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Chromodacryorrhea and Parasympathetic Action of Cyclopropane.

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The effects of anesthetic drugs upon the autonomic nervous system are of recent interest. Those of ether upon the sympathetic division have been described.[1] Parasympathetic stimulation by cyclopropane has been suggested from laboratory observations in dogs.[2] The results of a study of this latter action and its *modus operandi* are contained in this report. Cyclopropane does not inhibit the activity of cholinesterase of human serum *in vitro*.[3] Two of us[4] have noted that perfusion of turtles' and frogs' hearts with solutions of cyclopropane produced parasympathetic effects. Perfusates from eserinized stomachs and hearts exhausted of the cyclopropane likewise produced parasympathetic stimulation when added to fresh eserinized hearts or to preparations of the frog's rectus abdominis muscle. Such results suggested the liberation of an acetylcholine-like substance. These results were not obtained with ethylene and ether. Recently Tashiro, *et al.*,[5] described a technic for the assay of acetylcholine by the response of chromodacryorrhea or "red tears" in the eserinized albino rat. This procedure was utilized here to demonstrate further the parasympathetic action of cyclopropane.

Procedure and Results. Sixty-one observations were made on 36 white adult male rats weighing 225 to 325 g. Fifty gamma of eserine salicylate per 100 g of rat were given intraperitoneally. Twenty minutes later ether, cyclopropane, or ethylene narcosis was induced and maintained in the first plane of surgical anesthesia for a minimum of 20 minutes. The eyes were examined for the presence of chromodacryorrhea: (1) 20 minutes after the injection of eserine before anesthesia was begun, (2) immediately after anesthesia was discontinued, and (3) 20 minutes after recovery. Thirty control observations were made on non-premedicated, unanesthetized rats

1 Bhatia, B. B., and Burn, J. H., *J. Physiol.*, 1933, **78**, 257.

2 Seevers, M. H., Meek, W. J., Rovenstine, E. A., and Stiles, J. A., *J. Pharm. and Exp. Therap.*, 1934, **51**, 1.

3 Adriani, J., and Rovenstine, E. A., *Anes. and Anal.*, 1940, in press.

4 Adriani, J., and Rovenstine, E. A., *Am. J. Physiol.*, 1940, **129**, 299.

5 Tashiro, S., Smith, C., Badger, E., and Kezur, E., PROC. SOC. EXP. BIOL. AND MED., 1940, **44** 658.

TABLE I.
Chromodacryorrhea in Eserinized Rats.

Anesthetic agent	Premedication	Observations No.	No. of rats showing chromodacryorrhea		
			Before Anesthesia	At end of Anesthesia	Twenty minutes after recovery
None	Eserine	64	3	0	0
Cyclopropane	None	18	0	0	0
Ether	"	12	0	0	0
Cyclopropane	Eserine	23	0	17	1
Ethylene	"	18	0	0	1
Ether	"	20	0	0	2

and on those anesthetized with cyclopropane and ether without the administration of eserine. Twelve rats were treated with acetylcholine and the occurrence of chromodacryorrhea noted, thus confirming the studies of Tashiro, *et al.*[5]

A positive response for chromodacryorrhea was obtained in 18 of 23 eserinized rats treated with cyclopropane (Table I). This response was noted immediately after anesthesia was terminated. It was delayed in one rat which showed a positive response 20 minutes after recovery. The response was negative in the remaining 5 anesthetized with cyclopropane. Two of the 20 rats anesthetized with ether and one of the 18 treated with ethylene developed a positive response. Three unanesthetized eserinized rats similarly showed chromodacryorrhea. In none of the non-premedicated unanesthetized rats or the non-premedicated rats anesthetized with cyclopropane or ether was chromodacryorrhea observed.

Discussion. Since chromodacryorrhea follows the injection of acetylcholine in eserinized rats,[5] the positive responses obtained from cyclopropane suggest that this drug liberates acetylcholine in rat tissue. The exceptional results obtained with the eserinized rats anesthetized with ether and ethylene may be due possibly to an increased acetylcholine secretion incident to handling or to variations in individual threshold since chromodacryorrhea may be elicited with larger doses of eserine. This may also account for the absences of chromodacryorrhea in the 5 eserinized rats given cyclopropane.

Summary. The phenomenon of chromodacryorrhea produced by cyclopropane in eserinized white rats indicates that acetylcholine is liberated in mammalian tissues and supports the contention that the drug is a parasympathetic stimulant.