The studies carried out *in vitro*, which demonstrated inhibition of Na K Mg-ATPase, are of interest since the degree of inhibition caused by diphenylhydantoin alone was minimal and not statistically significant. This inhibition was markedly augmented by the presence of ouabain especially in concentrations of 10^{-4} M and 10^{-5} M. This effect of diphenylhydantoin in inhibiting Na K Mg-ATPase in the presence of ouabain was statistically significant and dose related and indicates that diphenylhydantoin *in vitro* may inhibit Na K Mg-ATPase to a small extent but that the inhibition is augmented by the presence of other inhibitors.

These results suggest that under certain circumstances diphenylhydantoin may act upon the Na K Mg-ATPase fraction of brain.

Departments of Pharmacology and Medicine (Neurology),
Yale University School of Medicine,
New Haven, Conn., U.S.A.

J. H. PINCUS
N. J. GIARMAN

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Anesthesia LXXII: Anesthesia with deuterochloroform*

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IN OUR previous studies[1] we showed that deuterated ethylene, evoked anesthesia in dogs similar to that induced by ethylene, and also that it did not sensitize the heart to challenging doses of epinephrine. In the latter respect it also resembles ethylene. Recently, our attention has again been focused on deuterated compounds[2] and their anesthetic properties. Having available a sample of deuterated chloroform we became interested in determining the character of the anesthetic syndrome it elicits, whether or not deuterium is exchanged for hydrogen during anesthesia, and whether deuterochloroform sensitizes the heart to epinephrine as does chloroform.

The deuterated chloroform was obtained from Volk and had an isotope purity better than 99·5 atom per cent.

The chloroform was "Chloroform for Anesthesia," N. F. Merck. The isotopic analyses were made with a CEC model 21103C mass spectrometer.

Anesthesia was conducted on Swiss-Webster albino mice ICR strain and mongrel dogs.

The mice, in groups of five, were placed in a 4-l. jar of oxygen with a gauze bag of soda lime. The anesthetic agent was introduced through a stopcock, and anesthesia was allowed to continue for 30 min. The gaseous contents of the jar were then drawn off by mild suction through a trap chilled with CO_2 ice and ethylene glycol monoethyl ether acetate. This was continued for 30 min. The frozen gases from the jar were thawed and subjected to mass spectrometric analysis.

The dogs were anesthetized via a mask with a closed-circuit Ohio infant inhalation set. The anesthetic was injected through a specially devised mask onto gauze.

The initial dose was 0·1 ml/kg. Additional chloroform was given during the course of the experiment to maintain anesthesia, as far as possible, in stage 3, plane 3. Control electrocardiograms (ECGs) (lead II) were obtained with a Sanborn Cardiette.

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Epinephrine was injected into the saphenous vein, 10 μg/kg of a 1:100,000 solution. An ECG was taken immediately after the injection. The dogs were allowed to recover promptly.

The same dogs were employed 2 days later, with deuterochloroform as the agent and the same procedure followed.

Mice. The animals responded to the anesthetic action of $CDCl_3$ as they had responded to $CHCl_3$. The anesthetic syndromes were similar quantitatively and qualitatively. There were three deaths in 20 mice with $CHCl_3$ and one with $CDCl_3$; this difference is not significant.

Deuterium–hydrogen exchange. The exhaled vapors of the mice were subjected to mass spectrometric analysis. The exhaled deuterated chloroform had the same isotopic content as the $CDCl_3$ before use, indicating the absence of exchange.

Cardiac sensitization (dogs). The anesthetic syndromes in dogs resulting from $CHCl_3$ and $CDCl_3$ appear essentially the same. It is our impression from these limited studies that $CDCl_3$ is slightly more potent, since 20 per cent more $CHCl_3$ was necessary to achieve apparently the same stage of anesthesia in the same five dogs. Also with $CDCl_3$, under like experimental conditions, three animals showed threatened respiratory arrest.

With $CHCl_3$, 5/5 animals responded to the epinephrine challenge with marked arrhythmias. A typical electrocardiogram is shown in Fig. 1. The epinephrine injection during $CDCl_3$ anesthesia produced marked arrhythmias in all animals also. One of the dogs exhibited an irreversible ventricular fibrillation with subsequent cardiac arrest. The electrocardiogram of the same dog shown in Fig. 1 is shown in Fig. 2 under $CDCl_3$ and epinephrine.

Our principal aim in this study was to determine whether, during anesthesia, there is atomic transfer between body tissues and the anesthetic agent. The question becomes especially pertinent since Van Dyke, *et al.*[3] have shown that many volatile anesthetics are partially metabolized. In addition, we were curious about the anesthetic syndrome of $CDCl_3$, since there are marked deviations in the pharmacologic responses of D_2O[4] and deuteroethanol[5] from their corresponding hydrogen analogs. This did not prevail with ethylene or ether, and in these studies it was shown that $CDCl_3$ and $CHCl_3$ elicit similar anesthetic responses.

In cardiac sensitization to epinephrine, it appears that the presence of the hydrocarbon in the cardiac tissue interferes with the wave of excitation, disrupting cardiac rhythm.[6] This interference is likely due to certain atomic and/or electronic configurations of the hydrocarbon. For example, the single electron shared bond between the carbon atoms in ethane causes interference and arrhythmias. The double electron pair shared in the ethylene molecule does not evoke this response. It therefore occurred to us that the additional neutron in the $CDCl_3$ might so modify the molecule as to change its behavior with respect to cardiac sensitization. The data clearly show that this does not obtain.

Our conclusions are that deuterochloroform causes an anesthetic syndrome similar to that of chloroform; deuterium does not exchange with tissue constituents for hydrogen during anesthesia with $CDCl_3$; and deuterochloroform sensitizes the heart of the dog to challenging doses of epinephrine.

Department of Chemistry,
Johns Hopkins University, and
The Huntingdon Research Center,
Baltimore, Md., U.S.A.

JOHN C. KRANTZ, JR.
WALTER S. KOSKI
CLAIRE K. LOECHER

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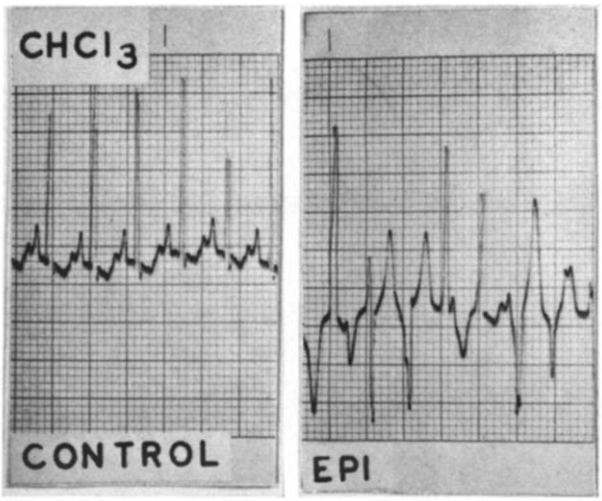

FIG. 1. Lead II, ECG. Dog anesthetized with $CHCl_3$; ECG after epinephrine challenge.

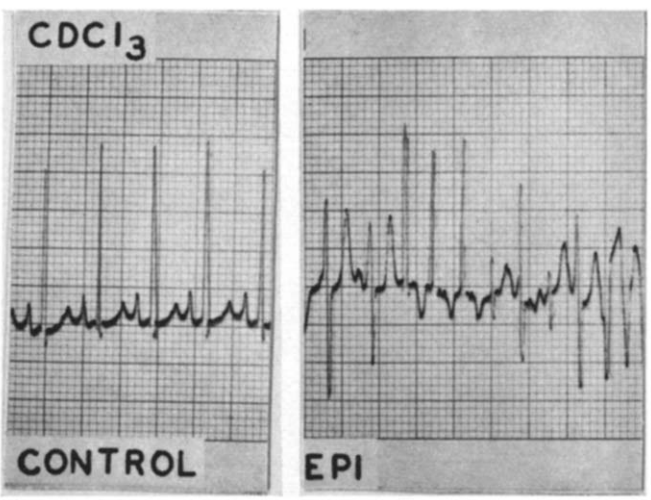

FIG. 2. Lead II, ECG. Dog anesthetized with $CDCl_3$; ECG after epinephrine challenge.