EFFECTS OF ENDOTOXIN ON MYOCARDIAL HEMODYNAMICS, PERFORMANCE, AND METABOLISM

L. B. Hinshaw, L. T. Archer, L. J. Greenfield, and C. A. Guenter

Technical Report No. 39
University of Oklahoma Medical Center THEMIS Contract

This document has been approved for public release and sale; its distribution is unlimited.

Reproduction in whole or in part is permitted for any purpose of the United States Government

MEDICAL CENTER RESEARCH AND DEVELOPMENT OFFICE
OF THE UNIVERSITY OF OKLAHOMA FOUNDATION, INC.
800 Northeast Thirteenth Street
Oklahoma City, Oklahoma 73104
Experiments investigating the cause of the decrease in cardiac output after endotoxin have demonstrated a decrease in venous return in both the canine and primate species (9,11-13,27). It appears therefore that systemic hypotension in endotoxin shock is in large part precipitated by peripheral rather than direct cardiac mechanisms.

Although it is generally agreed that the heart will ultimately fail in shock, its possible contributory role in the development of irreversibility is in serious question. It is postulated by some that heart failure is seen only late in shock subsequent to prolonged inadequate coronary perfusion (2). However, others have developed a "cardiac theory" which assumes that irreversible shock is due to a sustained depressed cardiac output of a dysfunctioning heart, failing as a relatively early event (14, 25). A cardiac-toxic theory has also been suggested in which a myocardial depressant factor is postulated to directly decrease cardiac performance (15-17).

The objective of the present study is to investigate the role of the heart in endotoxin shock, to determine if it is directly damaged by endotoxin or fails as a result of deleterious hemodynamic or respiratory alterations set into motion by the shock state.

Experiments designed to distinguish between direct and indirect cardiac factors, have been carried out and results exclude a direct cardiotoxic action of endotoxin; demonstrate a strong resistance of the myocardium in endotoxin shock; and suggest that myocardial failure may occur only after extensively prolonged systemic hypotension.
METHODS

Experiments were carried out on adult mongrel dogs intravenously anesthetized with sodium pentobarbital, 30 mg/kg. The basic procedure was to support an isolated left ventricle by blood exchanged with a heparinized support animal. The donor heart dog was anesthetized, and the chest opened by median sternotomy after the animal was placed on a constant volume respirator. The azygous vein and subclavian artery were ligated and divided. Ligatures were loosely placed around the thoracic aorta distal to the subclavian artery, the brachiocephalic artery, and superior and inferior vena cavae. The pericardial sac was opened along its ventral surface and the animal was heparinized (3-5 mm/kg). The vagi were then cut in the neck and the brachiocephalic artery was cannulated with a tygon tube elevated to a height of 100-125 cm above the heart level. The superior vena cava was cannulated with a blood filled plastic tube led through a roller-type blood pump prepared to draw blood from the aorta of the support dog. To transfer the donor heart to the external perfusion system without interruption of coronary flow, the brachiocephalic outflow from the heart was opened, allowing blood to fill the tubing against a hydrostatic pressure in order to provide adequate coronary perfusion. The aorta of the isolated heart was then tied distal to the origin of the brachiocephalic artery, the superior vena caval inflow from the pump was commenced at about 120 cc/minute, and the inferior vena cava was immediately ligated. Blood from the aortic outflow of the isolated heart was collected in a plastic reservoir (Figure 1) and returned to the dog, perfusing the heart at a flow rate equal to the superior vena caval inflow. The heart
and lungs were then removed from the chest and supported by the trachea in
the external system with adequate coronary pressure and flow constantly
provided. The lungs of the isolated heart were not ventilated, and the
support animal was respiring spontaneously.

A strain gauge arch was sutured under stretch to the lateral wall of
the left ventricle for measurement of myocardial contractile force (3).
Left ventricular pressure was measured simultaneously for end diastolic
pressure (0-40 mm Hg), and systolic pressure (0-200 mm Hg) by means of
separate Statham pressure transducers attached by a "Y"-connector to a
plastic cannula inserted through a purse-string suture in the apex of
the left ventricle.

