ELECTROCARDIOGRAPHIC STUDIES DURING ENDOTRACHEAL INTUBATION. III. EFFECTS DURING GENERAL ANESTHESIA AND INTRAVENOUS DIETHYLAMINOETHANOL* †

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In previous communications it was indicated that the incidence and the severity of cardiac arrhythmias that occur during endotracheal intubation were significantly reduced when procaine hydrochloride was injected intravenously during general anesthesia prior to endotracheal intubation (1, 2). Since it has been shown that procaine is rapidly hydrolyzed after intravenous administration to diethylaminoethanol (hereafter referred to as DEAE) and para-amino benzoic acid (3), it was deemed desirable to investigate the effects of DEAE upon the cardiac disturbances produced by endotracheal intubation. Recent studies on DEAE have indicated that this primary hydrolytic product of procaine, like procaine itself, is capable of reverting ventricular arrhythmias produced by cyclopropane-epinephrine to sinus rhythm (4). Larger doses of DEAE (about ten times that of procaine) are required to obtain this therapeutic effect but DEAE has been found to be almost devoid of any toxic manifestations. Indeed, it was found to be effective and nontoxic in conscious humans: it has suppressed ventricular premature contractions for short periods and it has been successful in reverting ventricular tachycardia to sinus rhythm.

In the present report, an analysis is made of the effects on the electrocardiograms in a series of 114 adult patients who were intubated during anesthesia with various anesthetic agents and in whom DEAE, 10 cc. of a 10 per cent concentration (1 Gm.), was injected intravenously one to five minutes before endotracheal intubation.

METHOD

As in the preceding series, control electrocardiograms of the first three leads were obtained in all patients before anesthesia. Subse-

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TABLE 1

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<td>Cyclopropane and cocaine</td>
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<td>Nitrous oxide, ether and cocaine</td>
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<td>Pentothal sodium intravenously</td>
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<td>Pentothal sodium and curare</td>
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<td>Pentothal sodium, curare and cocaine</td>
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<td><strong>Total</strong></td>
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Fragmented lead 2 electrocardiographic tracings were taken during anesthesia, at the time of injection of DEAE, one minute after the injection, at the time of intubation and after intubation at frequent intervals. Tracings were completed on 114 patients who underwent surgical procedures in which endotracheal intubation was an elective procedure. An attempt was made to approximate the number of different anesthetic agents employed with that of the preceding series (table 1).

### Results

**Cyclopropane and Ether.**—Completed electrocardiographic records were obtained in 35 cases in which anesthesia was induced with cyclopropane and maintained with ether. Intubation was carried out at a depth of second plane in 23 cases and in third plane in 12 cases. In each instance 1 Gm. of DEAE in a 10 per cent concentration was injected intravenously one to five minutes before intubation.

Of the 23 patients who were intubated during cyclopropane-ether anesthesia in the second plane, 10 showed no change at any time in the electrocardiograms. This compares well with the previous series in which procaine hydrochloride, 100 mg., was injected instead of DEAE and in which 11 out of 26 patients showed no change on the electrocardiogram under similar conditions. In both instances there was a significant improvement over the first series in which only 3 of 24 patients showed no electrocardiographic change when the only difference was omission of the intravenous procaine or DEAE. In addition to the 10 uneventful cases, a transitory nodal rhythm developed in one patient about thirty seconds after the injection of DEAE. This nodal rhythm returned to normal in two minutes and remained normal during and after intubation.

Sinus tachycardia was produced at the time of intubation in only one instance; this is in contrast to an incidence of 11 in the series in which procaine or DEAE had been omitted. The case in question was that of a patient whose control electrocardiographic tracings before anesthesia showed inverted T waves in the second and third leads. Follow-
ing anesthetization with cyclopropane and excess oxygen, the T waves became upright as soon as the first plane of surgical anesthesia was attained. They remained upright after the administration of DEAE and thereafter for the remainder of the operation. During the moment of intubation, the heart rate increased from 100 to 140 per minute and this tachycardia persisted for two minutes.

In 8 patients there was no electrocardiographic change before or during intubation, but one to four minutes after intubation the patients manifested a “bucking” reaction, and sinus tachycardia developed at that time. In 3 instances the rate increased to 120 per minute, in 4 it increased to 130 per minute, and in 1 case to 140 per minute. The tachycardias so produced were maintained for several minutes until the inserted tube was tolerated.

In one instance, arrhythmia did not occur until one minute after intubation when “bucking” was manifested. This was followed by frequent ventricular premature contractions which were sustained for five minutes.

