SUMMARY Twenty-one dogs were studied under conditions of normal oxygenation and hypoxia with the microsphere distribution method to determine the effect of arterial oxygen saturation on the regional distribution of cardiac output. The dogs were anesthetized and artificially ventilated. Cannulas were placed in the left ventricle to administer microspheres and in a peripheral artery to determine cardiac output. Each dog received two microsphere injections: (1) while normally oxygenated (room air), and (2) under hypoxia (10% oxygen-90% nitrogen in 10 dogs and 5% oxygen-95% nitrogen in 11 dogs). Absolute cardiac output increased from $87 \pm 15$ ml/min per kg to $101 \pm 14$ ml/min per kg during mild hypoxia (10% oxygen) ($P < 0.05$), and from $73 \pm 17$ ml/min per kg to $120 \pm 24$ ml/min per kg during severe hypoxia (5% oxygen) ($P < 0.01$). Absolute blood flow increased to all organs except skin and muscle during hypoxia, although there were decreases in the fractional distribution of cardiac output to the splanchnic bed and kidney. Striking changes were found in coronary, hepatic, and cerebral circulation, and the organ with greatest response to hypoxia was the heart, with increased coronary flows of 37% and 285% during exposure to 10% and 5% oxygen, respectively. Hence, low oxygen levels in blood cause redistribution of cardiac output and arterial content plays an important role in blood flow regulation.

THE LEVEL of oxygen in the blood is one of the important factors determining the regional distribution of cardiac output. For example, the pulmonary circulation is extremely sensitive to decreases in the partial pressure of oxygen, which alter the regional distribution of pulmonary arterial blood flow. The coronary circulation also is extremely sensitive to local decreases in Po$_2$ and responds by marked vasodilation. The effect of a decreased partial pressure of oxygen in other organs also has been evaluated, but no evaluation has been made of the overall redistribution of cardiac output in the intact animal under conditions of decreased oxygen tension. Therefore, we have examined the changes in the distribution of cardiac output in the intact anesthetized dog during normal oxygenation and following 20 minutes of equilibration with either 10% oxygen or 5% oxygen.

Methods

Carbonized microspheres (3M Co.) 50 $\pm$ 10 $\mu$m in diameter and labeled with either strontium-85 or cerium-141 at a specific activity of $10 \mu$Ci/mg, were used to evaluate the regional distribution of blood flow. The dose employed for each determination was 40-50 $\mu$Ci (100,000 particles). Female mongrel dogs weighing approximately 20 kg were anesthetized with intravenous pentobarbital sodium (25-35 mg/kg of body weight) and were ventilated with a Harvard respirator. A catheter was inserted into the right brachial artery into the left ventricle to permit injection of microspheres and in a peripheral artery to determine cardiac output. The coronary circulation also is extremely sensitive to local decreases in Po$_2$ and responds by marked vasodilation. The effect of a decreased partial pressure of oxygen in other organs also has been evaluated, but no evaluation has been made of the overall redistribution of cardiac output in the intact animal under conditions of decreased oxygen tension. Therefore, we have examined the changes in the distribution of cardiac output in the intact anesthetized dog during normal oxygenation and following 20 minutes of equilibration with either 10% oxygen or 5% oxygen.

A blood sample was drawn from the brachial artery over a period of 30 seconds beginning a few seconds prior to tracer administration for the determination of cardiac output. The distribution of cardiac output was determined in each of 21 dogs on two occasions: (1) during a control period during which the dog breathed room air at a fixed rate and a volume determined on the basis of the surface area of the dog, and (2) following 20 minutes of ventilation with either 10% oxygen and 90% nitrogen or 5% oxygen and 95% nitrogen. Ventilation was maintained at the same rate and volume throughout the experiment. Eleven dogs were studied while breathing room air (control) and 5% O$_2$,95% N$_2$; 10 other dogs were studied while breathing room air (control) and 10% O$_2$,90% N$_2$. Arterial blood samples were collected for determination of pH, PO$_2$, and PCO$_2$ before and after administration of these gases to each of the dogs. In one dog, a third catheter was placed in the coronary sinus with fluoroscopic guidance to determine venous PO$_2$. After the second administration of tracer the dogs were killed with intravenous sodium pentothal. The heart was removed and the position of the catheter tip in the left ventricle was confirmed. In all dogs the catheter was found to be

