

ELECTROCARDIOGRAPHIC CHANGES DURING ETHYL CHLORIDE AND VINYL ETHER ANESTHESIA IN THE DOG AND MAN * †

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IN spite of numerous fatalities which have occurred in the past from ethyl chloride many practitioners continue to use it as an inhalation anesthetic for brief surgical procedures or as a preliminary anesthetic agent to ether by the open drop technic. Fatalities from the use of this agent usually occur without warning shortly after administration is begun (1). The exact mechanism causing them has never been defined, although it has been assumed that they result from ventricular fibrillation or cardiac standstill.

In view of continued use of the drug with apparent success we decided to review its pharmacology and re-evaluate its properties as an anesthetic agent. Data on many aspects of the pharmacology of ethyl chloride are lacking. Discussions in current textbooks are largely résumés of observations of Embley (2). Additional data on its cardiac effects, particularly electrocardiographic changes, appeared desirable; therefore, we undertook this present study. Inasmuch as vinyl ether (vinethene) is used for the same purposes and in the same manner as ethyl chloride and has, to a large extent, supplanted it, a comparative study of its effects upon the heart was also undertaken.

METHOD

Both dogs and human subjects were studied. The open drop technic was used for induction of both drugs, inasmuch as this is the technic most frequently employed clinically. After induction the dogs were intubated and anesthesia was maintained on a closed, to-and-fro carbon-dioxide absorption system. Anesthesia in the human subjects was maintained by the open drop technic throughout the entire course of anesthesia. Control electrocardiographic tracings were taken prior to anesthesia or premedication. Continuous tracings, using lead II, were taken from the moment of induction until either death or complete recovery ensued. Concurrent blood pressure studies were not made.

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RESULTS USING ETHYL CHLORIDE IN DOGS

Thirty dogs were used in the study. A group of 21 unpremedicated dogs was first studied. Later one group was given atropine, 0.1 mg. per kilogram, intravenously fifteen minutes before anesthesia, to observe the effects of depressing the vagus nerve; another morphine, 2 mg. per kilogram to observe the effects of sedation, and another a combination of morphine and atropine to observe the combined effects of sedation and depressing the vagus nerve. The animals were deliberately given an overdose at the conclusion of the experiment, and attempts were made to resuscitate them.

Ethyl chloride appeared to affect the heart in two ways: (1) Inhibition of the conducting mechanism owing to vagal stimulation; and (2) direct depression of the cardiac tissues. Inhibition due to vagal stimulation preceded cardiac depression in every instance. It usually appeared eighteen to 120 seconds after induction and was noted during plane 1 or 2 of stage III anesthesia. In several instances, the animal was still in stage II when vagal inhibition appeared. The first manifestation of inhibition (fig. 1) was depression of the S-A node, with a shift of the pacemaker from the head to the tail of the node or to the wall of the atrium. In most cases the P wave changed from its normal upright to a markedly widened biphasic contour. Almost immediately after the appearance of the abnormal P wave either an A-V block, with a slow idioventricular rhythm, or a nodal rhythm or ventricular fibrillation developed. When A-V block developed, the auricles maintained a separate rhythm but showed a bizarre spread of conduction through the auricular tissue. The ventricular rate was sometimes as low as 5 or 6 per minute. The A-V block and bradycardia could be reversed by discontinuing and washing the ethyl chloride out of the lungs by controlled respiration.

Ventricular fibrillation occurred within the first two minutes in 2 of the unpremedicated animals (fig. 2). We are unable to explain how this vagal stimulation precipitated ventricular fibrillation. The dogs ceased breathing after the fibrillation began. Fibrillation could not be reversed by artificial respiration with oxygen. Other methods of cardiac resuscitation were not attempted. The vagal inhibition appeared in all animals not premedicated with atropine. It was absent in all animals which received atropine. It is noteworthy that the dose of atropine employed is nowhere near that ordinarily stated as being necessary to block the vagus completely (1 to 2 mg. per kilogram). As the vagal effects disappeared the complexes assumed their normal appearances until the direct depressant effects became established.

The depressant effects of ethyl chloride on the cardiac tissues occurred later in the course of anesthesia and always followed the vagal inhibition when the latter occurred. They were preceded in most instances by brief periods of excitation manifested by tachycardia. In 20 instances they were noted in plane 2, 3 or 4 of stage III. In others

they appeared after respiration had ceased from overdosage (stage IV). The periods of anesthesia varied from one to thirty minutes, with an average duration of ten minutes.