Moderate laryngeal spasm developed in one case when ether was administered following the cyclopropane induction. As a result the heart rate increased from 75 to 105 per minute. No arrhythmia was produced at any time and intubation was uneventful.

In 2 patients, arrhythmias apparently disappeared at the moment of intubation. One patient manifested persistent ventricular premature contractions which suddenly disappeared at the time the endotracheal tube was inserted. The other had auricular fibrillation before anesthesia. After cyclopropane and ether anesthesia, this shifted to sinus tachycardia with ventricular premature contractions. One minute after the administration of DEAE, the rhythm became regular sinus tachycardia at a rate of 120 per minute; the regular sinus rhythm was maintained at intubation and during the rest of the operation.

When endotracheal intubation was performed following cyclopropane induction supplemented by ether until the third plane was reached, and DEAE was injected before intubation, there were no electrocardiographic changes in 11 of 12 cases at the moment of intubation. The one patient who displayed an arrhythmia at intubation had auricular fibrillation before anesthesia. The auricular fibrillation persisted, and at intubation it was complicated by the appearance of premature ventricular contractions. In one instance, a nodal rhythm developed about one minute after the administration of DEAE and lasted for ninety seconds. This nodal rhythm reverted spontaneously to regular sinus rhythm before intubation and there was no further change at or after intubation. In another instance, no change occurred until one minute after intubation when the heart rate increased from 80 to 105 per minute. In 2 patients, frequent ventricular premature contractions were produced during cyclopropane-ether anesthesia. They were eliminated sixty to ninety seconds after the intravenous injection of
DEAE and no further alteration in cardiac rhythm occurred thereafter. Figure 1 illustrates one of these cases.

*Cyclopropane, Ether and Cocainization.*—Endotracheal intubation performed during cyclopropane-ether anesthesia and intravenous DEAE combined with 10 per cent cocaine spray of the glottis was studied in a group of 13 cases. Five patients were intubated during second plane and 8 during third plane anesthesia. As in the procaine series, the results showed fewer disturbances compared to the first series when intravenous procaine or DEAE was not administered.

Three of the 5 patients who were intubated during second plane under these conditions showed no electrocardiographic disturbance at the time of intubation. In one of the patients, sinus tachycardia at a rate of 135 per minute was produced at intubation. In another, frequent ventricular premature contractions developed at intubation and persisted for five minutes.

![Figure 1](image)

**Fig. 1.** Clearance of ventricular premature contractions during cyclopropane-ether anesthesia one minute after the intravenous administration of diethylaminoethanol. The upper tracing (a), control lead 2, shows a regular sinus rhythm at a rate of 60 per minute. In the middle tracing (b), during second plane cyclopropane-ether anesthesia, bigeminal ventricular premature contractions are recorded. The lower tracing (c), taken one minute after the intravenous injection of 1 Gm. of diethylaminoethanol, shows a regular sinus rhythm at a rate of 95 per minute.

Six of the 8 patients who were intubated during third plane cyclopropane-ether anesthesia complemented by DEAE and cocainization of the glottis had no electrocardiographic change at the time of intubation. In one instance, sinus tachycardia at a rate of 120 per minute occurred at intubation. In another case, ventricular premature contractions appeared at intubation.

In one case, there was no cardiac change until one minute after intubation when a transitory nodal rhythm developed. In another case a transitory nodal rhythm occurred twenty-five seconds after the intravenous injection of DEAE; a regular sinus rhythm returned quickly and there was no further alteration either at or after intubation. In another patient, bidirectional auricular tachycardia at a rate of 150 to 210 per minute was produced two minutes after spraying the glottis
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with 10 per cent cocaine during cyclopropane-ether anesthesia. The intravenous injection of 1 Gm. of DEAE was ineffective in causing any change in this arrhythmia. Four minutes later the condition was complicated by the appearance of frequent ventricular premature contractions. A second dose of DEAE was then injected. One minute later, there was a change to sinus tachycardia at a rate of 125 per minute with occasional bidirectional ventricular premature contractions. Two minutes later, a regular sinus rhythm was observed. No change occurred during and after intubation (fig. 2). This case, we believe, illustrates the sympathetic stimulating effects of absorption of cocaine during inhalation anesthesia and its treatment by a procaine derivative.

