Stroke Volume in the Dog During Graded Exercise

BY YANG WANG, M.D., ROBERT J. MARSHALL, M.D., M.R.C.P., AND JOHN T. SHEPHERD, M.D., M.CH., D.SC.

RUSHIMER and his colleagues, using a sonar teelmic to monitor changes in the diameter of the left ventricle and in thoracic aortic blood flow in the dog during exercise, concluded that, contrary to earlier experience, stroke volume remains relatively constant. Barger and associates, using the direct Fick principle in exercising dogs, did not find a constant relation between stroke volume and cardiac output.

In the present study, dogs were taught to run on a horizontal treadmill but were otherwise untrained. The indicator-dilution method was used to measure the cardiac output during graded exercise. The stroke volume showed little or no increase over the whole range of activity.

Method

Seven mongrel dogs weighing 13.6 to 19 Kg. were used. Cardiac output was measured by the indicator-dilution method, using cardio-green dye (indoeyeamine green dye). Catheters were inserted under either thiopental or local procaine anesthesia (table 1).

One catheter was introduced via an external jugular vein into the pulmonary artery and used for injection of indicator, a no. 6 Lehman catheter, 40 cm. long (dead space, 0.4 ml.), was inserted via a carotid artery into the aortic root. This was connected to a Wood oximeter or a densitometer for continuous photographic recording of dye concentration in the arterial blood. Dye was injected manually, or by means of a power-driven syringe. Calibrations for the indicator-dilution curves were obtained by drawing known concentrations of dye in aliquots of the dog's own blood through the oximeter or densitometer. Cardiac output was calculated from the dilution curve by the method of Stewart, as modified by Kinsman and associates.

An indicator-dilution curve was recorded with the dog standing quietly on a horizontal treadmill. The treadmill was started at 4 km. per hour (km.p.h.), and after 2 minutes, to permit the dog to achieve a steady state (unpublished data), an indicator-dilution curve was recorded during the exercise. The speed of the treadmill was increased by steps of 2 to 4 km.p.h. up to the maximum that the dog could maintain for more than 2 minutes, usually 12 to 14 km.p.h. After 2 minutes at each speed, an indicator-dilution curve was recorded during the exercise. Each procedure entailed the removal of not more than 30 ml. of blood from the aorta which was reinfused immediately after completion of the curve. The dogs did not appear to be disturbed by the presence of the catheters and were able to run unencumbered.

In 1 dog, the following additional measurements were made: with the dog running at 12 km.p.h., the cardiac output and the heart rate were measured after both 2 and 3 minutes. Later, the dog was made to run at 8 km.p.h., and similar measurements were made after 2, 3, and 8 minutes of exercise. Finally, the dog was made to run at 8 km.p.h., during intravenous infusion of epinephrine and of levarterenol, in doses of 16 and 32 μg. of the base per minute, and similar observations were made at the end of each second-minute period while the dog was still running.

The heart rate was recorded by means of the electrically damped aortic pressure tracing immediately before and after inscription of the dye-dilution curve, while the dog was still performing the exercise. The rates before and after the curve never differed by more than 12 beats per minute and were assumed to give the heart rate during inscription of the curve. In 2 dogs, a third catheter was wedged into a distal branch of the pulmonary artery. With the dog at rest, the pulmonary artery wedge tracing showed chiefly respiratory fluctuations. During exercise, however,
STROKE VOLUME DURING EXERCISE

DOG (15 kg.)

RESTING

RUNNING (12 km./hr.)

AORTA

2.5 mg. Cardio-green into Pulmonary Artery

CARDIAC OUTPUT 2.7
HEART RATE 144
STROKE VOLUME 19

2.5 mg. Cardio-green into Pulmonary Artery

CARDIAC OUTPUT 6.3 (L./minute)
HEART RATE 294 (beats/minute)
STROKE VOLUME 21 (ml.)

Figure 1

Typical recordings at rest and during exercise at 12 km. per hour in a dog (weight 15 Kg.). From above: the first tracing shows indicator-dilution curves recorded from the aorta following sudden injection of cardio-green dye into the pulmonary artery. The scale to the right shows the dye concentration in milligrams per liter in the arterial blood. The second tracing shows electrically damped aortic pressure tracing. The third tracing is the pulmonary artery wedge (P.A.W.) pressure tracing. These pressure tracings were used to count the ventricular rate. Note that with the dog at rest the contour of the pulmonary artery wedge pressure is dominated almost entirely by respiratory fluctuations. Only during exercise is there sufficient amplification of this pressure to give the ventricular rate.

The amplitude of the pulsations was increased so that this tracing could also be used to count the heart rate. The rate was identical with the rates counted from the aortic pressure tracings immediately before and after inscription of the curve (fig. 1).

Results

Figure 1 shows indicator-dilution curves recorded with a dog standing and running at 12 km.p.h. The cardiac output increased from 2.7 to 6.3 L./min. The heart rate increased from 144 to 294 min. Thus the change in stroke volume was only from 19 to 21 ml.

The results of the 11 experiments in the 7 dogs are shown in figure 2 and table 1. With the dogs standing at rest, the cardiac output ranged from 2.9 to 4.3 L./min., the heart rate from 100 to 158/min., and the stroke volume from 16 to 37 ml. At the maximal exercise achieved, when the cardiac output was increased by 1.5 to 3.5 (average 2.4) times, 5 dogs showed less than 5 per cent increase in stroke volume over resting values; in the remainder, the increases at maximal exercise over resting values were 8, 11, 11, 14, 15, and 19 per cent. Of the 4 dogs in which duplicate experiments were carried out, 2 dogs (dogs 1 and 5, table 1) showed similar stroke volumes on the 2 occasions. In dogs 2 and 3, although values obtained for cardiac output and stroke volume differed somewhat between the 2 sets, there was good agreement within the sets. The difference could well be due to discrepancies in the calibration curves on the 2 occasions.

The details of the comprehensive experiment on 1 dog are given in table 2. Both during graded exercise from 4 to 12 km.p.h. and during continuous exercise at 8 km.p.h., the stroke volume was 26 to 30 ml., which was
Eleven series of observations on 7 dogs (13.6 to 19 Kg.) standing at rest and at various grades of exercise. Lines join points obtained during the same experiment. Note that in the individual dogs there is little change in stroke volume (a) so that heart rate and cardiac output increase nearly proportionately (b).

similar to that at rest (28 ml.). In the final series of observations, the cardiac output, heart rate, and stroke volume were first determined at the end of the second minute of exercise at 8 km.p.h. to serve as a control. The values were 5.3 L/min., 187 beats/min. and 28 ml., respectively. During exercise at 8 km.p.h., combined with infusion of epinephrine at 16 µg./min., there was little change in cardiac output (from 5.3 to 5.5 L/min.), while the heart rate fell from 187 to 150/min. There was thus a rise in stroke volume from 28 to 37 ml. With infusion of epinephrine at 32 µg./min., the cardiac output was 5.7 L/min., the heart rate 147/min., and the stroke volume 39 ml. When levarterenol was infused at 16 µg./min. for 2 minutes while the dog was running at 8 km.p.h., there was a slight fall in cardiac output from 5.3 to 4.9 L/min.; heart rate slowed from 187 to 135; the stroke volume increased to 36 ml. When levarterenol was infused at 32 µg./min., the cardiac output was 4.7 L/min., the heart rate fell to 84/min., and the stroke volume reached 56 ml., which was double its normal value.

Discussion

The indicator-dilution technic, with continuous recording of the changes in dye concentration in the arterial blood, is well suited for measurement of cardiac output and stroke vol-

Figure 2
Eleven series of observations on 7 dogs (13.6 to 19 Kg.) standing at rest and at various grades of exercise. Stroke index (solid circles) and heart rate (open circles) are plotted against cardiac index. The linear regression equation correlating stroke index and cardiac index is statistically significant (r = 0.85; S.E. = 0.21, p<0.001). The data plotted in this way should be compared with figure 2. This plot illustrates the fallacy of assuming that expressing cardiac output per unit of body surface necessarily renders the data capable of analysis as a homogenous group. From such a plot, one might draw the erroneous conclusion that stroke volume increases significantly with exercise.