The direct effects were ushered in by sinus tachycardia with rates as high as 300 beats per minute. As anesthesia deepened an A-V block,

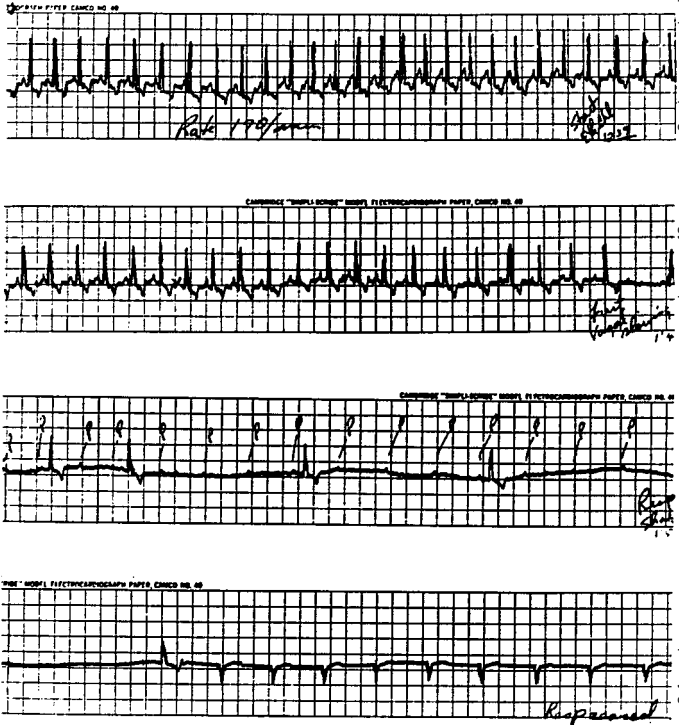


FIG. 1. Segments of continuous electrocardiographic tracings (lead II) of unmedicated dog showing onset of vagal inhibition of cardiac tissues.

idioventricular rhythm, and widening and slurring of the QRS complexes appeared, which were interpreted as manifestations of a depression of both automatic tissue and myocardium. As the concentration was further increased death ensued from asystole in 13 animals and from ventricular fibrillation in 9 animals.

These changes could be reversed if the drug was discontinued and artificial respiration instituted before the development of widened QRS complexes or ventricular fibrillation or cardiac standstill. Manifestation of some degree of cardiac depression appeared in every experiment. Atropine afforded no protection to the heart from the direct de-

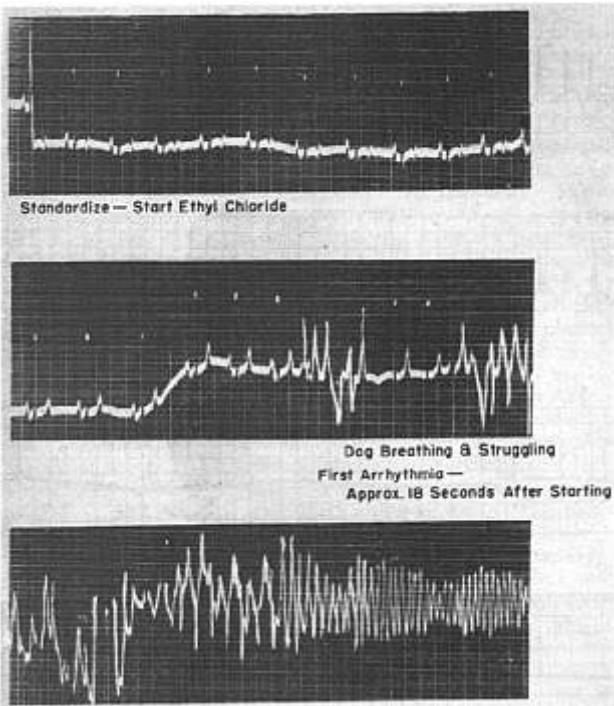


FIG. 2. Segments of continuous electrocardiographic tracings (lead II) of unmedicated dog showing onset of ventricular fibrillation approximately eighteen seconds after starting ethyl chloride anesthesia.

pressant action of the drug. The effect of larger doses of atropine on the depressant action was not studied as it seemed reasonable to assume they would afford no protection.

