological deficit. On this evidence, the authors claimed that the ankle clonus test is a safe, sensitive, and easily performed test of spinal cord integrity.

The promise of such a non-invasive test holds considerable attraction for anesthesiologists and surgeons who care for children undergoing spinal surgery. Current monitoring techniques include the Stagnara "wake-up" test,[2] which can be very difficult to execute safely in children, and continuous somatosensory evoked potential monitoring,[3] which requires expensive equipment and a dedicated technician, and is limited to sensory column monitoring.

The results from Hoppenfeld *et al.*, however, are at variance with earlier investigations of neurologic phenomena during emergence. Rosenberg and colleagues[4] studied 29 healthy male patients undergoing superficial surgery during halothane-$N_2O$, enflurane-$N_2O$ and narcotic-$N_2O$ anesthesia. They found that the incidence of ankle clonus during emergence was 92% with enflurane, 63% with halothane and only 33% with narcotic based anesthesia. Furthermore, "sustained clonus" (which they did not define) occurred in only 50% of patients after enflurane, 12.5% of patients after halothane and did not occur at all following narcotic-$N_2O$ anesthesia. In a similar study of 30 healthy adults, McCulloch and Milne[5] compared enflurane and isoflurane. They found sustained ankle clonus (defined as clonus lasting greater than five seconds) in 57% of patients emerging from enflurane anesthesia and 31% of those emerging from isoflurane.

A weakness common to these studies is the failure to measure the end-tidal concentration of volatile anesthetic agent. From animal studies, we know that hyperreflexia occurs at subanesthetic concentrations of both fixed agents, such as barbiturates,[6,7] and volatile agents such as halothane.[8] It is believed that selective inhibition of descending inhibitory pathways by low concentrations of anesthetic agents raises the excitability of the motor neuron pool.[9] Reflex activity increases as motor neuron threshold decreases. A long conduction distance in the reflex pathway, for example between ankle flexors and extensors, increases the likelihood of rhythmic oscillations as the phase lag between stretch and muscle activity increases.[10] This is one explanation of the origins of ankle clonus and the rationale for the ankle clonus test as a monitor of spinal cord function.

Based on the aforementioned studies, the incidence of clonus in children will probably differ among the different volatile anesthetic agents. The reasons for this may have as much to do with pharmacokinetics as with pharmacodynamics. Halothane, for example, will have a slower decline in neuraxial concentration during emergence than a less soluble agent like sevoflurane. Signs of hyperreflexia, like ankle clonus, may be more likely during a slow emergence from anesthesia. Additionally, some anesthetic agents appear to have a propensity to cause excitatory phenomena. Etomidate[11] and enflurane[12] are such agents, and sevoflurane may be another.[13]

In this prospective, observer-blinded investigation, we sought to determine the overall validity of the ankle clonus test in healthy children undergoing general anesthesia for surgical procedures unrelated to spinal surgery. Furthermore, we hypothesized that the use of sevoflurane, with a low blood solubility, would be associated with a shorter recovery time and time to the onset of clonus than would isoflurane. We therefore tested this hypothesis by comparing the incidence of bilateral sustained ankle clonus during emergence from isoflurane or sevoflurane anesthesia in two randomized groups of children.

## Methods

The study was approved by the local Health Research Ethics Board. After obtaining written informed parental or guardian consent, we enrolled 32 children, ASA physical status I and II, aged between three and 13 yr, undergoing dental surgery of at least 30 min duration. We excluded children with known neurological or musculoskeletal abnormality, as well as children taking drugs that might interfere with spinal cord reflexes. This included anticonvulsants and methylphenidate.[14] We allocated each child randomly to one of two groups. Those in Group I received isoflurane for maintenance of anesthesia and those in Group S received sevoflurane.

