Burnham,[7] however. Incidentally, the fact that it was possible to neutralize the interfering anti-A and anti-B isoagglutinins in human sera without affecting the irregular isoagglutinins, by the simple expedient of adding solutions of group substances from saliva, is evidence that the properties Rh and M are absent from saliva, in contrast to A and B.[8]

From the clinical standpoint, the case illustrates the difficulties that may be encountered on rare occasions in finding compatible donors for blood transfusion. That three subsequent transfusions from two different selected donors of type ONRh- were successful indicates that such obstacles can be overcome.

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Adrenolytic Action of Cyclopropane.*

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Previous work[1, 2, 3] has shown that 30 minutes of cyclopropane anesthesia sensitizes the heart of the dog so that ventricular tachycardia follows the injection of 0.01 mg of adrenalin† per kilogram. The only ventricular effect of this dose in the unanesthetized animal is extrasystoles. In studying the mechanism of this sensitization it was observed that some dogs which showed 30 seconds or more of

7 Levine, P., Katzin, E. M., and Burnham, L., PROC. SOC. EXP. BIOL. AND MED., 1940, **45**, 346.

8 Dr. Philip Levine (personal communication) has also found that the property Rh is probably restricted to the blood cells.

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

2 Orth, O. S., Leigh, M. D., Mellish, C. H., and Stutzman, J. W., *J. Pharm. and Exp. Therap.*, 1939, **67**, 1.

3 Allen, C. R., Stutzman, J. W., and Meek, W. J., *Anesthesiology*, 1940, **1**, 158.

† Parke Davis adrenalin hydrochloride.

cyclopropane-adrenalin tachycardia after 30 minutes of anesthesia had no irregularities when adrenalin was injected subsequently after the anesthesia had continued for a longer time. This paper is an investigation of this adrenolytic action of cyclopropane on the cardiovascular system. By adrenolytic action is meant the blocking of the response of the effector organs to the injection of adrenalin. In this study blood pressure and cardiac responses were used as indicators.

In order to determine the percentage of dogs that develop this tolerance to adrenalin within 5 hours of cyclopropane anesthesia 31 dogs were anesthetized without premedication, intubated to insure an open airway, and connected through a soda-lime carbon

TABLE I.

Duration of Ventricular Tachycardia in Dogs Following the Injection of 0.01 mg Adrenalin per Kilogram under Cyclopropane Anesthesia.

	Minutes of cyclopropane anesthesia							
Dog No.	5	30	90	120	150	210	300	Remarks
	sec	sec	sec	sec	sec	sec	sec	
1	12	0						Complete protection
2	30	0						
3		18	0					
4		28	0					
5		30	0					
6		40	0					
7		44	0					
8		55	0					
9		65			0			
10		37	48		31	0		
11		65		40		0		
12		70	72		64	0		
13		71	45		17	0		
14		29	40		44	35	0	
15		32	45		30	30	0	
16		52	25		30		0	
17		65	30		30	25	0	
18		76	63		63		0	
19		79		73		66	0	
20		79	66		38	36	15	Partial protection
21		76	72		35	25	18	
22		70	68		65	70	20	
23		60	50	50	50	50	30	
24		60	70		45	47	40	
25		76	67			64	51	
26		51	51	35	42	41	38	No protection
27		50	49		45	44	43	
28		48	64		61	54	73	
29	Ventricular fibrillation							
30	,,		,,					
31	,,		,,					

dioxide absorber to a 100 liter bag containing a 32% mixture of cyclopropane in oxygen. In dogs this concentration of the anesthetic agent produces deep surgical anesthesia with at least partial intercostal paralysis. After 30 minutes of this constant mixture the dogs were injected intravenously with 0.01 mg of adrenalin per kilogram in 5 cc of normal saline at a constant rate of 1 cc per 10 seconds. The duration of ventricular tachycardia was determined by electrocardiograms (lead II) taken throughout a 5-minute period beginning with the injection. The injection of adrenalin was repeated after 90, 150, 210, and 300 minutes of cyclopropane anesthesia or until no ventricular tachycardia occurred. Direct blood pressure tracings were made of 9 of the dogs.

From Table I it can be seen that 19 of the 31 dogs developed a complete protection to cyclopropane-adrenalin tachycardia in 300 minutes or less of anesthesia. Of these animals 2 had no ventricular tachycardia after 30 minutes; 6 after 90 minutes; 1 after 150 minutes; 4 after 210 minutes; and 6 after 300 minutes. Of the remaining 12 dogs 6 had an average ventricular tachycardia of 70 seconds' duration when adrenalin was injected after 30 minutes of anesthesia but had an average of only 29 seconds tachycardia following the injection after 300 minutes. These dogs were considered as being partially protected. Three of the remaining dogs showed no protection within 300 minutes of anesthesia and 3 died of ventricular fibrillation as a result of the first injection of adrenalin.