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Henry N. Wagner, Jr., M.D.
positioned properly in the left ventricle, well away from the aortic outflow tract. The lungs, heart, kidneys, stomach, pancreas, spleen, small bowel, large bowel, muscle, bone, skin, and brain were removed and weighed, and their content of radioactivity was measured in a sodium iodide well-sci-
tillation detector (diameter = 5 inches) at the appropriate gamma photon energy for each of the two radionuclides. Large organs, i.e., liver and bowels, were cut into multiple pieces; the activity in each piece was measured and the total activity in the entire organ was obtained by summing the counts of individual samples after background correction. The gamma photon energies examined were 100-200 keV for cerium-141 and 450-550 keV for strontium-85. Less than 8% of the activity from strontium-85 was found to be at the energy of the cerium window. There was no significant cerium activity in the strontium window. Appropriate corrections were made for strontium activity in the cerium window.

The percent of cardiac output reaching each organ was calculated as the amount of nuclide in the organ divided by the dose of the tracer.4** Cardiac output was calculated as the product of the dose of the tracer and the reference blood flow divided by the amount of nuclide in the blood sample withdrawn from the brachial artery.5 Absolute blood flow to each organ and tissue was calculated by multiplying the percentage of cardiac output by the absolute cardiac output. Student's t-test was used to determine whether there were significant differences in the flow to each organ, comparing the control and the hypoxic state.

**Results**

The arterial oxygen tension decreased from a control value of 81 ± 6.5 (mean ± SD) mm Hg to 41 ± 5.3 mm Hg when the dogs were ventilated with 10% oxygen, and to 24 ± 5.8 mm Hg when the dogs were ventilated with 5% oxygen. The PCO₂ and pH remained essentially unchanged during the control and hypoxic periods. Arterial pressure and heart rate increased under the influence of hypoxia (Table 1). The control cardiac output was 87 ± 15 ml/min per kg for the first group of 10 dogs and 73 ± 12 ml/min per kg for the second series of experiments (11 dogs). During mild hypoxia, the cardiac output increased to 101 ± 14 ml/min per kg, whereas during the severe hypoxia (5% oxygen) the cardiac output increased to 120 ± ml/min per kg (Table 1). These values were significantly different from those obtained during the control states.

The effect of severe hypoxia (5% oxygenation) on the distribution of cardiac output was greater than that resulting from breathing 10% oxygen. With 10% oxygen only the liver and diaphragm received a significant increase in the fraction of cardiac output. The fractions distributed to the ileum and skin both were significantly diminished. When expressed in terms of blood flow per 100 g of tissue, flow to the heart, liver, diaphragm, and intercostal muscle was significantly increased (Table 2). During severe hypoxia (5% oxygen) there was a significant increase in the fraction of cardiac output going to the heart, kidneys, brain, and diaphragm. In terms of absolute blood flow, there were significant changes from control in flow to the heart, lungs, liver, brain, pancreas, stomach, jejunum, diaphragm, and intercostal muscle (Table 3). The data expressed as a percent change from control value are illustrated in Figure 1 for the percent cardiac output and Figure 2 for the absolute blood flow in ml/100 g per min.

Since the changes in flow to the heart were most striking, additional calculations were made of left ventricular cardiac work, coronary vascular resistance, myocardial oxygen extraction, myocardial oxygen consumption, and cardiac efficiency. The mean value of coronary vascular resistance (calculated from the mean arterial pressure divided by coronary blood flow) was 1.8 mm Hg/ml per min in the control state and decreased to 1.57 mm Hg/ml per min under the influence of 10% oxygen and to 0.57 mm Hg/ml per min, under the influence of 5% oxygen. Cardiac work (cardiac output times mean arterial pressure) was 2.2 kg-m/min in the control state and increased to 3.0 kg-m/min under the influence of 10%, and to 4.3 kg-m/min under the influence of 5% oxygen. To calculate myocardial oxygen extraction, coronary venous PO₂ was calculated from the regression equation of Feinberg et al.6 The validity of this regression equation was checked for one dog in which the coronary sinus was catheterized. Under controlled circumstances the regression equation predicted a coronary sinus PO₂ of 5.2; the measured value was 4.5. Under conditions of 10% hypoxia the equation predicted a value of 4.5; the measured value 3.2, and under 5% hypoxia the regression equa-