No premedication was given. Absence of ankle clonus was confirmed in each patient prior to induction of anesthesia. We induced anesthesia in all children with sevoflurane and $N_2O$. Tracheal intubation was facilitated by mivacurium 0.2 $mg \cdot kg^{-1}$ and the lungs were ventilated with air and $O_2$ and either isoflurane 2% to 2.5% or sevoflurane 3.5% to 4%, titrated to signs of anesthetic depth. This was delivered at 150 $mL \cdot kg^{-1} \cdot min^{-1}$ via a pediatric circle system with a $CO_2$

TABLE

| | *Group I* | *Group S* |
|---|---|---|
| *Patients (n)* | 15 | 17 |
| Age (yr) | 7.3 ± 2.6 | 5.8 ± 1.6* |
| Weight (kg) | 27.7 ± 11.3 | 20.4 ± 4.9† |
| Duration of anesthesia (min) | 97.8 ± 41.8 | 80.3 ± 28.2 |
| Temperature at end of surgery (°C) | 36.1 ± 0.4 | 36.3 ± 0.6 |
| Time to onset of clonus (min) | 7.5 ± 2.0 | 10.2 ± 7.2‡ |
| Time to extubation (min) | 11.6 ± 3.0 | 15.2 ± 4.7§ |
| Patients with clonus (*n*) | 13 (87%) | 15 (88%) |
| Patients with bilateral sustained clonus (*n*) | 4 (27%) | 4 (25%) |
| Individual clonus scores | 23.6 ± 25.9 | 13.2 ± 12.6 |
| Somnolence score at clonus onset [median (range)] | 3.77 (3 - 4) | 3.73 (3 - 4) |

*$P < 0.05$. †$P < 0.05$. ‡$P = 0.017$(unpaired t test). §$P = 0.012$ (unpaired t test). Values are mean ± SD except where otherwise specified.

absorber. After neuromuscular transmission returned, as evaluated by train-of-four peripheral nerve stimulation, and each patient resumed spontaneous respiration, we gave *im* codeine phosphate 1 mg·kg$^{-1}$ and *iv* ondansetron 0.05 mg·kg$^{-1}$. The end-tidal concentration of isoflurane or sevoflurane was measured by side sampling from the circuit Y-piece using an AS/3 monitor (Datex-Ohmeda, Helsinki, Finland). Core temperature was measured by a rectal thermistor.

At the end of surgery, the volatile anesthetic agent was discontinued. A second observer, blinded to the anesthetic agent by a screen across the AS/3 monitor, checked for ankle clonus by dorsiflexing the patients' ankles in turn, every 60 sec. The anesthesiologist contemporaneously recorded the end-tidal concentrations of volatile anesthetic agent and $CO_2$. The number of beats of clonus, if present, was recorded for each foot. We defined sustained clonus as 5 or more beats. For each subject, the total number of beats of clonus during emergence was summated as a "clonus score".

The degree of somnolence of the patient was recorded according to the following scale:

1. Awake, responding to commands
2. Drowsy, opens eyes to commands
3. Spontaneous movement, swallowing or coughing
4. No spontaneous movement except respiration

We extubated the trachea when we judged that the patient's protective reflexes were adequate. End-tidal $CO_2$ and volatile concentration monitoring ceased after tracheal extubation.

On the basis of previously quoted incidences of clonus,[1] we calculated that a sample size of 15 would be required to detect a difference between two groups with incidences of ankle clonus of 40% and 90%, with an α-error of 0.05 and a power of 0.8. All data analyses were carried out according to a pre-established analysis plan. Data were analyzed using Intercooled Stata version 7 (Stata Corporation, College Station, TX, USA). Demographic data for each group were compared by unpaired t test. Group comparisons of clonus scores were made by Mann Whitney U-test. The proportions of patients with bilateral sustained clonus were compared between the two groups by Fisher's exact test. The times to onset of clonus and tracheal extubation were compared, between groups, after logarithmic transformation, by unpaired t test. For all analyses, $P < 0.05$ was considered statistically significant.

## Results

There were 15 patients (7 boys and 8 girls) in the isoflurane group and 17 (12 boys and 5 girls) in the sevoflurane group. Mean age (yr) and weight (kg) were greater in Group I than Group S (7.3 ± 2.6 *vs* 5.8 ± 1.6 ($P < 0.05$), and 27.7 ± 11.3 *vs* 20.4 ± 4.9 ($P < 0.05$) respectively). Details of anesthesia and emergence are shown in the Table.

