INTRODUCTION: Halothane lowers the dose of epinephrine needed to induce ventricular arrhythmias in experimental animals and in patients. A previous study in dogs suggested that a higher concentration of halothane (2.0 MAC) appeared to sensitize the heart less to epinephrine arrhythmias than a lower concentration (1.2 MAC); however no statistical analysis was performed. Our study was designed to definitively determine whether varying halothane concentration over a clinically relevant range (0.5% to 2.0%) alters the arrhythmogenic dose of epinephrine (ADE).

METHODS: Anesthesia was induced and maintained in unmedicated dogs with halothane in oxygen. Tracheal intubation was performed without muscle relaxants and ventilation was controlled to achieve normocarbia. Maintenance fluids consisted of 5% dextrose in 0.2% NaCl supplemented with 89 mg/dl of NaHCO3 to prevent the metabolic acidosis observed with repeated epinephrine infusions. End-tidal CO2 and halothane, arterial blood pressure, and lead II of the EKG were continuously recorded.

The ADE was measured according to the method of Pace et al. A fresh 100 µg/kg solution of epinephrine in 5% dextrose was infused via a syringe pump for three minutes at a constant rate. If the arrhythmia threshold (4 or more ventricular ectopic beats in a 15 second period or any tachyarrhythmia producing a life-threatening drop in blood pressure) was not achieved, the animal was allowed to recover from the epinephrine infusion before a logarithmically spaced higher dose was infused. This process of progressively larger doses of epinephrine was continued until the ADE was established.

MAC for halothane in the dog is 0.9%; therefore the ADE assessment at 0.5% halothane may be affected by endogenous epinephrine release secondary to light anesthesia. NaHCO	extsubscript{3} and barbiturates were avoided because both of these supplemental anesthetic agents sensitize the myocardium to epinephrine; etomidate has not previously been investigated in this regard. We sought to demonstrate that etomidate does not enhance epinephrine arrhythmogenicity so that it could be used as a supplemental agent in this study. Therefore, 10 dogs were anesthetized with halothane as described above. After the baseline ADE was determined with halothane alone, an intravenous loading dose of etomidate, 1 mg/kg, was given and followed by a continuous infusion of 4 mg/kg/hr. Blood samples taken at intervals confirmed that therapeutic levels of etomidate were achieved.

After a steady-state of etomidate was established, the ADE was again determined. Statistical analysis by the t test for paired data revealed no significant difference in the ADE values with and without etomidate (p > 0.05).

For the definitive study, the ADE was determined in 10 dogs at each of four end-tidal concentrations (0.5, 1.0, 1.5 and 2.0%). The initial concentration and the order of subsequent concentrations was varied amongst animals.

The ADE values at each concentration of halothane were compared by analysis of variance for repeated measures. A p value of < 0.05 was considered significant.

RESULTS: Halothane concentration was shown to have no significant influence on the ADE (p > 0.05).

<table>
<thead>
<tr>
<th>HALOTHANE (%)</th>
<th>ADE (µg/kg/min)</th>
<th>mean ± SD</th>
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<tbody>
<tr>
<td>0.5</td>
<td>3.45 ± 1.84</td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td>3.31 ± 1.57</td>
<td></td>
</tr>
<tr>
<td>1.5</td>
<td>2.93 ± 1.81</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>3.20 ± 1.71</td>
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</table>

DISCUSSION: Our study showed that the ADE for halothane was not dose dependent, the simple presence of halothane producing a consistent and reproducible ADE independent of its concentration throughout a clinically relevant range. This suggests that in the patient who manifests ventricular arrhythmias due to exogenous epinephrine administration the potentiation of these arrhythmias by halothane will persist until the end-tidal halothane concentration drops to at least 0.5%. Adjusting halothane concentration to reduce these arrhythmias is a maneuver that may take many minutes, depending upon the initial concentration and the duration of the anesthetic to that moment. Other therapeutic modalities may be required before the effects of reducing the halothane concentration may be seen.

Additionally, etomidate was shown not to alter the ADE in dogs anesthetized with halothane. Etomidate, rather than thiopental, may therefore be the preferred induction agent for patients with a history of malignant ventricular arrhythmias.

REFERENCES: