lesions over normal animals and only about 20% reduction compared to desalivated animals not subjected to fluorine in their prenatal period. The relatively low number of fractures in nonfluorinized animals subjected to desalivation suggests that early breaks rapidly become carious. The higher number of fractures in the normal animals indicates the reverse condition, but in the fluorinized animals of Groups 3 and 4 it would be difficult to say to what degree the high frequency of breaks was due to greater friability of hypoplastic fluorinized teeth.

Summary. Some of the factors operative in suppressing rat caries have been tested in this experiment. By using animals in which the salivary glands have been removed it has been possible to test the relative effects of fluorine prenatally incorporated in the teeth. When the caries score of operated rats with mottled or fluorinized teeth are compared with that of nonfluorinized animals without glands there is a measurable reduction in caries. When the percentage of reduction is compared with the caries score of normal animals, however, there is evidence that the saliva offers greater protection than the fluorine in tooth substance.

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Prevention of the Anti-Curare Action of Epinephrine by Dibenamine.

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The effects of N, N-dibenzyl-beta-chloroethylamine (Dibenamine) on the responses of various visceral effectors to epinephrine have been studied by Nickerson and Goodman.[1] They have reported adrenolytic actions of Dibenamine in various visceral effectors which have an excitatory adrenergic innervation. Epinephrine is known to exert an anti-curare action at the skeletal neuromuscular junction.[2,3] The mechanism of this action is unknown. It does not appear to be related to any influence on adrenergic neuro-effector systems. In the present study it is demonstrated that Dibenamine prevents the anti-curare action of epinephrine.

Methods. Seven dogs were used. Intravenous sodium pentobarbital was the anesthetic employed in 6 dogs. In one animal, intratracheal ether anesthesia was used following the administration of 15.0 mg morphine sulfate. The peripheral portion of the cut peroneal nerve was drawn across 2 glass-shielded platinum electrodes, and single shocks of supramaximal strength were applied every 2 seconds by means of an electronic stimulator (Electrodyne, model 461). Relatively isometric contractions of the tibialis anticus muscle were recorded on a revolving drum by means of a Meyerhof type of myograph. The femoral artery of the same side was exposed for intra-arterial injections. The femoral vein of the opposite side was exposed for intravenous injection.

The curare preparation used was Intocostrin, 20 units per cc (E. R. Squibb and Sons). This preparation has the same potency as a solution containing 2.7 mg of anhydrous d-tubocurarine chloride per cc. The following general procedure was used in each of the 7 experiments. Intocostrin was diluted with isotonic saline so that each cc contained 2 units, and this was injected intravenously in amounts sufficient to depress the amplitude of muscular contraction to between one-fourth and one-half of the original height. Then epinephrine (Adrenalin, Parke-Davis and Co.) was injected rapidly intra-arterially. After demonstrating the anti-curare action of