---

**Table 1 Hemodynamic and Arterial Blood Gas Analysis Data**

<table>
<thead>
<tr>
<th>Arterial</th>
<th>Arterial</th>
<th>Arterial blood pressure</th>
<th>Heart rate</th>
<th>Cardiac output</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>Po₂ (mm Hg)</td>
<td>Po₂ (mm Hg)</td>
<td>(mm Hg)</td>
<td>(beats/min)</td>
</tr>
<tr>
<td>Control</td>
<td>7.40 ± 0.05</td>
<td>80.5 ± 6.5</td>
<td>41.2 ± 4.9</td>
<td>145 ± 13</td>
</tr>
<tr>
<td>Mild hypoxia (10% oxygen)</td>
<td>7.43 ± 0.08</td>
<td>41.2 ± 5.3*</td>
<td>37.8 ± 6.1</td>
<td>164 ± 10*</td>
</tr>
<tr>
<td>(n = 10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>7.43 ± 0.06</td>
<td>83.1 ± 8.2</td>
<td>38.3 ± 5.0</td>
<td>144 ± 17</td>
</tr>
<tr>
<td>Severe hypoxia (5% oxygen)</td>
<td>7.43 ± 0.04</td>
<td>24.3 ± 5.8*</td>
<td>35.6 ± 5.6</td>
<td>171 ± 15*</td>
</tr>
<tr>
<td>(n = 11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD.

* Values significantly different from controls are symbolized:

† P < 0.01

‡ P < 0.05

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equation was a valid means of determining coronary sinus
PO
. The myocardial oxygen consumption was calculated

from these data (coronary arteriovenous O_2 difference mul-
tiplied by coronary blood flow) as 7.2 ml of oxygen per min
per 100 g of myocardium during control, 7.6 under 10% o-
oxgen, and 9.9 under 5% oxygen. Myocardial efficiency

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Distribution of Cardiac Output in Mild Hypoxia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td></td>
<td>Distribution (%) Q</td>
</tr>
<tr>
<td>Heart</td>
<td>5.2 ± 1.6</td>
</tr>
<tr>
<td>Lungs</td>
<td>3.2 ± 1.7</td>
</tr>
<tr>
<td>Kidneys</td>
<td>13.0 ± 2.3</td>
</tr>
<tr>
<td>Liver (hepatic artery)</td>
<td>3.0 ± 1.0</td>
</tr>
<tr>
<td>Brain</td>
<td>1.4 ± 0.4</td>
</tr>
<tr>
<td>Spleen</td>
<td>2.5 ± 1.1</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.7 ± 0.4</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.8 ± 0.7</td>
</tr>
<tr>
<td>Duodenum</td>
<td>1.0 ± 0.4</td>
</tr>
<tr>
<td>Jejunum</td>
<td>4.9 ± 1.6</td>
</tr>
<tr>
<td>Ileum</td>
<td>4.8 ± 1.8</td>
</tr>
<tr>
<td>Colon</td>
<td>3.2 ± 1.0</td>
</tr>
<tr>
<td>Total splanchnic</td>
<td>18.5 ± 5.7</td>
</tr>
<tr>
<td>Hepatosplanchnic</td>
<td>21.8 ± 6.5</td>
</tr>
<tr>
<td>Muscle (leg), 100 g</td>
<td>0.43 ± 0.24</td>
</tr>
<tr>
<td>Skin (leg), 100 g</td>
<td>0.33 ± 0.21</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bone</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ribs, 100 g</td>
<td>0.40 ± 0.13</td>
<td>5.2 ± 1.7</td>
<td>0.47 ± 0.31</td>
<td>7.2 ± 4.7</td>
</tr>
<tr>
<td>Femur, 100 g</td>
<td>0.16 ± 0.06</td>
<td>2.1 ± 0.8</td>
<td>0.18 ± 0.10</td>
<td>2.8 ± 1.5</td>
</tr>
<tr>
<td>Diaphragm, 100 g</td>
<td>0.39 ± 0.16</td>
<td>5.1 ± 2.1</td>
<td>0.99 ± 0.54*</td>
<td>15.2 ± 8.3*</td>
</tr>
<tr>
<td>Intercostal muscle, 100 g</td>
<td>0.31 ± 0.10</td>
<td>4.1 ± 1.3</td>
<td>0.37 ± 0.11</td>
<td>5.7 ± 1.7*</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 10 dogs.
Values significantly different from controls are symbolized:
* P < 0.05
† P < 0.01
† P < 0.10