After the development of complete protection higher doses of adrenalin were given to 13 dogs. Table II indicates the results. Each of the 10 dogs receiving 2 times the control dose showed no tachycardia. Three of 9 dogs had ventricular tachycardia following the injection of 5 to 10 times the control dose. There was no case of ventricular fibrillation with high doses of adrenalin even though 4 of the animals received 1 mg per kilogram, which is 100 times the control dose and more than the M.L.D. for the unanesthetized dog.[4] The degree of protection appears to be of the same order as that produced by decerebration, by bilateral sympathectomy,[3] by blocking the sympathetics with sympatholytic agents, or by protecting the heart with adrenolytic drugs.[5]

The blood pressure levels and the responses to the injections of adrenalin before and after complete protection from cyclopropane-adrenalin tachycardia are listed in Table III. The average pressure

[4] Parkins, W. M., Swingle, W. W., Taylor, A. R., and Hays, H. W., *Am. J. Physiol.*, 1938, **123**, 669.

[5] Orth, O. S., and Allen, C. R., *Am. J. Physiol.*, in press.

TABLE II.
Increased Doses of Adrenalin under Cyclopropane Anesthesia.
Duration of Ventricular Tachycardia.

Dog No.	Before adrenolytic action Control dose sec	After adrenolytic action Same dose sec	2x's dose sec	5x's dose sec	10x's dose sec	100x's dose sec	Time for adrenolytic action to occur min
3	61	0	0				210
4	28	0	0	0			120
5	30	0	0	85			90
6	40	0		15		30	90
7	44	0	0	0			90
10	37	0	0	40			210
16	52	0	0	*		210	210
17	65	0				370	300
32	50	0			0		120
33	30	0	0		0	60	90
34	52	0	0		0		90
35	43	0	0				90
36	53	0	0				240

*40 sec of shifting pacemaker (S-A and ventricular).
The control dose in each case was 0.01 mg adrenalin per kilogram. Fifteen minutes were allowed for recovery between injections of higher doses. All dogs recovered from Tachycardia.

in the dogs while subject to tachycardia was 140 mm Hg, and the average after protection had developed was 136 mm Hg. A response of ventricular tachycardia following the injection of adrenalin was always accompanied by a rise in blood pressure. After protection developed the response to adrenalin was a rise in pressure for 4 of the dogs and either no change or a reversal for the other 5. From the responses of the first 4 animals it is concluded that cyclopropane exerts its adrenolytic action on the heart before it has this effect on the peripheral vascular system. In the remaining 5 dogs cyclopropane had produced an adrenolytic effect upon both the heart and the blood vessels.

Repeated injections of adrenalin in doses of the magnitude used in this study cause comparable blood pressure rises in normal animals.[6] That this failure to obtain cyclopropane-adrenalin tachycardia is not due to the repeated injections of adrenalin is shown in Table I. Nine dogs had complete protection from ventricular tachycardia on the second injection; while after the fifth injection dogs 1, 3 and 13 had irregularities comparable in duration to those obtained with the first injection.

Furthermore, that the adrenolytic action of cyclopropane is not the result of general debilitation from prolonged anesthesia is evi-

[6] Sollmann, T., *A Manual of Pharmacology*, 5th ed., Saunders, 1940, p. 418.

TABLE III.
Blood Pressure under Cyclopropane Anesthesia.

Dog No.	Minutes of cyclopropane	Blood pressure: Level before adrenalin (mm Hg)	Blood pressure: Response to adrenalin (mm Hg)	Duration ventricular tachycardia sec
8	30	156	+ 34	45
	210	140	+ 30	0
10	30	154	+ 56	37
	210	142	+ 46	0
3	30	150	+ 80	18
	90	174	+ 58	0
17	30	100	+ 51	65
	300	140	+ 25	0
22	30	136	+ 74	70
	330	120	0	0
13	30	156	+104	71
	210	155	— 8	0
14	30	145	+ 25	29
	300	105	— 10	0
7	30	122	+ 38	48
	90	130	— 18	0
12	30	144	+ 76	70
	210	122	— 30	0

The dose of adrenalin in each injection was 0.01 mg per kilogram.
Direct blood pressure determinations were made from the femoral artery.

dent from the following: In Table I it is seen that 8 dogs developed protection with no more than 90 minutes of cyclopropane; while 9 dogs still gave a response after 5 hours anesthesia. Blood pressure levels before and after the development of protection are comparable as shown in Table III. An analysis of the electrocardiogram before the injection of the test dose of adrenalin did not indicate whether the adrenolytic effect had developed. There were no significant changes in the P and T waves and the QRS complexes. The average heart rate before the development of protection was 127 beats per minute as compared to an average of 153 after the development of protection.

Conclusion. Although cyclopropane initially sensitizes the dog's heart so that the injection of adrenalin causes ventricular tachycardia, subsequently it may exert an adrenolytic effect on the cardiovascular system.