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**Fig. 2.** Clearance of arrhythmia following diethylaminoethanol during cyclopropane-ether anesthesia and cocaineization. Tracing (a), during second plane cyclopropane-ether anesthesia, shows a regular sinus rhythm at a rate of 70 per minute. Tracing (b), two minutes after cocaine spray of the larynx, shows bidirectional auricular tachycardia at the rate of 150 to 210 per minute. In tracing (c), there is no change. This is eight minutes after cocaineization and one minute after the intravenous injection of 1 Gm. of diethylaminoethanol. In tracing (d), twelve minutes after cocaineization and one minute after a second injection of 1 Gm. of diethylaminoethanol, there is a sinus tachycardia at a rate of 125 per minute with occasional bidirectional ventricular premature contractions. Tracing (e) taken three minutes later, shows a sinus tachycardia at a rate of 110 per minute.

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*Cyclopropane.*—Electrocardiographic tracings were obtained in 30 patients who were intubated following anesthetization with cyclopropane and the intravenous injection of DEAE. Twenty were intubated in second plane and 10 in third plane anesthesia.

Twelve of the 20 cases in which intubation was performed during second plane anesthesia showed no electrocardiographic change. As in the procaine series, this is a significant improvement over the first series in which intravenous procaine or DEAE had been omitted.

In 4 cases, transitory electrocardiographic changes were observed one to three minutes after intubation. These changes consisted of sinus tachycardia in 2 cases (115 and 125 per minute), ventricular premature
contractions in bigeminois form in another case and sinus bradycardia (at 55 per minute) in the fourth case.

Sinus tachycardia was produced at the moment of intubation in 3 cases; it was mild and transitory, ranging at rates of 105, 110 and 115 per minute.

In one case, a nodal rhythm became evident during cyclopropane anesthesia; this persisted until one and a half minutes after the injection of DEAE when a regular sinus rhythm returned and was maintained thereafter.

When endotracheal intubation was performed during third plane cyclopropane anesthesia and DEAE, 7 of 10 patients showed no electrocardiographic change. In 2 of the other 3 patients, the changes consisted of a few ventricular premature contractions at the moment of intubation in one, and ventricular premature contractions in bigeminois form in the second case. In the third case, sinus tachycardia at a rate of 120 per minute developed one minute after the intravenous injection of DEAE; this lasted for two minutes, after which no further change was observed.

Cyclopropane and Cocaine.—In 10 cases, endotracheal intubation was performed during second plane cyclopropane anesthesia, intravenous DEAE, and following the spraying of the glottis with 10 per cent cocaine.

Three patients had no electrocardiographic disturbance.

In 4 cases gross arrhythmias developed in from one to three minutes after spraying the glottis with cocaine. In each instance this consisted of ventricular premature contractions in bigeminois form which persisted for several minutes.

In the other 3 cases, sinus tachycardia at rates of 120 to 140 per minute was manifested one to two minutes after intubation.

Nitrous Oxide and Ether.—Electrocardiographic tracings were obtained in 6 patients who were intubated after nitrous oxide induction followed by ether and oxygen to second or third plane and in whom DEAE was injected intravenously before intubation. There were no electrocardiographic disturbances in 4 patients. In one, the heart rate increased from 65 to 105 per minute one minute after the injection of DEAE. In another patient, the heart rate increased from 65 to 125 per minute one minute after intubation and this tachycardia lasted six minutes.

Nitrous Oxide, Ether and Cocaine.—In 4 patients who had been anesthetized with nitrous oxide and ether, the glottis was sprayed with 10 per cent cocaine. This was followed by the injection of DEAE intravenously before intubation. All 4 patients were intubated in mid or deep second plane.

Two of the 4 patients showed no electrocardiographic change.

In one case, frequent ventricular premature contractions developed two minutes after cocainization during ether anesthesia. This ar-
rhythmia persisted until about one minute after the intravenous injection of DEAE when a regular sinus rhythm was restored. The patient's course during and after intubation was uneventful.

In the fourth case frequent ventricular premature contractions were manifested immediately after intubation and persisted for four minutes.

Pentothal Sodium.—Three of 4 patients who were intubated following the intravenous injection of 4 per cent pentothal sodium (750 mg.) supplemented by the intravenous injection of DEAE (1 Gm.) showed no electrocardiographic disturbance before, during or after intubation. The fourth patient manifested a decrease in the voltage of the T wave which coincided with the appearance of apnea ninety seconds after the injection of pentothal. At the time of intubation, a tachycardia of 110 per minute, developed and was sustained for two minutes.

