



$P_{CO_2}$  readings were reproducible to  $\pm 1$  mm. of mercury.

Cardiac output was measured by the dye dilution method. Indocyanine green dye was injected high in the inferior vena cava about the level of the right atrium through a polyethylene catheter passed through the femoral vein, and arterial sampling was made through a catheter placed in mid-aorta via the femoral artery. Arterial blood was drawn at a constant rate by a Harvard withdrawal pump through the cuvette of a Gilford densitometer and the resulting dye curve was recorded. The cardiac output was computed from the area under the curve.<sup>10</sup> Cardiac output determination was made from duplicate dye curves and the average used. The difference between duplicates was less than 10 per cent.

A polyethylene catheter was placed in mid-aorta via the other femoral artery and blood pressure was monitored using a Statham P23 transducer.

The left chest was opened and the heart exposed. A modified Cushny myocardiograph (fig. 1) was sutured to the wall of the left ventricle along the axis of maximal shortening, care being taken to avoid damage to coronary vessels. End-diastolic segment length (EDL) was measured and then by stretching the segment of myocardium between the feet of the myocardiograph, tension at various lengths could be recorded. Tension was plotted against percentage increase in length presented as: Increase in length  $\times 100$ /EDL and the tension at 10 per cent increase in length was measured from this graph.

After the animal had been ventilated with the anesthetic mixture for two hours to achieve a steady circulatory state, control heart rate, length-tension relation and cardiac output were measured. The tension measurements were made before the injection of dye. Propranolol 0.2 mg./kg. was then administered intravenously, and 20 minutes later these parameters were measured again. All recordings were made on a Sanborn Model 565 Oscillograph.

Mean blood pressure was derived from the formula: Mean BP = (diastolic pressure + (systolic - diastolic)/3). Heart rate was measured from the blood pressure tracing immediately before the injection of dye. Stroke

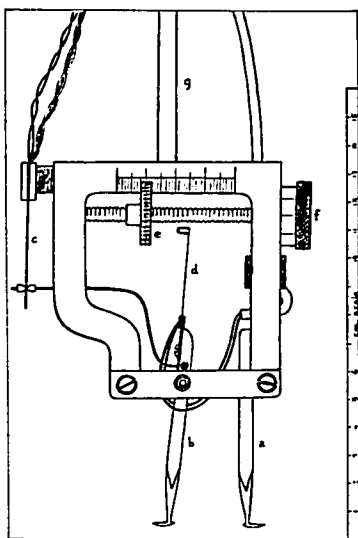


FIG. 1. (a) Fixed leg, (b) movable leg, (c) strain gauge, (d) strain gauge, (e) movable stop, (f) calibrated screw, and (g) support. Feet (a) and (b) are sutured to the myocardium. When stop (e) is at the left, leg (b) is free to move with shortening of the muscle. This shortening is recorded by strain gauge (c). When stop (e) is brought to the right to keep leg (b) in the resting position then as the muscle contracts leg (b) cannot move and the resulting tension is recorded by strain gauge (d). One turn of the screw (f) moves stop (e) 1 mm. to the right and lengthens muscle segment by 1 mm.

volume was calculated by dividing the cardiac output (CO) by the heart rate. Peripheral resistance (PR) was calculated from the formula:  $PR = (\text{mean BP} \times 1,333/\text{CO in ml. per sec.}) \text{ dynes. sec. cm.}^{-5}$ .

Each dog acted as its own control. Because of variation in the size of the animals and therefore in their cardiac outputs, and because the length of the strip of myocardium used to determine length-tension relationship varied, all data are presented as percentage change from control, i.e., (Experimental-Control/Control)  $\times 100$ . The mean of these values for each parameter was recorded as "percentage change" in table 1.