The right heart was then bypassed after first placing a saline filled
plastic tube into the right ventricle via the atrium, and then cannulating
the pulmonary artery from a "T"-connector previously secured to the superior
vena cava inflow tubing. The cannulation of the pulmonary artery required
only a few seconds during which time the coronary vessels were retrograde-
perfused with blood by hydrostatic pressure from the aortic outflow tubing.
Coronary venous blood was collected from the right ventricular drain into
a plastic reservoir and returned together with brachiocephalic outflow to
the support dog via a second pump. Cardiac output was taken as the sum of
aortic outflow and coronary flow, both measured with a cylinder and stop
watch (Figure 1). Temperature of coronary venous blood was monitored with
a temperature probe. Aortic pressure, left ventricular pressures, cardiac
contractility of the isolated heart, and systemic pressure of the support
dog were monitored continuously on a Sanborn recorder. The first derivative
of the left ventricular pressure, \( \frac{dP}{dT_{\text{max}}} \), was also continuously recorded
by means of a resistance-capacitance differentiating network. Mean aortic
pressure and cardiac output were increased steadily in the isolated heart preparation by adjustment of a screw clamp on the aortic outflow and elevation of pump speed supplying the pulmonary artery. Coronary arterial and venous \( P_{O_2} \), \( P_{CO_2} \), and pH were followed by utilizing an Instrumentation Laboratories blood gas analyzer calibrated prior to each determination with known gas mixtures. Oxygen content of coronary arterial and venous blood was measured by a Van Slyke manometric blood gas analyzer. Simultaneously obtained coronary blood flow measurements permitted the calculation of oxygen uptake and carbon dioxide production from the product of coronary flow and A-V oxygen or carbon dioxide differences.

During the equilibration period of the isolated heart preparation, aortic pressure was stabilized at an average of 118 mm Hg with a cardiac output of 76 cc/min/kg body weight (based on the weight of the heart donor dog). These pressure and flow values supported and maintained left ventricular systolic and diastolic pressure, coronary blood flow, and myocardial oxygen uptake in the physiological range, and were maintained during the thirty-minute control period in all experiments. At the end of the control period, an \( LD_{90} \) of \( E. \) coli endotoxin, 1.2 mg/kg (Difco, Detroit), was injected both intravenously into the support dog and into the pulmonary artery of the isolated heart. The mean coronary arterial pressure of the isolated heart was adjusted to that of the mean systemic pressure of the support animal by changing pulmonary blood flow rate with the blood pump. At 200 minutes post-endotoxin, coronary pressure and cardiac output were returned to pre-endotoxin values and cardiac performance, metabolic and hemodynamic parameters were evaluated. In addition, coronary pressure and cardiac output in all experimental and control studies were equalized at 60 and 180 minutes after zero time.
The control experiments, \((N = 6)\) not given endotoxin, were conducted in order that mean coronary pressures and mean cardiac outputs of the isolated hearts were matched to those of the previous experimental group \((N = 7)\) by pump adjustment at precisely the same times up to a terminal point of 200 minutes after zero time.

**Stroke work** in gram-meters was calculated from the formula used by others (19):

\[
(MAP - LVEDP) (SV) \times (1.36)/100
\]

where \(MAP\) = mean aortic pressure (mm Hg); \(LVEDP\) = left ventricular end diastolic pressure (mm Hg) and \(SV\) = stroke volume in cc, determined by dividing cardiac output by heart rate. The acceleration component of left ventricular stroke work was disregarded in the calculations on the basis that it represents less than 1 per cent of total stroke work (20). **Cardiac power** was calculated and expressed as work per second. The maximum change in pressure \((dP/dT_{\text{max}})\) occurring during isometric contraction of the left ventricle (10,19) was continuously recorded and expressed as the first derivative of the pressure rise. Calibration of the \(dP/dT\) recording was carried out by analysis of the slope of a line drawn tangentially to the steepest portion of the left ventricular isovolumetric tracing and expressed as mm Hg/sec (5).

Coronary blood flow averaged 160 cc/min/100 gms left ventricle at zero time (range 99-290) in 13 experiments.

Oxygen uptake was assumed to be negligible in atria and right ventricle (bypassed) as was reported by others (21) and averaged 11 cc/min/100 gms left ventricle at zero time (range 7-16 cc/min) in 13 experiments.
RESULTS

Figure 2 illustrates mean values for aortic pressure, cardiac output and blood temperature in control and endotoxin isolated working heart preparations. Mean aortic pressure changes in the endotoxin-series reflect alterations in mean systemic pressure of the support dog, except at the 200 and 180 minute readings when pressures were matched to zero time and 60 minute values respectively, by pump adjustment. Thus, two sets of matching points were achieved, one at the hypotensive value, and the last at the normotensive pressure level and cardiac output was similarly adjusted at the same time intervals. The mean values ± SE of the experimental group for blood temperature (Tb), cardiac output (CO) and aortic pressure (MAP) at 0 and 200 minutes respectively are as follows:

\[
\begin{align*}
T_b &= 38.50 \pm 0.54, 38.70 \pm 0.37; \\
CO &= 482.7 \pm 28.8, 481.6 \pm 28.9; \\
MAP &= 118.4 \pm 4.2, 117.3 \pm 3.9.
\end{align*}
\]