The mean time to onset of clonus, and the mean time to tracheal extubation were significantly greater in Group S. Thirteen of 15 subjects (87%) in Group I, and 15 of 17 (88%) in Group S exhibited either sustained or non-sustained clonus. Bilateral sustained clonus occurred in only 4/17 patients (24%) in Group S and 4/15 (27%) in Group I. Mean individual clonus scores were not significantly different between the two groups: 23.6 (range 0–78) in Group I *vs* 13.2 (range 0–45) in Group S ($P = 0.17$). At the onset of clonus, somnolence scores were either 3 or 4 in all subjects. None of the subjects had evidence of neurologic impairment in the recovery room. All patients were normothermic during the observation period. The relationships between

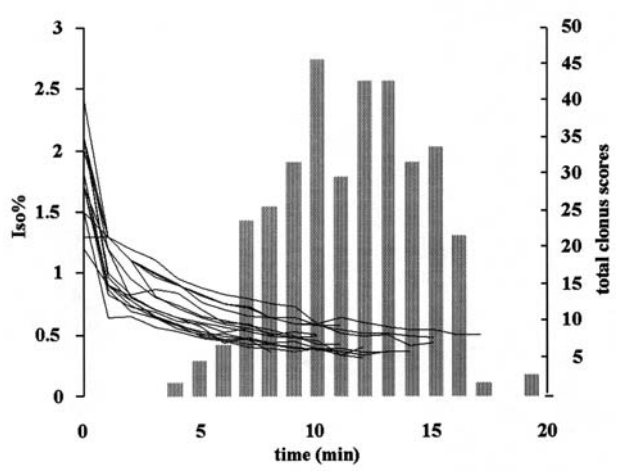


FIGURE 1 Solid lines show the washout curves for each subject during the first 20 min after emergence from isoflurane (Iso). Bars represent the summated clonus scores for all subjects in the Iso group during emergence.

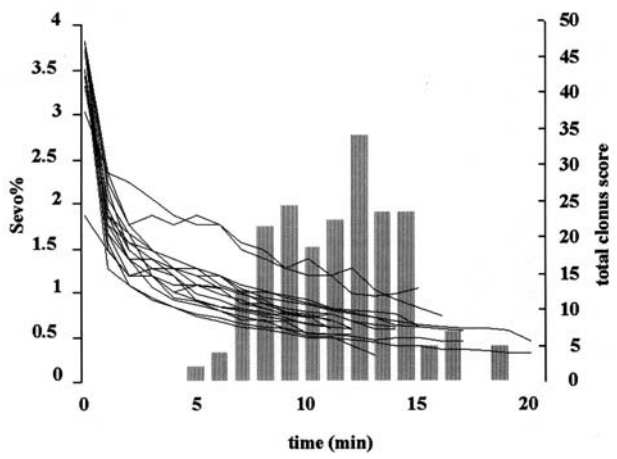


FIGURE 2 Solid lines show the washout curves for each subject during the first 20 min after emergence from sevoflurane (Sevo). Bars represent the summated clonus scores for all subjects in the Sevo group during emergence.

emergence time, group ankle clonus scores and the end-tidal concentrations of isoflurane and sevoflurane are displayed in Figures 1 and 2.

## Discussion

Our study confirms that flexion-induced ankle clonus is a common phenomenon during emergence from general anesthesia in children. We used a much less stringent definition of sustained clonus ($\geq$ 5 beats·min$^{-1}$) than McCulloch and Milne ($\geq$ 5 sec duration).[5] Despite this, fewer than a third of our neurologically intact patients exhibited sustained bilateral clonus during emergence. Although we evaluated both clonus scores and the presence of sustained bilateral clonus, in practice the clinician would use only the latter clinical sign, and we have demonstrated this to be an unreliable indicator of spinal cord integrity.

