FAILURE OF PROCAINE TO REVERSE CYCLOPROPANE-EPINEPHRINE VENTRICULAR FIBRILLATION * †

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THE fact that procaine serves as a myocardial depressant and thereby reduces cardiac irregularity has been shown repeatedly (1, 2, 3). In a series of papers, Burstein *et al.* (4) suggested the existence of a protection by procaine and drugs closely related to it in chemical structure against certain cardiac irregularities initiated by the intravenous injection of epinephrine during cyclopropane anesthesia. Not only did these workers feel convinced that ventricular tachycardia and ventricular fibrillation could be prevented by an injection of the protecting drugs preceding administration of epinephrine, or when mixed with it for simultaneous injection, but they believed that after the cardiac irregularities were aroused they could be stopped and normal sino-auricular rhythm restored by a later injection of procaine. This last result has been quoted rather widely, particularly with respect to the treatment of ventricular fibrillation (5).

In work on the same subject (6), we found that much higher dosages of procaine than reported by Burstein (16 mg. rather than 5 mg. per kilogram of body weight) were necessary to prevent ventricular tachycardia. In our studies there had been several unsuccessful attempts to stop fully developed ventricular fibrillation with procaine but at that time the number of instances were too few to be conclusive. In subsequent studies on the dog, during cyclopropane anesthesia, whenever epinephrine was to be injected, our established effective dose of 16 mg. of procaine per kilogram of body weight was placed in a syringe and an appropriate needle attached to permit rapid administration if fibrillation developed. Methods of administration of the anesthetic agent were the same in both laboratories and are as reported by Burstein.

In experiments with almost 200 animals, there have been 27 instances of ventricular fibrillation following the intravenous injection of epinephrine. The electrocardiographic beam (lead II) was observed routinely, and as rapidly as possible after evidence of the condition appeared procaine was given by an intravenous or intracardiac injection. There was never a lapse of more than thirty seconds before

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its administration was completed. Many of the experiments were performed with the anterior thoracic wall removed and the heart visible so that the injections could be finished within ten seconds.

Table 1 gives the results of the 27 experiments. They can be summarized by stating that they were *uniformly unsuccessful;* not a single animal recovered from its fibrillation.

TABLE 1

RESULTS IN 27 DOGS OF THE TREATMENT OF VENTRICULAR FIBRILLATION BY THE INTRAVENOUS OR INTRACARDIAC INJECTION OF PROCAINE HYDROCHLORIDE

Sixteen milligrams of procaine per kilogram of body weight was administered after the onset of ventricular fibrillation and all injections of it were completed within thirty seconds. The animals had been equilibrated against cyclopropane-oxygen mixtures for twenty-five minutes or more.

No. of Animals	Cyclopropane in Oxygen	Amount of Epinephrine	Volume of the Epinephrine Soln. Injected*	Route of Procaine Injection	Time before Procaine Injection was Completed	Effect on Ventricular Fibrillation
	per cent.	mg./Kg.	cc.		sec.	
1	22	0.01	3	Intravenous	15	None
3	31	0.01	3, 3, 5	Intravenous	15, 25, 10	None
1	22	0.005	5	Intracardiac	<30	None
2	22	0.01	5, 5	Intracardiac	<30	None
2	22	0.02	4, 4	Intracardiac	<30	None
3	27	0.01	1½, 3, 4	Intracardiac	<30	None
2	29	0.005	3, 5	Intracardiac	<30	None
5	30	0.005	2½, 3, 3, 5, 5	Intracardiac	<30	None
5	30	0.01	3, 3, 4, 5, 5	Intracardiac	<30	None
2	31	0.005	3, 5	Intracardiac	<30	None
1	31	0.02	5	Intracardiac	<30	None

* Epinephrine was used on the mg./Kg. basis indicated and made up to a total volume of 5 cc. with physiologic saline solution. It was then injected intravenously at a steady rate of 1 cc. per ten seconds. The total volume indicated as being injected for the respective animals in each group caused the onset of ventricular fibrillation.

It is rather difficult to harmonize these findings with the apparently successful experiments of Burstein *et al.* Whereas they produced ventricular fibrillation in from one-half to three-quarters of the animals in a group, they often did so by injecting multiples of the test dose of 0.01 mg. of epinephrine per kilogram of body weight. The dosage of 0.01 mg. is rather uniformly effective in eliciting ventricular tachycardia and is comparable to the amount which is liberated from the adrenal glands either from electrical stimulation of the preganglionic fibers leading to them or by simultaneous manual massage of the two glands (7). From their protocols, it would seem that the initial injection of the sympathomimetic drug was made within fifteen or twenty minutes after induction of cyclopropane anesthesia when sensitization of the cardiac automatic tissue is relatively high (8). Also, their animals were usually maintained in only the second plane of surgical anesthesia, whereas deeper planes increase the sensitivity (9). The assumption

that the increased test dosages of epinephrine would routinely cause fibrillation is also unwarranted since in some animals apparently no amount of epinephrine produces such a result (8).

Some of the records published (4a) (figs. 4D and 5D) do not seem to be indicative of ventricular fibrillation. There are in our files innumerable records similar to 4D, where bizarre but regular QRS-T complexes of varying height return either progressively, or after a brief period of cardiac arrest, to sino-auricular rhythm. We also have three records similar to the first four complexes of 5D, where a ventricular flutter at a rate of 750 per minute persisted for ten seconds, yet spontaneous recovery occurred *without any treatment* whatsoever. Undoubtedly the duration of ventricular tachycardia can be shortened or the irregularity abolished by the administration of procaine, but spontaneous recovery is practically assured in the dog if unequivocal ventricular fibrillation has not developed within a few seconds after the onset of tachycardia. The cause of the early appearance of fibrillation, if it is to appear at all, awaits explanation. The injected procaine at the time of fibrillation is not well circulated through the heart and it can therefore hardly be expected to be effective. Even massaging the heart did not improve the results.

SUMMARY

In 27 of several hundred dogs anesthetized with cyclopropane, the injection of epinephrine produced unequivocal ventricular fibrillation. This fibrillation was treated by the intravenous or intracardiac injection of 16 mg. of procaine per kilogram of body weight. Despite the fact that the administration of procaine was completed within a period of less than thirty seconds, not a single instance of fibrillation was altered by this treatment. While the use of electrical shock may prove effective in the exposed, fibrillating heart there is no practical method available at the present time for abolishing ventricular fibrillation if it occurs in the intact animal during cyclopropane anesthesia.

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