These parameters were controlled because of their direct influence on performance, metabolic and hemodynamic characteristics of the myocardium (4, 21) and in order that the effects of endotoxin on the heart could be clearly discernable. In addition, control experiments were carried out after the completion of the endotoxin studies, with pressures and flows similarly matched by pump adjustment as in the experimental group. Results show no significant differences in values between the two series in all measured parameters at all recorded time periods.

With the foregoing protocol carefully executed, another set of parameters dealing with performance, metabolism and hemodynamics were measured or calculated and these are illustrated in the remaining figures.

Figure 3 characterizes the typical findings obtained in an isolated heart preparation treated with an LD_{50} of endotoxin. Only values during the matching periods, when pressures and flows were rigidly controlled, are shown in the figure. Results show that the heart performs normally both metabolically and
in regard to energy output at times of comparable aortic pressure and cardiac outputs after endotoxin administration. Findings at 180 minutes clearly resemble those at 60 minutes, while those at 200 minutes are very similar to those at -30 minutes and zero time. Thus, endotoxin is seen to have no adverse effects on myocardial performance characteristics including left ventricular contractile force, $dP/dT_{\text{max}}$, and power (work/sec) and no deleterious action was seen in the metabolic parameters of oxygen uptake and carbon dioxide production. Relationships between after-load (mean aortic pressure) and pre-load (left ventricular end diastolic pressure [LVEDP]) remained clearly similar during the control and post-endotoxin periods. Results strikingly demonstrate the notable effects of aortic pressure and cardiac output on contractility, $dP/dT$, coronary flow, LVEDP, power, and $O_2$ uptake and $CO_2$ production.

These results emphasize the importance of controlling pressure and flow in the isolated heart preparation in order to assay the effects of endotoxin. In order to compare the response of the heart exclusively to changes in aortic pressure and cardiac output in the absence of endotoxin, a second series of control experiments was carried out. Typical results from such an experiment are shown in Figure 4, and no significant differences in the response of any parameter from those of the endotoxin group are discernable from the various measurements and calculations of performance and metabolic characteristics.

Figure 5 summarizes mean results from control and endotoxin shock experiments. Particular evaluation of data was made at two time periods, 180 and 200 minutes, when aortic pressure and cardiac output are matched with earlier values at 60 minutes and zero time, respectively. The mean values ± SE of the experimental group for $dP/dT_{\text{max}}$, stroke work (SW), heart rate (HR),
power (P) and LVEDP at 0 and 200 minutes respectively are as follows:

\[
dP/dT_{\text{max}} = 2473 \pm 173.00, 2658 \pm 379.36; \quad SW = 5.91 \pm 0.37, 4.89 \pm 0.34;
\]

\[
HR = 127.1 \pm 4.7, 146.4 \pm 4.5; \quad P = 12.41 \pm 0.65, 11.90 \pm 0.74; \quad \text{and} \quad \text{LVEDP} = 3.96 \pm 1.20, 7.86 \pm 4.03.
\]

It is seen that all parameters show similar changes regardless of the presence or absence of endotoxin. Findings clearly illustrate that the decreases of the various performance characteristics of the heart including dP/dT, stroke work and power, at 60 and 180 minutes (p < 0.01) are due to lowered aortic pressure and cardiac output, rather than endotoxin directly. When aortic pressure and flow are elevated to control values at 200 minutes (Figure 2), these performance characteristics return to the normal values observed at zero time. Mean LVEDP, though decreasing (p < 0.05) in the control at 60 minutes is insignificantly changed at 180 minutes. LVEDP is insignificantly decreased at 60 and 180 minutes in the endotoxin group and insignificantly elevated at 200 minutes when pressure and flow are restored in both the control and endotoxin series. The observed mean increase in LVEDP in both groups at 200 minutes was due to the fact that each group contained one experiment in which LVEDP was elevated above 20 mm Hg.