Our results showed that there was no difference in the incidence of clonus between the two groups, nor were the mean clonus scores statistically different between the two groups. The small size of this study increases the possibility of a type II error with respect to clonus score comparison, but we do not believe that we have failed to detect any clinically important difference between the two agents. As well, the more clinically useful indicator, the presence of sustained clonus, was elicited in very similar numbers across the two groups.

Our results are considerably at odds with those of Hoppenfeld *et al.*[1] One possible explanation for this finding is that the mean age of our study population (dental patients at the Alberta Children's Hospital) was significantly younger than the population of scoliosis surgery patients. Although the external validity of our study may appear low, we chose dental patients for several reasons. They all required tracheal intubation, which facilitated measurement of end-tidal volatile anesthetic concentration, and the procedures were usually of more than 30 min duration, which allowed for tissue equilibration of anesthetic agent.

We chose ranges of maintenance concentrations of isoflurane and sevoflurane that we considered equipotent.[15] Given the lower blood solubility of sevoflurane, compared with isoflurane, we expected that recovery time (time to extubation) and time to onset of clonus, would be shorter in Group S. The converse was true, suggesting that the depth of anesthesia at the beginning of emergence was greater in those children receiving sevoflurane. One possible confounding variable was the difference in ages and weights between the two groups. Although this was a statistically significant difference, the mean ages, for example, were unlikely to be clinically important (7.3 *vs* 5.8 years in Group I and Group S respectively). Nevertheless we acknowledge that this represents a potential weakness of our study.

Another important difference between our study and that of Hoppenfeld *et al.* relates to the time of surgery and consequent exposure to anesthetic agent. Our contention was that the presence of clonus would be related primarily to the end-tidal agent concentration. It is logical to suppose, however, that the time of the onset and duration of clonus will vary with the end-tidal concentration of agent just before closure of the vaporizer and to the length of anesthesia. This latter effect will vary with the solubility of the agent used. In any event, there were no significant differences between our two groups in terms of anesthesia time, but the exposure was likely less than in those studied by Hoppenfeld. Additionally, we closed off the vaporizer abruptly at the end of surgery, whereas we can speculate that Hoppenfeld used a more stepwise reduction in agent concentration.

Finally, there may be differences in core temperature among our subjects and those of some other investigators. The subjects of Rosenberg and colleagues' investigation were all normothermic.[4] McCulloch[5] measured, but did not report axillary temperature, and Hoppenfeld *et al.*[1] did not report core temperature. Shivering thermogenesis occurs in almost all hypothermic individuals after anesthesia but thermoregulation is only part of the etiology of postanesthetic clonus. Sessler and colleagues[16] have shown that spontaneous ankle clonus occurs commonly in hypothermic adults at isoflurane concentrations of between 0.5% and 0.1%, but flexion-induced clonus may occur at end-tidal isoflurane concentrations as high as 0.7%, and in normothermic individuals. Ankle clonus is but one of several signs of motor neuron hyperexcitability that have been variously described as "shakes", "spasticity" and "shivering".[17] Both shivering and flexion-induced clonus are large-amplitude involuntary oscillations with similar electromyographic signatures and a relatively consistent frequency range of 5 to 8 Hz.[18] This suggests that a common spinal reflex is responsible for both phenomena. Core temperatures in our subjects did not change significantly throughout the observation period. We did not measure rectal temperature prior to induction, but rectal temperatures immediately after induction ranged from 35.3° to 37.3°C, and no subject had a decrease of more than 0.2°C during the observation period.

Notwithstanding the methodological differences between out study and that of Hoppenfeld, we have demonstrated some serious deficiencies of the ankle clonus test. Our data show that ankle clonus is likely to be elicited at end-tidal concentrations of isoflurane or sevoflurane that are close to the MAC awake measured during slow emergence.[19] Other investigators[17] have demonstrated a close temporal relationship, during emergence, among onset of clonus, somatic response to pain, and awakening. In our subjects, the mean time from onset of clonus to tracheal extubation was less than five minutes in both groups. The utility of the ankle clonus test may well be limited by the risks of involuntary somatic responses to painful stimuli during testing. Its use as a less daunting alternative to the "wake-up" test includes a significant risk of awareness. For some patients, the difference between the ankle clonus test and the "wake-up test" may be moot. Our data demonstrated that, under the conditions of this study, neither sevoflurane nor isoflurane offers a specific advantage over each other with respect to their propensity to cause flexion-induced clonus. Although it may be a useful adjunct to other methods of monitoring spinal cord function during scoliosis surgery, the specificity of the ankle clonus test is too low to be clinically useful as a stand-alone alternative to the Stagnara "wake-up" test.

