capable of paralyzing postganglionic fibers, and Dibenamine capable of blocking the same fibers, do not abolish the vasoconstrictor action of nicotine. Serial sections of the vessels of the frog's hind legs have shown the absence of ganglion cells.

It appears, therefore, that in the L-T preparation the site of action of nicotine is peripheral to the postganglionic fibers, possibly directly on the blood vessels. In the intact animal, it may be assumed that in addition to its known sites of action on ganglion cells, and adrenal medulla, nicotine may also act directly on the neuroeffector cells of the blood vessels.

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Effects of Intrathecal Administration of Epinephrine on Cardiac Rhythm in Dogs Anesthetized with Cyclopropane.

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Recently there has been a trend in clinical anesthesia to combine epinephrine with local anesthetic drugs to prolong the duration of spinal anesthesia. At times it is necessary to supplement spinal anesthesia with a rapidly acting drug such as cyclopropane. It is well established that cyclopropane increases cardiac irritability and this increased irritability is further enhanced by epinephrine. In dogs, as little as .01 mg of epinephrine per kilo intravenously precipitates ventricular premature beats, tachycardia or fibrillation during deep cyclopropane anesthesia. There is some evidence that vasopressors do not quickly pass from the subarachnoid space into the blood stream. Bray, Katz, and Adriani[1] have shown that epinephrine, neosynephrine, ephedrine and oenethyl cause no vasopressor response when administered intrathecally in therapeutic doses in man. Inasmuch as so little epinephrine causes serious circulatory changes, it is important to know whether or not the passage of epinephrine from the subarachnoid space into the general circulation is sufficiently rapid to be a hazard under such circumstances.

Method. Observations were made on 6 dogs. Thirty mg of nembutal per kilo was administered intraperitoneally to facilitate the insertion of an endotracheal tube. Cyclopropane and oxygen were administered by the carbon dioxide absorption technique to the point of intercostal paralysis and maintained at this level. After 20 minutes of cyclopropane anesthesia control electrocardiograms were obtained using lead II.

The first dog was given the standard test dose of .01 mg kilo body weight in 5 cc normal saline intravenously until ventricular tachycardia occurred. Meek[2] *et al.* have found that dose produces reflex vagal inhibition of the pacemaker with or without escape of the A-V node bundle or ventricle but without tachycardia or fibillation. With cyclopropane this same dose causes ventricular premature beats, tachycardia or fibrillation. After the rhythm had returned to normal 1 mg of epinephrine was administered intrathecally. One milligram is the upper limit of the dose usually employed clinically. Continuous electrographic recordings were made prior, during and immediately after the injection. The dog was observed for 1 hour, at the end of which time the standard test dose of epinephrine was repeated intravenously. The second dog was prepared as the first except that at the end of 1 and 2 hours 2 mg and 5 mg of epinephrine

[1] Bray, K., Katz, S., and Adriani, J., in press.

[2] Meek, W. J., Hathaway, H. R., and Orth, O. S., *J. Pharm. and Exp. Therap.*, 1937, **61**, 240.