Figure 6 demonstrates the effects of endotoxin on coronary blood flow, coronary vascular resistance, oxygen uptake and carbon dioxide production. Coronary flow changes insignificantly (p > 0.05) in all experiments up to 180 minutes while coronary vascular resistance falls during the total post-endotoxin period in the experimental group (p < 0.05). Notable findings were the large increases in coronary flows occurring in both groups at 200 minutes greatly exceeding those during the control periods (p < 0.05). Both mean oxygen uptake and carbon dioxide production returned to control values at termination of all studies. The significant reduction of O₂
uptake and CO₂ production (p ≤ 0.05) at 180 minutes is seen in both the control and endotoxin series. Mean RQ values from -30 to +200 minutes in endotoxin studies are 0.83, 0.90, 0.99, 0.88, 0.91 and in control experiments are 0.83, 0.76, 0.91, 0.86, 0.91. There were no significant changes in the RQ values.

Tables Ia and Ib summarize mean oxygen and carbon dioxide pressures, contents, and pH changes in coronary arterial and venous blood observed in both endotoxin and control experiments. It is noted that the endotoxin series showed significant acidosis by 200 minutes (p ≤ 0.05) while pH was seen to remain relatively constant in the control group. Coronary venous oxygen content was not elevated at termination of the endotoxin experiments although increases were seen in the control series. Results demonstrate a lower mean coronary venous oxygen content at the same mean Po₂ in the endotoxin treated heart in comparison to the control group at 200 minutes.
DISCUSSION

The primary purpose of the present study was to determine possible direct toxic effects of endotoxin on canine myocardial tissue. To this end, two kinds of experimental controls were devised and executed: (a) cardiac performance and metabolism were assayed after the end of a three hour period of hypotension by requiring the heart to work at the precise pre-shock levels of cardiac output and aortic pressure; and (b) the degree of hypotension and depressed cardiac output in the isolated heart preparation in shock studies was mimicked by pump adjustment in the absence of endotoxin. In addition, the heart was also evaluated at 180 minutes at cardiac output and aortic pressure values obtained at 60 minutes.

Three hours of systemic hypotension and depressed cardiac output followed by restoration of pressure and flow to control values by pump adjustment, revealed statistically insignificant differences in results between the endotoxin or control groups in which endotoxin was not administered. Myocardial contractility, cardiac power (work/sec.), dP/dT, O₂ uptake and CO₂ production at 200 minutes post-endotoxin were statistically unaltered from control pre-endotoxin values. These observations appear to preclude any significant direct toxic action of endotoxin on myocardial performance and metabolism. Although findings reveal a strong resistance of the myocardium to endotoxin, the effects of prolonged systemic hypotension may ultimately impair cardiac function. In single heart experiments in both the endotoxin and control series, LVEDP rose above control values at 200 minutes upon restoration of aortic pressure and cardiac output.

The studies show that the heart treated with endotoxin exhibits marked changes in hemodynamics which appear to assure its high level of performance and metabolism: coronary flow markedly increases when the heart is required to work at the pre-shock level and the coronary venous oxygen content remains
at a normally low value, and oxygen uptake is adequately achieved even when 

pH has fallen to significantly depressed values. Thus, increased blood flow, 

achieved by marked coronary vasodilatation coupled with an adequate extraction 

of oxygen from capillary blood, and the ability of the heart to achieve normal 

oxidative metabolism in an acid medium provides the necessary essential re- 

quirements permitting the heart to operate at normal 1-vels of performance. 

Results from the present study show that dP/dT, cardiac power and aortic 

pressure are directly related to oxygen uptake of the myocardium. These 

results are in agreement with the view that heart failure is probably only 

seen late in shock subsequent to prolonged inadequate coronary perfusion (2). 

No evidence was obtained to support recent observations in hemorrhagic and 

endotoxin shock, that a myocardial depressant factor is released which directli 

decreases cardiac performance (15-17). Results from the present study fail to 

reveal a single instance of endotoxin toxicity on myocardial work performance 

or oxidative metabolism. These observations support the conclusions of some 

investigators (2,5,18,27) but are in disagreement with others (14,23,24-26). 

The postulation that primary heart failure is an early event in shock (1,6-8), 

and initiates the irreversible state, is not supported by the findings of the 

present investigation.