## References


1 *Hoppenfeld S, Gross A, Andrews C, Lonner B.* The ankle clonus test for assessment of the integrity of the spinal cord during operations for scoliosis. J Bone Joint Surg Am 1997; 79A: 208–12.

2 *Vauzelle C, Stagnara P, Jouvinroux P.* Functional monitoring of spinal cord activity during spinal surgery. Clin Orthop 1973; 93: 173–8.

3 *Grundy BL.* Intraoperative monitoring of sensory-evoked potentials. Anesthesiology 1983; 58: 72–87.

4 *Rosenberg H, Clofine R, Bialik O.* Neurologic changes during awakening from anesthesia. Anesthesiology 1981; 54: 125–30.

5 *McCulloch PR, Milne B.* Neurological phenomena during emergence from enflurane or isoflurane anaesthesia. Can J Anaesth 1990; 37: 739–42.

6 *Ewen A, Archer DP, Samanani N, Roth S.* Hyperalgesia during sedation: effects of barbiturates and propofol in the rat. Can J Anaesth 1995; 42: 532–40.

7 *Archer DP, Samanani N, Roth SH.* Nocifensive reflex thresholds in rats: measures of central nervous system effects of barbiturates. Can J Anaesth 1997; 44: 765–74.

8 *Zhang Y, Eger EI 2nd, Dutton RC, Sonner JM.* Inhaled anesthetics have hyperalgesic effects at 0.1 minimum alveolar anesthetic concentration. Anesth Analg 2000; 91: 462–6.

9 *Tanelian DL, Kosek P, Mody I, MacIver MB.* The role of the $GABA_A$ receptor/chloride channel complex in anesthesia. Anesthesiology 1993; 78: 757–76.

10 *Hidler JM, Rymer WZ.* A simulation study of reflex instability in spasticity: origins of clonus. IEEE Trans Rehabil Eng 1999; 7: 327–40.

11 *Meinck HM, Mohlenhof O, Kettler D.* Neurophysiological effects of etomidate, a new short-acting hypnotic. Clin Neurophysiol 1980; 50: 515–22.
12 *Rosen I, Soderberg M.* Electroencephalographic activity in children under enflurane anesthesia. Acta Anesthesiol Scand 1975; 19: 361–9.
13 *Komatsu H, Taie S, Endo S, et al.* Electrical seizures during sevoflurane anesthesia in two pediatric patients with epilepsy. Anesthesiology 1994; 81: 1535–7.
14 *Brichard G, Johnstone M.* The effect of methylphenidate (Ritalin) on post-halothane muscular spasticity. Br J Anaesth 1970; 42: 718–21.
15 *Mapleson WW.* Effect of age on MAC in humans: a meta-analysis. Br J Anaesth 1996; 76: 179–85.
16 *Sessler DI, Rubinstein EH, Moayeri A.* Physiologic responses to mild perianesthetic hypothermia in humans. Anesthesiology 1991; 75: 594–610.
17 *Soliman MG, Gillies DM.* Muscular hyperactivity after general anaesthesia. Can J Anaesth 1972; 19: 529–35.
18 *Pozos RS, Iaizzo PA.* Shivering and pathological and physiological clonic oscillations of the human ankle. J Appl Physiol 1991; 71: 1929–32.
19 *Katoh T, Suguro Y, Kimura T, Ikeda K.* Cerebral awakening concentration of sevoflurane and isoflurane predicted during slow and fast alveolar washout. Anesth Analg 1993; 77: 1012–7.