TABLE 1

	Cyclopropane				Halothane			
	Control†	Propranolol†	Difference	Percentage Change‡	Control†	Propranolol†	Difference	Percentage Change‡
Systolic B.P. (mm. Hg)	187	143	- 44	-22.8* ± 4.1	134	134	0	0 ± 8.2
Diastolic B.P. (mm. Hg)	107	95	- 12	-11.6 ± 8.9	105.4	101.6	- 3.8	- 4.6 ± 3.1
Mean B.P. (mm. Hg)	134	111	- 23	-13 ± 6.5	96	94	- 2	- 3.0 ± 2.1
Heart Rate (beats/min.)	132	117	- 15	-11.0 ± 5.6	113.4	100.0	-13.4	-10.0 ± 3.1
Cardiac Output (ml./min.)	3941	2064	-1877	-47.4* ± 5.3	1870	1878	+ 8	4.0 ± 16.7
Stroke Volume (ml.)	31.8	19.2	- 12.6	-41.2* ± 4.7	16.8	19.2	+ 2.4	12.5 ± 9.7
Contractility (grams)	83.4	55.9	- 27.5	-41.0* ± 11.0	67.4	59.0	- 8.4	- 7.4 ± 16.9
Peripheral Resistance (dynes·sec./cm. <sup>2</sup> )	3603	6177	+2574	+41.7* ± 7.9	5345	5444	+99	0.6 ± 12.5
EDL (mm)	21.9	23.8	+ 1.9	7.5 ± 3.7	24.3	26.8	+ 2.5	1.8 ± 2.4

\* Significant  $P < 0.05$ .

† Mean values.

‡ Mean  $\pm$  standard error of the mean.

The results in each group were subjected to statistical analysis to determine whether the changes after propranolol were significant. This was done by assuming that when the 95 per cent confidence interval of the mean (CI), calculated from the formula,  $CI = \text{Mean} \pm (t_{0.05} \times \text{Standard Error of the Mean})$  does not include zero, the result is significant.<sup>11</sup>

### Results

In the cyclopropane group, propranolol caused a statistically significant decrease in cardiac output (47.4 per cent), stroke volume (41.2 per cent), myocardial contractility (27.5 per cent), systolic blood pressure (22.8 per cent), and increase in peripheral resistance (41.7 per cent). Changes not significant at the 5 per cent level were a fall in mean and diastolic blood pressure and in heart rate. End-diastolic segment length was unchanged in one

animal and increased in the other four animals (mean increase 7.5 per cent). This value was not statistically significant.

In the halothane group, the only significant finding was a reduction in heart rate of 10 per cent after the administration of propranolol.

### Discussion

With the exception of a mild bradycardia, propranolol did not produce significant cardiovascular changes in the dog anesthetized with halothane. On the other hand, in the animal anesthetized with cyclopropane, the changes following propranolol were marked. Cardiac output and stroke volume were reduced by more than one-third. Myocardial contractility was also decreased considerably. The increase in peripheral resistance was probably due to the absence of the vasodilating effect of catecholamines on beta receptors

(probably in muscle) while the vasoconstricting effect on the alpha receptors remained unaltered.<sup>12</sup> The decrease of systolic blood pressure, despite an increase in peripheral resistance, was probably secondary to the decrease in cardiac output.

We were unable to find a significant increase in the end-diastolic segmental length. If left ventricular end-diastolic volume had increased, one would expect a significant increase in EDL. Our data certainly suggest that performance capability of the heart was decreased markedly in the cyclopropane group. In the absence of a significant increase in EDL, it is unlikely that this had progressed to failure. However, if the function of the myocardium were impaired by ischemia or disease, it is quite possible that the administration of propranolol could lead to acute cardiac failure. It is therefore suggested that propranolol should not be used in patients with heart disease for the treatment of cardiac arrhythmias during cyclopropane anesthesia.

The lack of significant changes in the halothane group is consistent with reports that propranolol is a pure beta receptor antagonist with minimal side effects.<sup>13</sup>

This work supports the findings of Bagwell *et al.*<sup>6</sup> that in dogs, cyclopropane releases catecholamines. This results in increased cardiac output and blood pressure in the lighter planes of anesthesia. The degree to which the circulation is supported by the action of catecholamines on beta receptors during cyclopropane anesthesia is demonstrated. The data also confirm the lack of significant sympathoadrenal response to halothane anesthesia.

### Summary

The response of the cardiovascular system to propranolol in the anesthetized dog varies with the type of anesthetic used.

Marked changes in cardiac output, stroke volume, systolic blood pressure, peripheral resistance, and myocardial contractility occurred when the animals were anesthetized with cyclopropane. When halothane was used, the only significant change was a mild bradycardia. In

this experiment, change in end-diastolic segment length was not significant.

### References

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