

## Postoperative Seizure Activity Following Enflurane Anesthesia

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Electroencephalographic and clinical evidences of seizure-like activity during administration of clinically useful concentrations<sup>1</sup> of enflurane have been documented in man, especially in the presence of respiratory alkalosis.<sup>2</sup> These responses can be terminated by reducing the enflurane concentration and/or returning the patient to normocarbia. Delayed postoperative seizure activity has been reported to occur in two patients without a history of previous seizure activity<sup>3</sup> and in one patient with a history of seizure activity.<sup>4</sup> This report describes the case of a patient in whom a generalized tonic/clonic convulsion that could have been related to enflurane anesthesia occurred in the immediate postanesthetic period.

## REPORT OF A CASE

A 23-year-old woman was hospitalized for evaluation of primary infertility with symptoms of endometriosis and irregular menses. She was taking no medication, had no known allergy, and had no personal or familial history of seizure activity. The remainder of her medical history and physical examination were unremarkable. Laboratory values and roentgenogram of the chest were normal.

The patient was premedicated with diazepam, 10 mg, orally, an hour prior to entering the operating room. After administration of *d*-tubocurarine, 3 mg, iv, anesthesia was induced with thiopental, 300 mg, iv. Endotracheal intubation was facilitated by the intravenous administration of succinylcholine. Anesthesia was initially maintained with 66 per cent nitrous oxide and enflurane at an inspired concentration of 2 per cent (Ohio<sup>®</sup> vaporizer) via a semiclosed circle CO<sub>2</sub> absorption system. The O<sub>2</sub> concentration was continuously monitored (Foregger<sup>®</sup> oxygen analyzer) and was never less than 30 per cent. Ventilation was controlled at a rate of approximately 12 breaths/min. Tidal volume was judged to be adequate on the basis of chest-wall movement and movement of the rebreathing reservoir. Pancuronium, 3 mg, was then given iv. Diagnostic laparoscopy with a tubal dye study revealed mild endometriosis, a 5 × 5-cm left ovarian cyst, and bilateral tubal patency. The intraoperative course was uneventful, and total anesthesia time was 45 min. The inspired concentration of enflurane during the operation was 2-3 per cent. Arterial blood pressures

ranged from 100/60 to 140/90 torr, and pulse rates ranged from 100 to 120 beats/min. Neuromuscular blockade was reversed with neostigmine, 5.0 mg, and atropine, 2.0 mg, iv. Blood loss was minimal, and lactated Ringer's solution with 5 per cent dextrose, 1,300 ml, was infused iv. Seizure activity was not observed intraoperatively. The patient resumed spontaneous respirations with an adequate tidal volume and was taken in good condition to the recovery room, where she breathed oxygen, 10 l/min, via a T-tube for 5 min. Then, after demonstration of good forced vital capacity, head lift for 5 sec, hand squeeze, and ability to follow voice commands, the trachea was extubated. The patient then received oxygen via face mask at 10 l/min. Blood pressure, pulse and respiratory rate remained stable in the recovery room. Level of consciousness varied from responses to painful stimuli only to adequate following of commands and answering questions appropriately. Approximately an hour after anesthesia, the patient had a generalized tonic/clonic convulsion lasting 90 sec that necessitated no therapy. For the next 15 min, her only responses to painful stimuli were withdrawal movements. Twenty minutes after the convulsion PaO<sub>2</sub> was 367 torr, PaCO<sub>2</sub> 40 torr, pH 7.40. Level of consciousness varied in a cyclic fashion over the next hour, from only responding to noxious stimuli with withdrawal movements to appropriate responses to questions. The remainder of her neurologic examination showed completely normal results. The patient did not experience any further seizure activity during the remainder of her three-day hospital stay. She remained alert, her condition was stable, and results of a complete neurologic examination at time of discharge were normal. Computerized axial tomography of the brain disclosed no abnormality. Electroencephalographic examination 12 days postoperatively revealed focal irregularities in the posterior right temporal lobe, while the electroencephalogram 40 days after anesthesia was normal.

