

These results suggest that the potencies of the human urinary gonadotropic rat units employed by the manufacturers vary greatly. To remedy this situation a uniform standard should be adopted.† This has already been accomplished with the estrogenic preparations.

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Protecting Action of Procaine Against Ventricular Fibrillation Induced by Epinephrine During Cyclopropane Anesthesia.

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There is much evidence indicating that several anesthetic agents sensitize the heart so that the addition of small amounts of epinephrine may cause ventricular fibrillation. Oliver and Schafer¹ were first to observe this as a frequent complication during chloroform anesthesia, and Levy² elaborated on the reaction. More recently, Meek, Hathaway and Orth³ have shown that the same effect may be produced in the dog during cyclopropane anesthesia. Experimental data accumulated by Kochman and Daels,⁴ Mautz,⁵ and Beck and Mautz⁶ serves to establish that procaine applied locally to the heart reduces irritability of the myocardium as evidenced by augmentation in intensity of stimulation necessary to produce extra-systoles or ventricular fibrillation. Hermann and Jourdan⁷ have reported that following subcutaneous injections of procaine a larger dose of epinephrine is necessary to produce ventricular fibrillation during chloro-

† Since the completion of these experiments, the League of Nations Health Organization has set up an international unit for the human chorionic gonadotropin. It is designated as 0.1 mg of a standard preparation of a gonadotropic extract from human pregnancy urine. This unit is supposed to produce an estrous type of smear in 21-day-old rats.

• ¹ Oliver, G., and Schafer, E. A., *J. Physiol.*, 1895, **18**, 230.

• ² Levy, A. G., *J. Physiol.*, 1911, **43**, 3.

• ³ Meek, W. J., Hathaway, H. R., and Orth, O. S., *J. Pharm. and Exp. Therap.*, 1939, **61**, 240.

⁴ Kochman, M., and Daels, F., *Arch. Internat. Pharm.*, 1908, **18**, 41.

⁵ Mautz, F. R., *J. Thoracic Surg.*, 1936, **5**, 612.

⁶ Beck, C. S., and Mautz, F. R., *Ann. Surg.*, 1937, **106**, 525.

⁷ Hermann, H., and Jourdan, F., *C. R. Soc. de Biol.*, 1931, **106**, 1153.

form anesthesia. Shen and Simon⁸ have shown that procaine, given to dogs simultaneously with epinephrine during chloroform anesthesia, protects against fibrillation. The present study was undertaken to determine whether similar results could be obtained during cyclopropane anesthesia.

Thirty-eight experiments were performed on fourteen dogs. Pre-anesthetic medication, morphine sulphate one mg per kilo and scopolamine hydrobromide 0.04 mg per kilo was injected subcutaneously one hour before each experiment. The carbon dioxide absorption technic was utilized for cyclopropane anesthesia. An unobstructed airway was assured by an endotracheal tube fitted with an inflatable cuff. Depth of anesthesia was maintained at second plane as evidenced by the loss of the lid reflex and maintenance of intercostal activity. Electrocardiograms (lead II) were taken before, during and after drug administration.

The test injection of epinephrine was 0.01 mg per kilo in 5 cc of normal saline, given intravenously at the rate of 1 cc per 10 seconds. The test injection of procaine was 5 mg per kilo in 5 cc of normal saline, given intravenously, 1 cc in 10 seconds. Electrocardiographic records were completed during cyclopropane anesthesia using epinephrine alone, procaine and epinephrine simultaneously, procaine preceding epinephrine and epinephrine preceding procaine.

The effects of injecting epinephrine alone were studied in 5 dogs. Three of the animals died of ventricular fibrillation. Two of these had recovered from previous experiments in which they had been treated with procaine prior to the intravenous injection of the test dose of epinephrine. Following an interval of several days these animals were given an identical dose of epinephrine alone and both developed ventricular fibrillation. Of the other 3 dogs 2 developed ventricular tachycardia but recovered; the third developed ventricular tachycardia, then fatal ventricular fibrillation.

Procaine and epinephrine were given simultaneously to 5 dogs. Two died of ventricular fibrillation. The 3 surviving animals developed electrocardiographic phenomena referable to the A-V node and the ventricles which rapidly shifted back to the sinus node. All revealed increased cardiac rates, which suggested an initial rapid and predominant epinephrine effect with gradual and slower ascendancy of the procaine effect and reestablishment of the pacemaking sinus node.

Procaine before epinephrine was given to 8 dogs, 7 recovered. One

⁸ Shen, T. C. R., and Simon, A., *Arch. Internat. de Pharm. et Therap.*, 1938, 59, 68.

of these animals died when an amount equal to 8 test doses of epinephrine was injected intravenously. This same dog had been studied twice before this fatal termination by injecting procaine before epinephrine, employing one test dose of epinephrine the first time and 3 test doses the second time, when the only electrocardiographic abnormality was short runs of ventricular tachycardia.

Epinephrine was given before procaine in 8 experiments with 5 dogs. The same experiment was repeated in 2 of the animals. All the animals survived and the results did not vary; that is, after ventricular tachycardia was established following the intravenous injection of a test dose of epinephrine, the intravenous or intracardiac injection of a test dose of procaine caused a change to auricular tachycardia which then reverted to a sinus rhythm.

Conclusions. The experiments presented support the contention that when procaine is administered to cyclopropanized dogs the incidence of ventricular fibrillation following epinephrine administration is reduced. Sixty percent of the animals developed ventricular fibrillation after injection of one test dose of epinephrine. When procaine was previously administered all animals were protected, and the introduction of 8 test doses of epinephrine were required to produce the fatal complication. The results also indicate that procaine may be efficient in the treatment of ventricular fibrillation induced in the dog by epinephrine during cyclopropane anesthesia. In every instance in which procaine was given intravenously at the time when ventricular tachycardia occurred following the administration of epinephrine, recovery was effected.

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Estrogenic Therapy by Implantation of Stilbestrol Pellets.

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The new synthetic estrogen, diethylstilbestrol (4:4-dihydroxy-alpha:beta-diethyl stilbene), announced by Dodds and coworkers,¹ has been found capable of producing in animals all the effects previously obtained with naturally occurring estrogens. Early reports

¹ Dodds, E. C., Lawson, W., and Noble, R. L., *Lancet*, 1938, 1, 1389.