1 Nickerson, M., and Goodman, L., *J. Pharm. and Exp. Therap.*, 1947, **89**, 167.

2 Rosenblueth, A., Lindsley, D. B., and Morison, R. S., *Am. J. Physiol.*, 1936, **115**, 53.

3 Wilson, A. T., and Wright, S., *Quart. J. Exp. Physiol.*, 1936-37, **26**, 127.

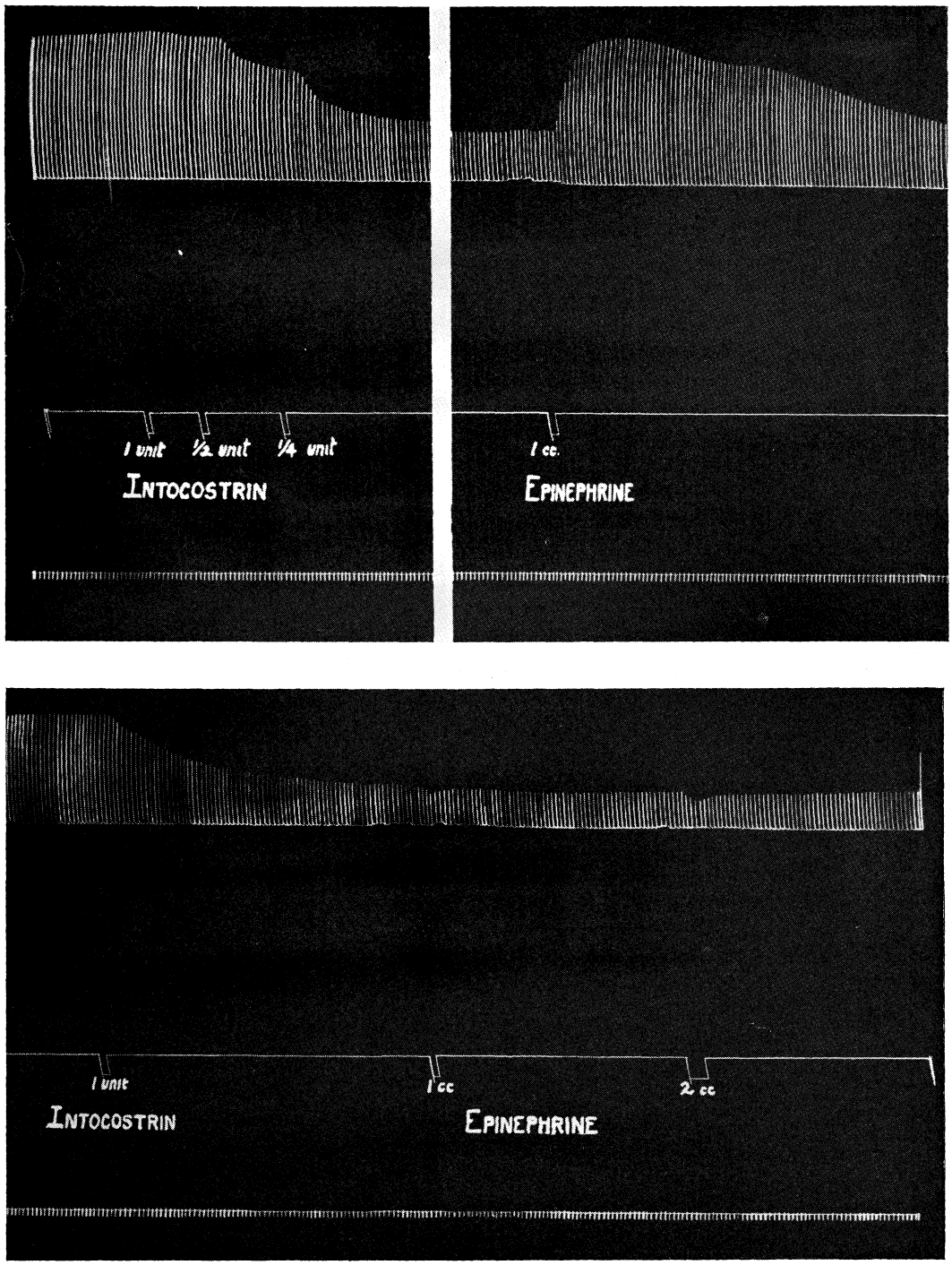

FIG. 1.

Prevention of the Anti-curare Action of Epinephrine by Dibenamine.

Upper Record. *Before Dibenamine.* From above downward record shows: (1) contractions of tibialis anticus muscle produced by stimulating the peroneal nerve at 2-second intervals. (2) times of intravenous injection of Intocostrin and intra-arterial injection of epinephrine

(1:100,000), and (3) time in 2-second intervals. At the break in the record a 3-minute section was removed, during which time an additional 0.25 unit of Intocostrin was injected.

Lower Record. *After Dibenamine.* Recording as in upper record. Animal had received 2 units of Intocostrin approximately 1 minute before the injection of Indocostrin indicated on the record.

epinephrine, Dibenamine was administered intravenously. The hydrochloride salt of Dibenamine was dissolved in propylene glycol (20 mg per cc) and then diluted with an equal amount of distilled water. Each dog was given between 25 and 45 mg of Dibenamine per kg within a period of 15 to 60 minutes. Within one to 3 hours after injection of Dibenamine, administration of curare and epinephrine was repeated.

Results. Intra-arterial injection of epinephrine (1.0 or 2.0 cc of a 1:100,000 solution of epinephrine in saline), following partial curarization, caused an immediate marked increase in the amplitude of muscular contraction in each of the 7 animals tested. A typical response is illustrated in Fig. 1, upper record.

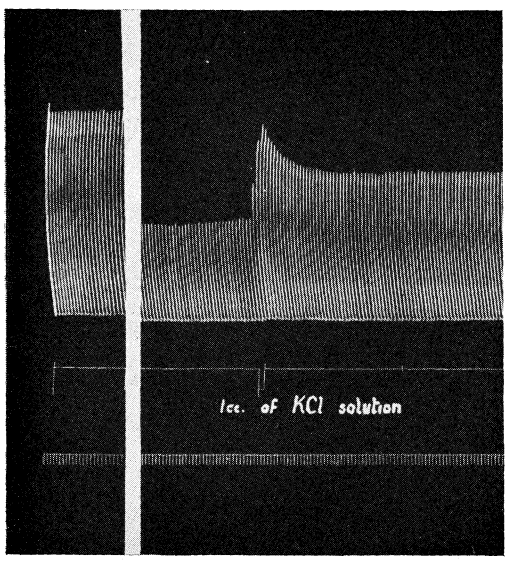

FIG. 2.

Anti-curare Action of Potassium after Dibenamine. Writing points are arranged as in Fig. 1. The record was obtained approximately 2 hours after administration of Dibenamine, 30 mg per kg. The break in the record indicates an 11-minute interval during which 1.2 units of Intocostrin were administered intravenously. Isotonic potassium chloride was administered intra-arterially.

After administration of Dibenamine, and subsequent partial curarization, the same dose of epinephrine failed to increase the amplitude of contraction in each of the 7 animals. An experiment is illustrated in Fig. 1, lower record. In fact, the injection of the epinephrine solution after Dibenamine and partial curarization produced a slight transient decrease in the amplitude of the contractions. The following controls indicate that the decreased amplitude was not due to the epinephrine but was related to the volume of the diluent. 1) In each of 2 dogs tested, injection of the same amount of epinephrine (20 μg) in 0.02 cc of fluid (*i.e.* 0.02 cc of a 1:1,000 solution of epinephrine) failed to have any effect on the amplitude of contraction. 2) The same slight depression in amplitude of contraction was produced in 3 dogs by the intra-arterial injection of 1.0 to 2.0 cc of isotonic saline or water.

The effects of large doses of epinephrine were tested in three dogs. A dose of epinephrine 100 times that used to demonstrate anti-curare action before Dibenamine had no anti-curare effect after Dibenamine.

Isotonic potassium chloride solution (1.15%), 1.0 to 5.0 cc was administered intra-arterially to 3 dogs following partial curarization. The well-known immediate increase in amplitude of contraction was noted both before and after Dibenamine. The anti-curare action of potassium chloride following the administration of Dibenamine is illustrated in Fig. 2.

Summary. The effects of Dibenamine on the anti-curare actions of epinephrine and of KCl have been studied in 7 dogs anesthetized with sodium pentobarbital or with morphine and ether. Dibenamine, in doses of 25-45 mg per kg, prevents the anti-curare action of epinephrine but does not prevent the anti-curare action of potassium chloride.