Pentothal Sodium and Curare.—Four patients were intubated after the intravenous injection of pentothal sodium (500 to 750 mg. of a 4 per cent concentration) and d-tubocurarine (50 to 60 units, or 7.5 to 9 mg.) followed one minute later by the intravenous injection of DEAE (1 Gm. in 10 cc.). In all 4 cases a normal electrocardiogram was maintained at all times.

Pentothal Sodium, Curare and Cocaine.—Electrocardiographic tracings were obtained in 3 patients who were anesthetized by first spraying the pharynx and glottis with 10 per cent cocaine. This was followed by the intravenous injection of pentothal sodium and curare as in the preceding group. One minute later, DEAE (1 Gm. in 10 cc.) was injected intravenously and endotracheal intubation was performed one minute after the last injection. Two patients showed no electrocardiographic change. In the third, a sinus tachycardia of 125 per minute developed after cocaineization and was maintained until three minutes after intubation.

Pentothal Sodium and Cocaine.—Two patients were treated as in the previous group except that curare was omitted. There were no electrocardiographic changes in one patient. The other “bucked” after intubation and one minute later there was a sinus tachycardia at a rate of 115 per minute which was maintained for three minutes.

Nembutal and Curare.—Three patients were intubated after anesthesia was induced in the following manner: nembutal (500 mg. in 20 cc.) was first injected intravenously. This was followed by d-tubocurarine (70 units in 3.5 cc.) One minute later, DEAE (1 Gm. in 10 cc.) was injected through the same intravenous route. Endotracheal intubation was accomplished about one minute later. The results in this group were exactly the same as in the procaine series. One subject maintained a normal electrocardiogram. At the time of intubation, a sinus tachycardia of from 80 to 120 per minute developed in a second patient and lasted ninety seconds. The third patient manifested a lowered T wave for six minutes.
DISCUSSION

The results obtained in this series with diethylaminoethanol are comparable to those of the preceding procaine series (2).

Of 114 cases studied in this series, 14 (12 per cent) showed some electrocardiographic disturbances at the time of intubation consisting of sinus tachycardia in 9 cases and ventricular premature contractions in 5 cases.

In 20 cases, electrocardiographic changes were observed one to three minutes after intubation following "bucking" on the insertion of an endotracheal tube. These consisted of sinus tachycardia, 16 cases; ventricular premature contractions, 2 cases, and one case each of nodal rhythm and sinus bradycardia.

Of 32 patients whose pharynx and larynx were sprayed with cocaine in addition to general anesthesia, 7 showed effects of stimulation of the cardio-accelerator nerve about one minute after cocainization. This consisted of sinus tachycardia in one case and frequent ventricular premature contractions in 6 cases. These effects seemed persistent but were alleviated by the intravenous injection of DEAE (fig. 2).

These results corroborate previous studies on DEAE which indicated that this hydrolytic product of procaine could prevent and suppress ventricular arrhythmias (3, 4). Although DEAE is considerably less toxic than procaine, its effective dose is at least ten times that of procaine. A significant advantage of DEAE is that it can be administered to the conscious patient in a single injection without producing convulsions or other toxic symptoms. This means of therapy may be employed as a prophylactic measure in cases in which stimulation of cardiac conductivity, produced by the administration of inhalation general anesthetic agents, is to be avoided.

SUMMARY

Electrocardiographic tracings were obtained in 114 adult patients who were given general anesthesia complemented by the intravenous injection of 1 Gm. of diethylaminoethanol in 10 cc. before endotracheal intubation. Electrocardiographic disturbances occurred in 12 per cent of the cases at the time of intubation. In a previous series under similar conditions but in which DEAE had been omitted, the incidence of electrocardiographic disturbances was 68 per cent.

In general, the changes in the electrocardiogram in this series were similar and comparable to those of the previous series in which procaine had been used instead of DEAE. The majority of the disturbances again consisted of sinus tachycardia and ventricular premature contractions.

Topical cocainization of the pharynx and larynx during general anesthesia seemed to enhance cardiac disorders. The injection of diethylaminoethanol alleviated these arrhythmias and reduced the inci-
dence and severity of cardiac disturbances usually produced at the time of endotracheal intubation.

The diethylaminoethanol used in this study was obtained from Dr. E. A. Ravenstine through the courtesy of Winthrop-Stearns, Inc., New York, N. Y., Novacol Chemical Mfg. Co. Inc., Brooklyn, N. Y., and E. R. Squibb and Sons, New Brunswick, N. J.

REFERENCES


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