Figure 3
Eleven series of observations on 7 dogs (13.6 to 19 Kg.) standing at rest and at various grades of exercise. Stroke index (solid circles) and heart rate (open circles) are plotted against cardiac index. The linear regression equation correlating stroke index and cardiac index is statistically significant (r = 0.85; S.E. = 0.21, p<0.001). The data plotted in this way should be compared with figure 2. This plot illustrates the fallacy of assuming that expressing cardiac output per unit of body surface necessarily renders the data capable of analysis as a homogenous group. From such a plot, one might draw the erroneous conclusion that stroke volume increases significantly with exercise.
STROKE VOLUME DURING EXERCISE

Table 1

Data From Eleven Experiments on Seven Dogs During Graded Exercise

<table>
<thead>
<tr>
<th>Dog</th>
<th>Weight (Kg.)</th>
<th>Cardiac output (L/min.)</th>
<th>Heart rate (beats/min.)</th>
<th>Stroke volume (ml.)</th>
<th>Cardiac output (L/min.)</th>
<th>Heart rate (beats/min.)</th>
<th>Stroke volume (ml.)</th>
<th>Cardiac output (L/min.)</th>
<th>Heart rate (beats/min.)</th>
<th>Stroke volume (ml.)</th>
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<th>Stroke volume (ml.)</th>
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<th>Heart rate (beats/min.)</th>
<th>Stroke volume (ml.)</th>
<th>Cardiac output (L/min.)</th>
<th>Heart rate (beats/min.)</th>
<th>Stroke volume (ml.)</th>
<th>Cardiac output (L/min.)</th>
<th>Heart rate (beats/min.)</th>
<th>Stroke volume (ml.)</th>
<th>Cardiac output (L/min.)</th>
<th>Heart rate (beats/min.)</th>
<th>Stroke volume (ml.)</th>
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<td>144</td>
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<td>135</td>
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<td>135</td>
<td>20</td>
<td>3.8</td>
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<td>24</td>
</tr>
</tbody>
</table>

* Catheters inserted under thiopental anesthesia.

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Stroke volume during exercise. The dog can run freely, repeated measurements can be made quickly and there is no mechanical hindrance to the action of the heart. Previous observations on stroke volume in exercising dogs using the indicator-dilution method have been confined to studies made immediately after exercise. From such studies, Gregg and associates concluded that there was no constant relation between stroke volume and cardiac output. In the present experiments, the indicator-dilution curves were obtained during exercise at a time when cardiac output, heart rate, and blood pressure have been previously shown to be relatively stable (unpublished data). This is supported by the observations on 1 dog running at 8 km.p.h. for 8 minutes, and at its "maximal" speed of 12 km.p.h. for 3 minutes (table 2) in which measurements of heart rate and cardiac output at repeated intervals gave similar results.

Examination of the data for individual dogs showed that at all grades of exercise, changes in stroke volume contributed relatively little to the increase in cardiac output. Even at maximal exercise, when the cardiac output had increased from 1.5 to 3.5 (average 2.4) times, the values obtained with the dog standing at rest, 5 experiments in 4 dogs showed no significant increase in stroke volume (less than...
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Table 2

Comprehensive Experiments in One Dog (Dog 7; Weight, 13.6 Kg.)

<table>
<thead>
<tr>
<th></th>
<th>Cardiac output (L./min.)</th>
<th>Heart rate (beats/min.)</th>
<th>Stroke volume (ml.)</th>
<th>Change in stroke volume from standing at rest (per cent)</th>
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<td>Graded exercise (speed)</td>
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<tr>
<td>Rest, standing</td>
<td>4.1</td>
<td>148</td>
<td>28</td>
<td>+4</td>
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<td>4 km. p.h.</td>
<td>5.1</td>
<td>177</td>
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<tr>
<td>8 km. p.h.</td>
<td>6.4</td>
<td>247</td>
<td>26</td>
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<tr>
<td>10 km. p.h.</td>
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<td>280</td>
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<td>12 km. p.h. (3 minutes)</td>
<td>8.1</td>
<td>274</td>
<td>30</td>
<td>+7</td>
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<td>Continuous exercise at 8 km. per hour (duration)</td>
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<tr>
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<td>111</td>
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<tr>
<td>2 minutes</td>
<td>5.1</td>
<td>194</td>
<td>26</td>
<td>-7</td>
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<tr>
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<tr>
<td>8 minutes</td>
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<td>208</td>
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<td>Exercise at 8 km. per hour*</td>
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<td>During intravenous infusion of epinephrine</td>
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<td>150</td>
<td>37</td>
<td>+32</td>
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<td>5.7</td>
<td>147</td>
<td>39</td>
<td>+39</td>
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<td>During intravenous infusion of levarterenol</td>
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<tr>
<td>16 /ig. per minute</td>
<td>4.9</td>
<td>135</td>
<td>36</td>
<td>+29</td>
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<td>32 /ig. per minute</td>
<td>4.7</td>
<td>84</td>
<td>56</td>
<td>+100</td>
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</table>

*Observations made at end of second minute.

