development of the nephrotic syndrome remains to be determined.

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Effect of Coronary Perfusion of Prostigmine on Ventricular Fibrillation in the Hypothermic Dog.* (20963)

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(Introduced by C. A. Maaske.)
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Ventricular fibrillation is a frequent event during cardiac surgery with inflow occlusion in the experimental hypothermic dog. Bigelow *et al.*(1), Rosenhain and Penrod(2), and Swan *et al.*(3) have demonstrated that the incidence of ventricular fibrillation increases with body temperatures below 25°C with CO_2 retention and with cardiac manipulation. To minimize the first 2 of these factors in the present work, the body temperature was lowered to the range between 23° and 26°C and the animals were vigorously hyperventilated with pure oxygen sufficiently to maintain a blood pH of about 7.6. A suitable pharmacological agent was then sought to alter the fibrillatory threshold during cardiac manipulation. The drug which significantly altered this fibrillatory threshold was prostigmine.

Methods. Mongrel dogs were placed in an ice water bath after being deeply anesthetized with I.V. sodium pentobarbital to prevent shivering. Following tracheal intubation, the dog was hyperventilated with pure oxygen. When 29°C rectal temperature was obtained, the dog was removed from the bath; a further drop of 3 to 6 degrees of temperature occurred. Using aseptic technic a right anterolateral thorocotomy incision was made through the 5th intercostal space. After entering the right thorax the azygos vein was ligated, the pericardial sac opened widely and both cavae were occluded. Fifteen seconds later the ascending aorta was occluded with a non-crushing clamp about one inch distal to the coronary ostia. A control series of dogs received no medications; the experimental group was treated as follows: Some received prostigmine intravenously before occlusion of circulation. In others, either prostigmine or acetylcholine was injected into the root of the aorta until the heart rate was reduced to 10 to 25 beats per minute. At this point injection of prostigmine was stopped; however, since its action is so brief, acetylcholine required a slow continuous perfusion to maintain the slow heart rate. This method of administration into the clamped aorta is termed coronary perfusion. To produce cardiac slowing, the range of dosage for prostigmine proved to be one to 2 ml of 1-4000 solution. For acetylcholine from one to 3 mg

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TABLE I. Summary of Data.

	No. dogs	Ventricular fibrillation	Resuscitation
Ventriculotomy as fibrillatory stimulus			
Control	23	23	0 of 23 attempts
Prostigmine in open circulation	15	7	5 of 5 "
Prostigmine by coronary perfusion	16	0	0 "
Acetylcholine	3	0	0 "
Catheterization of coronary sinus as fibrillatory stimulus			
			(Prostigmine given after fibrillation occurred)
Control	10	10	10 of 10 attempts
Prostigmine coronary perfusion	10	0	0 "

were required. A 5 cm incision was made in the right or left ventricle; occasionally a ventricular septal defect one cm in diameter was created. The septal defect was closed with interrupted sutures and after filling the heart with saline, the ventricular wall was also sutured. This accomplished, the aortic clamp was removed followed by simultaneous release of both cavae. The total occlusion time varied from 6 to 14 minutes, the average being 8 minutes.

Results. Right ventriculotomy is a fibrillatory stimulus in the cold dog. Our control series of 23 dogs all incurred ventricular fibrillation during ventriculotomy. Many succumbed to fibrillation with the initial needle-prick. Resuscitation by massage and electric shock was uniformly unsuccessful. Potassium chloride was not used(4). When prostigmine (.05 ml of 1-4000 solution per kg body weight) was administered in the general circulation before inflow occlusion to the heart, the incidence of fibrillation was reduced to about 50%. Table I shows that 8 of 15 dogs had no fibrillation. The remaining 7 suffered ventricular fibrillation. Resuscitation was successful in each of the 5 animals in which it was attempted. In the hope of a more direct administration of prostigmine to the heart yielding more consistent results, this agent was administered in another series of 16 animals by coronary perfusion. In this group ventriculotomy was performed without the occurrence of ventricular fibrillation. Eight of these dogs also had creation of a small ventricular septal defect with closure.

As an incidental finding to other work it was found that catheterization of the coronary sinus in the cold dog was attended by a high incidence of ventricular fibrillation. This maneuver was also used as a fibrillatory stimulus. Table I shows that 10 of 11 dogs subjected to this procedure incurred ventricular fibrillation. However, when prostigmine was given by coronary perfusion prior to catheterization, no ventricular fibrillation occurred in a group of 10 animals. It was found that when ventricular fibrillation occurred in the unprotected animals resuscitation was uniformly unsuccessful. After failure of the attempted resuscitation prostigmine was given by coronary perfusion with massage. Electric shock was then again instituted with 100% success. Seven of these dogs reverted directly from ventricular fibrillation to normal sinus rhythm following electric shock; the other 3 required massage. Since it seemed likely that the antifibrillatory effect of prostigmine was due to an accumulation of acetylcholine, this agent was administered by coronary perfusion in 3 animals. Table I indicates that ventriculotomy was successfully performed in all 3 of these animals without the occurrence of ventricular fibrillation.

Summary. Prostigmine is shown to have an antifibrillatory effect in the hypothermic dog. This agent is more effective when given by coronary perfusion than when given intravenously. When ventricular fibrillation occurs in the unprotected animal, coronary perfusion of prostigmine will allow conversion to a normal rhythm by massage and electric shock. It is felt that the antifibrillatory effect of prostigmine is probably due to an accumulation of acetylcholine.

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