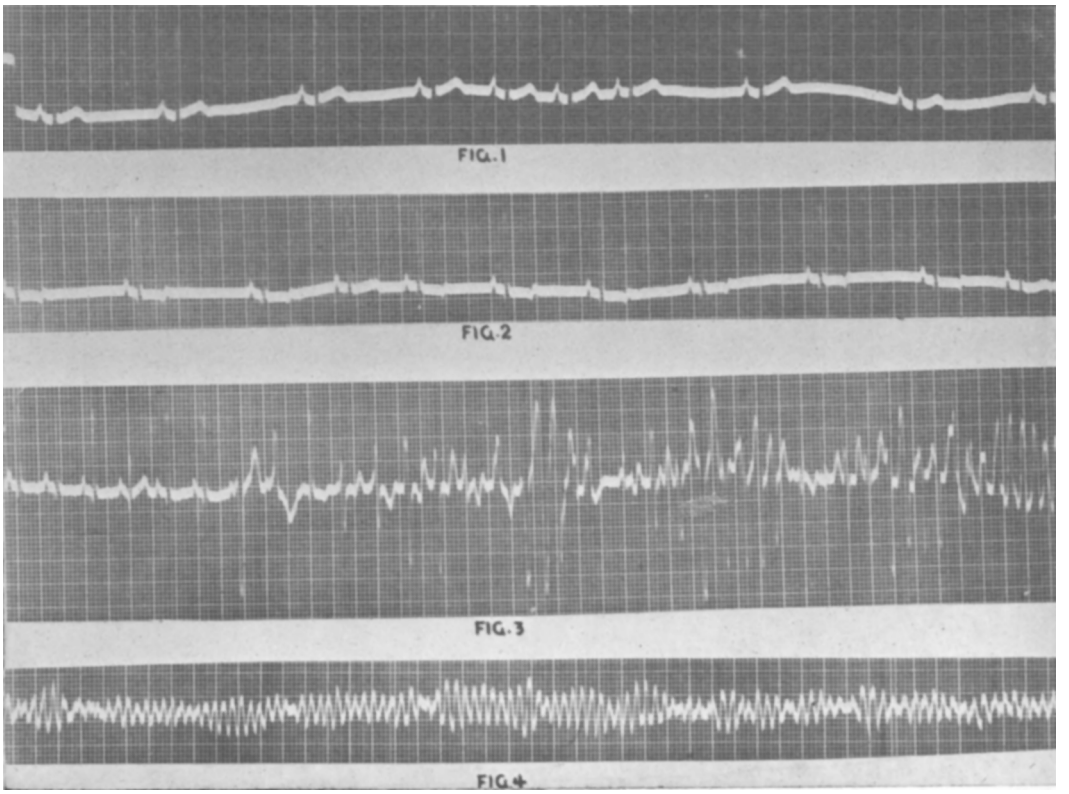

FIG. 1. Electrocardiogram. Control after nembutal and cyclopropane anesthesia.
FIG. 2. After 1 cc epinephrine intrathecally during cyclopropane anesthesia.
FIG. 3. After ½ cc spinal fluid intravenously (withdrawn one hour after epinephrine injection). Ventricular premature beats proceeding to ventricular tachycardia.
FIG. 4. Ventricular fibrillation resulting from injection of spinal fluid.

respectively were administered intrathecally. At the end of the third hour the standard test dose of epinephrine was administered intravenously. The last 3 dogs were initially given 1 mg of epinephrine intrathecally but not the intravenous standard test dose. At the end of one hour the third dog received the standard test dose intravenously. Spinal fluid was withdrawn from the fourth and fifth dogs after one hour and 0.5 cc undiluted injected intravenously. Cardiac rhythm was consistently observed on the electrocardiograph prior, during and immediately after each intrathecal or intravenous injection.

Results. In all dogs ventricular tachycardia appeared after the intravenous test dose of epinephrine. When 1 mg of epinephrine was given intrathecally no change in cardiac rhythm was noted during the one hour period in any of the dogs during cyclopropane anesthesia. In dog 2 no changes in cardiac rhythm were noted after the second hour after 2 mg of epinephrine were administered intrathecally. During the third hour the 5 mg dose intrathecally produced paroxysms of ventricular tachycardia 88 seconds after injection. Rhythm returned to normal in 3 minutes. Although in all dogs 1 mg intrathecally caused no change in rhythm over a period of 1 hour, the standard test dose caused ventricular premature beats, tachycardia and fibrillation when given intravenously at the end of the hour. Dog 1 died from ventricular fibrillation. Spinal fluid withdrawn and given intravenously 1 hour after 1 mg of epinephrine had been introduced into the subarachnoid space apparently still contained epinephrine. One half cubic centimeter undiluted, given intravenously caused ventricular tachycardia to develop in 18.2 seconds in dog 4 and in 11.8

seconds in dog 5. Dog 5 then developed ventricular fibrillation and died. In order to observe what might occur if epinephrine is inadvertently injected into the intraspinous ligaments instead of intrathecally, 1 mg was injected at this site in dog 6. A-V nodal rhythm, ventricular premature beats appeared 30 seconds later.

Summary and Conclusions. Epinephrine was administered intrathecally to 5 dogs anesthetized with cyclopropane. The characteristic changes which occur after intravenous epinephrine is given did not occur. At the end of one hour epinephrine was still present in sufficient quantities in the spinal fluid to cause disturbances in cardiac rhythm when the spinal fluid was withdrawn and given intravenously. Presumably the passage of epinephrine from the intrathecal space into the blood stream does not occur or occurs so slowly that it is of little consequence in dogs anesthetized with cyclopropane. The same is not true if epinephrine is given intravenously or into the interspinous tissues.

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Further Studies on Nutritional Requirements of the Cotton Rat. (*Sigmodon hispidus hispidus*).*

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Previous studies[1] showed that the cotton rat (*Sigmodon hispidus hispidus*) requires thiamin, riboflavin, pantothenic acid, vitamin B_6, nicotinic acid and inositol in the diet for optimum growth. Since these animals are very susceptible to dental caries[2,3] and are also susceptible to virus infections[4-6] it was of interest to extend the results obtained on their nutritional requirements. Studies have been carried out on the rate of growth obtained when diets low in choline, biotin, folic acid or nicotinic acid were fed. Preliminary studies on the reproduction performance have been conducted with the use of purified diets with and without the addition of liver extract.

Experimental—Care of Animals. Weanling cotton rats, 15-25 g in weight, obtained from our stock colony, were used in the growth studies. Litter mates and males and females were distributed as uniformly as possible among the groups within each experimental series. The animals were housed singly in screened bottom cages and food and water were provided *ad libitum*. The rate of growth for the different groups was observed over a period of 4-6 weeks.

In the reproduction studies one male and 1 or 2 females were housed in a colony cage with the screened bottom removed. Wood shavings and a metal can were included in each cage. The animals were placed together at an early age, usually before they were 6

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