5 per cent) over resting values. In the 6 other experiments, the increases in stroke volume were only 8, 11, 14, 15, and 19 per cent. These contrast with corresponding increases in heart rates of 133, 216, 270, 222, 236, and 182 per cent. These results are in good agreement with those of Rushmer and associates1, 2 who used different methods.

Figure 3 shows the results of all the experiments plotted as cardiac output per square meter of body surface against the heart rate and stroke volume per square meter of body surface. The surface area was obtained from Meek’s formula (11.2 X weight^{2/3}). The purpose of the plot is to illustrate the common fallacy, emphasized by Tanner, 21 of assuming that the use of such factors as surface area to normalize data will necessarily render such data comparable and susceptible of analysis as a homogeneous group. In the present case, the regression line calculated from such a plot might lead one to believe that stroke volume does indeed show a major increase with exercise, a conclusion which would be completely erroneous as it is not borne out by the experiments on individual dogs (fig. 2).

This relative constancy of the stroke volume in the dog during exercise contrasts with the large changes in stroke volume which may occur under other circumstances. Tachycardia in the resting dog, induced by electric stimulation of the atria, 5 is associated with marked reduction in stroke volume. In dogs with complete atrioventricular block in which the ventricular rate was controlled by electric stimulation, Warner and Toronto 13 found that at ventricular rates between 140 and 250 per minute the cardiac output was independent of heart rate during both rest and exercise. In the present experiments, when epinephrine was infused during exercise, the increase in cardiac output was due to moderate increases in both heart rate and stroke volume over resting values. When levarterenol was infused at 32 /ig./min. during exercise, the heart rate was actually less than at rest, and the increase...
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in cardiac output over resting values was achieved by doubling the stroke volume.

Summary

Measurements of stroke volume were made in dogs during graded exercise on a horizontal treadmill up to the maximal exercise which they could maintain for 2 to 3 minutes. Eleven series of experiments were performed on 7 dogs. The cardiac output was measured by the indicator-dilution technic and the heart rate was measured from the aortic pressure tracing. At all grades of exercise, there was little or no change in stroke volume. Even with severe exercise, when the cardiac output had increased from 1.5 to 3.5 (average, 2.4) times the values obtained with the dog standing at rest, the stroke volume showed less than 5 per cent change over resting values in 5 experiments on 4 dogs, while in the remainder the increases were 8, 11, 11, 14, 15, and 19 per cent. Thus, the increase in cardiac output in the untrained exercising dog is almost directly proportional to the increase in heart rate. This is in contrast to other situations, such as the combination of exercise with infusion of catecholamines, where an increase in stroke volume may make an important contribution to the increase in cardiac output.

Acknowledgment

The authors wish to thank Dr. H. J. Somler for his co-operation and W. A. Mocker and Julius Zarins for their assistance.

Summario in Interlingua

Le volumino systolic esseva mesurate in canes subjicito a grados progressive de exercitio in un ambulatorio horizontal, usque al maximo mantenable durante 2 a 3 minutas. Deze-un series de experimentos esseva executate in 7 canes. Lo rendimento cardiac esseva mesurate per le technica a dilution de indicatore, e le frequentia cardiac esseva determinate super le base del registration del tension aortic. A omne le vario grados de exercitio, pauc o nulla alteration esseva notate in le volumine systolic. Memio con sever grados de exercitio—quando le rendimento cardiac habeva crescite usque a inter 150 e 350 pro cento del valor de reposo—le volumine systolic esecleva le correspondente valor de reposo per minus que 5 pro cento in 5 experimentos in 4 canes, durante que in le remanente experimentos le procentage del

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