The problem of the precise role of the heart in the development of irrever-

sible endotoxin shock is complicated by events occurring in the periphery 

which most assuredly adversely influence cardiac output (9,11-13,22,27), causin 

gs decrease on the basis of diminished venous return due to peripheral pooling 

of blood. In addition, the resultant prolonged systemic hypotension may assure 

the precipitation of a vicious cycle by virtue of the adverse effects of 

diminished coronary perfusion pressure and flow on myocardial integrity. Care-

ful future consideration of adverse indirect hemodynamic or respiratory effects
on the myocardium is suggested from data in the present study in order to
assay more clearly the role of the heart in septic shock (24,26).

*Acknowledgement: Appreciation is expressed to R. T. Brantley, Janet Camp,
Hubert Jennings, Mary Lane, Susan Owen, Mary Harple, and Mary Carol Whitaker
for valuable technical assistance.
REFERENCES


**LEGEND FOR FIGURES**

**Figure 1.** Schematic diagram of isolated perfused heart preparation.
(Blood is obtained from aorta of support dog and subsequently returned to femoral vein. Arrows show direction of blood flow. Lungs are not ventilated.)

PA ........ pulmonary artery
A ........ aorta
BC ........ brachiocephalic artery
RA ........ right atrium
RV ........ right ventricle
AZ ........ azygous vein
SVC ........ superior vena cava
IVC ........ inferior vena cava
LVC ........ left ventricular pressure catheter
CVC ........ coronary drainage catheter
AC ........ aortic pressure catheter
SC ........ adjustable screw clamp
SGA ........ strain gauge arch
TP ........ temperature probe
WB ........ water bath at controlled temperature

**Figure 2.** Parameters controlled in isolated heart experiments. Mean blood temperature is maintained relatively constant in both control and experimental preparations. Mean aortic pressures of endotoxin-treated hearts are matched with intact support animal following endotoxin injection (Mean ± S.E.), and values at 180 minutes and 200 minutes matched those at 60 minutes and zero time, respectively.
Cardiac output and mean aortic pressure of control isolated heart preparations are also matched with endotoxin shock studies by adjustment of pump and screw clamp (as shown in Figure 1).

Figure 3. Effects of endotoxin (LD₉₀) on performance and metabolism of isolated working heart. (Single experiment).

Figure 4. Single, control experiment showing effects of decreasing cardiac output and aortic pressure on myocardial performance and metabolism. Mean aortic pressure and cardiac output values were adjusted to equal mean values of shock experiments at -30, 0, +60, +180, +200 minutes (adjustments were also made at 15 min. intervals).

Figure 5. Effects of endotoxin (LD₉₀) on myocardial performance characteristics including $\frac{dP}{dT}_{\text{max}}$, stroke work, heart rate, power and left ventricular end diastolic pressure (mmHg). (Mean ± S.E.; 6 control and 7 endotoxin experiments). Mean aortic pressure and cardiac output values of all control heart preparations were adjusted to equal mean values of endotoxin studies at -30, 0, +60, +180, +200 minutes (Blood temperature constant).

Figure 6. Effects of endotoxin (LD₉₀) on myocardial hemodynamics and metabolism (Mean ± S.E.; 6 control and 7 endotoxin experiments). Mean aortic pressure and cardiac output values of all heart control and experimental preparations are equal at -30, 0, +200 minutes, and those at 60 and 180 minutes are also equal. (See Figure 2). (Blood temperature constant).
Table 1b. Coronary Arterial and Venous Blood Gas and pH Values (M ± S.E.)
(7 experimental and 6 control studies)