Scopolamine, 0.1 mg. per kilogram, was used in 3 instances and also found to be effective in protecting against the vagal inhibition. Ban-

thine (β -diethylaminoethyl xanthine-9-carboxylate methobromide), 5 mg. per kilogram, was administered intravenously fifteen minutes prior to anesthesia in 4 instances. This drug is both a peripheral anticholinergic and autonomic ganglionic blocking agent. It behaved qualitatively similar to atropine. The release of endogenous epinephrine from stimulation during light anesthesia has been assumed to be the cause of ventricular fibrillation in a heart sensitized by ethyl chloride. A sympatholytic drug should prevent this. Prisolone (2-benzylimidazoline hydrochloride), 5 mg. per kilogram, intravenously, was administered fifteen minutes prior to anesthesia in three experiments. It afforded no protection whatsoever. Morphine quieted the animals but appeared to offer no protection against either the vagal inhibition or the direct cardiac depression. Painful stimuli, induced by external stimulation of the pharyngeal and tracheal mucosa by ether vapor, neither precipitated nor aggravated any disturbances in conduction.

RESULTS USING ETHYL CHLORIDE IN MAN

Eighteen unoperated subjects between the ages of 5 and 12 were next studied. In view of the foregoing observations, subjects premedicated with atropine were first studied. Depth of anesthesia was carefully controlled and maintained as nearly as possible between plane 1 and 2 of stage III. No notable changes in the electrocardiographic record were observed. Ether was then added or the subject was allowed to recover. As in the case of the dog, painful stimuli and ether were without effect. Subjects were then anesthetized without preanesthetic medication with atropine. The identical early changes due to vagal inhibition observed in the experiments in the dog appeared. The drug was immediately discontinued and atropine, 0.25 mg., was injected intravenously. Reversal of the vagal inhibition occurred within twenty or more seconds. Tachycardia followed, which was probably the result of loss of vagal tone. Anesthesia was maintained in plane 1 of stage III, and no attempt was made to demonstrate the depressant effects of drug upon the myocardium.

RESULTS USING VINYL ETHER IN DOGS AND MAN

Three dogs and 12 human subjects were similarly studied during vinyl ether anesthesia without preanesthetic administration of atropine or morphine. Neither the vagal inhibition nor the depression of cardiac tissues, which were noted with ethyl chloride, occurred. As stage IV was approached the complexes assumed a low voltage or evidence of an interference dissociation appeared in both animals and human subjects. These observations confirm those of Meek and his associates (3). None of the dogs anesthetized with vinyl ether died. Resuscitation by artificial respiration was successful in every instance in which apnea resulted from overdose.

DISCUSSION

The electrocardiographic changes during ethyl chloride anesthesia herein described are of a serious nature and shed some light on the possible cause of sudden death during clinical use of the drug. Anesthetists rely largely upon the character of respiration as a guide to depth of anesthesia. The fact that respiration may continue for some moments after effective cardiac action has ceased during ethyl chloride anesthesia must be stressed. Any drug behaving in this manner is unsafe for clinical use. Although Embley used methods other than the electrocardiogram for studying heart action, he likewise concluded that ethyl chloride causes an evanescent initial inhibition due to vagal stimulation and a later direct depression of cardiac tissues. He attached little significance to the vagal inhibition and did not indicate that ventricular fibrillation or asystole is a possible sequela. It is difficult to say what role the vagal inhibition may play in causing fatalities. Certainly, when the doses of atropine ordinarily employed in clinical anesthesia afford protection to the vagal inhibition, the use of ethyl chloride without atropine is not justified under any circumstance. It is not unreasonable, however, to infer that fatalities are largely the result of cardiac depression from overdosage. From the standpoint of cardiac action, vinyl ether appears to be preferable to ethyl chloride as an inhalation anesthetic.

SUMMARY

During ethyl chloride anesthesia electrocardiographic changes suggest a twofold effect on the heart: (1) an inhibition due to vagal stimulation, which appears early in the course of anesthesia, and (2) a direct depression of the cardiac tissues. The vagal inhibition is prevented by premedication with anticholinergic drugs. Asystole or ventricular fibrillation occurs as a result of these effects even before respiration ceases. Vinyl ether does not cause these changes.

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