## DISCUSSION

Ohm *et al.*<sup>3</sup> describe two adult female patients in whom seizure activity developed six and eight days following enflurane anesthesia. Neither of these patients had a history of previous seizure activity, but one of them had a strong family history of seizure disorders. Follow-up neurologic examinations of these two patients revealed no abnormality. Opitz *et al.*<sup>4</sup> described the case of a 9-year-old child with a history of epilepsy who had a generalized convulsion shortly after anesthesia and another convulsion an hour later.

Electroencephalographic activity characterized by high-amplitude spikes, spike-wave complexes with burst suppression, and myoclonic movements are known to occur during enflurane anesthesia in animals and man.<sup>5,6</sup> In studies performed on cats<sup>7</sup> with chronically implanted electrodes, high-voltage electroencephalographic activity was found to originate

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in the nuclei of the limbic system (amygdalae and hippocampus), and to a lesser extent, in midline thalamic nuclei, during enflurane anesthesia. The animals manifested occasional facial movements and were awake within 1 to 2 min following discontinuance of enflurane with loss of high-voltage spikes. By the second postoperative day high-voltage electroencephalographic activity occurring at short intervals was observed in the cortex and thalamic nuclei. This abnormal electroencephalographic activity reached a maximum four days after enflurane anesthesia. Spike activity was decreasing in intensity and frequency by the eighth postanesthetic day, and by the sixteenth day, the electroencephalogram appeared normal. Recently, Bassell repeated this experiment in cats and found no behavioral or electroencephalographic changes as long as four weeks following enflurane anesthesia.<sup>¶</sup>

Burchiel<sup>1</sup> anesthetized 12 healthy volunteers with enflurane. In six of these patients, either electroencephalographic or clinical evidence of seizure activity developed during the anesthesia. Eight patients showed posterior intermittent delta activity, and all subjects had significantly slowed alpha activity, persisting from 6 to 30 days following enflurane administration. At no point did *de novo* spike activity appear in any subject following enflurane. Burchiel<sup>8</sup> found that three of seven healthy volunteers experienced *de novo* sharp wave activity in the first week, lasting as long as 30 days following halothane anesthesia. Five patients had posterior delta or theta activity, and all showed significant slowing of alpha activity. Several cases where electroencephalographic seizure activity during enflurane anesthesia has developed into a grand mal pattern followed by postictal slowing have been reported.<sup>9</sup>

Darimont and Jenkins<sup>10</sup> have shown that in animals diazepam may lower the threshold for spiking activity by shifting leftward the curve relating spiking activity and enflurane concentration. Castro,<sup>\*\*</sup> in a human study, found that diazepam potentiated enflurane-induced electroencephalographic seizure activity in man by increasing the number of spikes and spike waves and prolonging the period of burst suppression. This patient was premedicated with diazepam, 10 mg,

approximately three hours prior to seizure activity. Small doses of thiopental during light enflurane anesthesia can transiently exacerbate electroencephalographic seizure activity.<sup>11</sup> At a greater depth of anesthesia, thiopental diminishes seizure activity. The patient received thiopental, 300 mg, iv, for induction of anesthesia, which was an adequate induction dose (6.0 mg/kg).

Seizure activity during induction and in the operative period may be masked due to the administration of barbiturates and muscle relaxants. The use of enflurane in patients with histories of seizures, mass intracranial and space-occupying lesions, and increased intracranial pressures should also be carefully considered. The effects of enflurane anesthesia in epileptic patients have been studied.<sup>4</sup> Nineteen of 21 epileptic patients did not show clinical evidence of convulsive activity. However, tonic/clonic activity developed in two patients, with a recurrence in one patient an hour after anesthesia. Whenever possible, an alternate anesthetic would seem more appropriate for these patients.

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