**CONTROL SERIES**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>-30</th>
<th>0</th>
<th>+60</th>
<th>+180</th>
<th>+200</th>
</tr>
</thead>
<tbody>
<tr>
<td>pO₂</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>75(6)</td>
<td>66(7)</td>
<td>61(6)</td>
<td>55(4)</td>
<td>55(4)</td>
</tr>
<tr>
<td>V</td>
<td>29(2)</td>
<td>28(2)</td>
<td>28(3)</td>
<td>27(2)</td>
<td>29(4)</td>
</tr>
<tr>
<td>O₂ Content</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>15.2(0.9)</td>
<td>14.3(0.9)</td>
<td>14.2(0.6)</td>
<td>13.7(0.9)</td>
<td>13.9(1.1)</td>
</tr>
<tr>
<td>V</td>
<td>7.5(0.9)</td>
<td>7.6(0.7)</td>
<td>7.2(0.6)</td>
<td>8.0(0.8)</td>
<td>8.8(0.6)</td>
</tr>
<tr>
<td>pCO₂</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>31(2)</td>
<td>31(3)</td>
<td>31(3)</td>
<td>28(2)</td>
<td>23(3)</td>
</tr>
<tr>
<td>V</td>
<td>34(3)</td>
<td>36(3)</td>
<td>34(4)</td>
<td>30(2)</td>
<td>26(3)</td>
</tr>
<tr>
<td>CO₂ Content</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>39.1(0.9)</td>
<td>40.1(1.3)</td>
<td>38.6(2.0)</td>
<td>34.6(1.2)</td>
<td>33.5(1.4)</td>
</tr>
<tr>
<td>V</td>
<td>45.8(1.6)</td>
<td>45.4(1.8)</td>
<td>45.0(2.5)</td>
<td>39.4(1.9)</td>
<td>37.8(1.9)</td>
</tr>
<tr>
<td>pH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>7.41(0.02)</td>
<td>7.42(0.04)</td>
<td>7.38(0.03)</td>
<td>7.42(0.02)</td>
<td>7.42(0.0)</td>
</tr>
<tr>
<td>V</td>
<td>7.39(0.03)</td>
<td>7.38(0.03)</td>
<td>7.37(0.04)</td>
<td>7.40(0.02)</td>
<td>7.42(0.0)</td>
</tr>
</tbody>
</table>
Table Ia. Coronary Arterial and Venous Blood Gas and pH Values (M ± S.E.)
(7 experimental and 6 control studies)

**ENDOTOXIN SERIES**

<table>
<thead>
<tr>
<th>Time (Minutes)</th>
<th>Parameter</th>
<th>-30</th>
<th>0</th>
<th>+60</th>
<th>+180</th>
<th>+200</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pO2</td>
<td>A</td>
<td>V</td>
<td>A</td>
<td>V</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>73(4)</td>
<td>23(1)</td>
<td>70(4)</td>
<td>22(2)</td>
<td>60(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>56(5)</td>
<td></td>
<td>61(6)</td>
</tr>
<tr>
<td></td>
<td>O₂ Content</td>
<td>A</td>
<td>V</td>
<td>A</td>
<td>V</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14.0(1.0)</td>
<td>6.1(0.9)</td>
<td>14.0(0.8)</td>
<td>5.8(1.0)</td>
<td>11.9(2.3)</td>
</tr>
<tr>
<td></td>
<td>pCO₂</td>
<td>A</td>
<td>V</td>
<td>A</td>
<td>V</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30(1)</td>
<td>37(2)</td>
<td>30(2)</td>
<td>34(2)</td>
<td>26(1)</td>
</tr>
<tr>
<td></td>
<td>CO₂ Content</td>
<td>A</td>
<td>V</td>
<td>A</td>
<td>V</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>39.2(0.9)</td>
<td>45.6(0.5)</td>
<td>38.3(0.9)</td>
<td>45.8(0.8)</td>
<td>28.5(1.0)</td>
</tr>
<tr>
<td></td>
<td>pH</td>
<td>A</td>
<td>V</td>
<td>A</td>
<td>V</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.40(0.03)</td>
<td>7.38(0.03)</td>
<td>7.42(0.03)</td>
<td>7.39(0.03)</td>
<td>7.34(0.03)</td>
</tr>
</tbody>
</table>
FIGURE 2
FIGURE 3
FIGURE 4
FIGURE 5
Figure 6

---

**MEAN CORONARY FLOW**

- Control: N=6
- Endotoxin: N=7

---

**MEAN CORONARY RESISTANCE**

- (mm Hg/cc/min)

---

**MEAN O₂ UPTAKE**

- (cc/min)

---

**MEAN CO₂ PRODUCTION**

- (cc/min)
The purpose of the present study was to determine possible direct adverse effects of endotoxin toxicity on canine myocardial tissue. Experiments were designed to assay cardiac performance, hemodynamics and metabolism in an isolated working left ventricle removed from a donor dog, exchanging blood with an intact support animal. Aortic pressure and cardiac output of the heart were decreased by pump adjustment in the experimental group to follow the support animal's mean systemic pressure after endotoxin or in the control group to mimic the previous cardiac endotoxin response. Three hours of systemic hypotension and depressed cardiac output followed by restoration of pressure and flow to control values by pump adjustment revealed insignificant differences between the endotoxin and control animals. Left ventricular end diastolic pressure, myocardial contractility, cardiac power (work/sec), dP/dT, O₂ uptake and CO₂ production were statistically unaltered from zero time control values after the sustained period of hypotension in both control and experimental groups. Findings indicate the absence of a direct toxic action of endotoxin on the myocardium.