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Distribution of Cardiac Output in Severe Hypoxia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td></td>
<td>Distribution (%) Q</td>
</tr>
<tr>
<td>Heart</td>
<td>5.5 ± 1.3</td>
</tr>
<tr>
<td>Lungs (bronchial artery)</td>
<td>3.7 ± 1.4</td>
</tr>
<tr>
<td>Kidneys</td>
<td>12.0 ± 2.8</td>
</tr>
<tr>
<td>Liver (hepatic artery)</td>
<td>3.7 ± 1.1</td>
</tr>
<tr>
<td>Brain</td>
<td>1.2 ± 0.3</td>
</tr>
<tr>
<td>Spleen</td>
<td>2.9 ± 1.1</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.7 ± 0.3</td>
</tr>
<tr>
<td>Stomach</td>
<td>2.1 ± 0.8</td>
</tr>
<tr>
<td>Duodenum</td>
<td>0.9 ± 0.4</td>
</tr>
<tr>
<td>Jejunum</td>
<td>4.4 ± 1.1</td>
</tr>
<tr>
<td>Ileum</td>
<td>4.1 ± 1.4</td>
</tr>
<tr>
<td>Colon</td>
<td>3.8 ± 1.0</td>
</tr>
<tr>
<td>Total splanchnic</td>
<td>18.8 ± 5.0</td>
</tr>
<tr>
<td>Hepatosplanchnic</td>
<td>22.5 ± 5.9</td>
</tr>
<tr>
<td>Muscle (leg), 100 g</td>
<td>0.48 ± 0.33</td>
</tr>
<tr>
<td>Skin (leg), 100 g</td>
<td>0.24 ± 0.13</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bone (2 dogs)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ribs, 100 g</td>
<td>0.47 ± 0.16</td>
<td>6.0 ± 2.0</td>
<td>0.33 ± 0.10†</td>
<td>6.9 ± 2.1</td>
</tr>
<tr>
<td>Femur, 100 g</td>
<td>0.15</td>
<td>1.9</td>
<td>0.10</td>
<td>2.1</td>
</tr>
<tr>
<td>Diaphragm, 100 g</td>
<td>0.33 ± 0.13</td>
<td>4.2 ± 1.6</td>
<td>1.00 ± 0.51*</td>
<td>21.0 ± 10.7*</td>
</tr>
<tr>
<td>Intercostal muscle, 100 g</td>
<td>0.27 ± 0.17</td>
<td>3.4 ± 2.2</td>
<td>0.37 ± 0.05*</td>
<td>7.8 ± 1.1*</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 11 dogs.
Values significantly different from controls are symbolized:
* P < 0.05
† P < 0.01
‡ P < 0.05
†† P < 0.10
Statistically significant: *P < 0.01; **P < 0.05; ***P < 0.10.

was calculated by dividing left ventricular cardiac work by myocardial oxygen consumption. In the control state efficiency was 13.2%, but under hypoxia the efficiency rose significantly, 17.5% under 10% hypoxia, and 18.1% under 5% hypoxia.

Discussion

Regional blood flow is controlled by factors intrinsic and extrinsic to the specific organs. It is regulated by the central nervous system and by humoral factors. Regional blood flow also is regulated by the conditions in the immediate vicinity of the blood vessels, for example, by changes in essential nutrients and by the accumulation of tissue metabolites. Oxygen is one of the most necessary nutrients, and many experiments in recent years lead to the conclusion that oxygen concentration in the tissues is the chief regulator of local blood flow to most organs.6-12

Smooth muscle in the precapillary arteriole sphincter requires oxygen to remain contracted:11 when the oxygen concentration in tissue falls, the precapillary sphincters open and result in increased blood flow and tissue oxygenation, the so-called oxygen demand theory.11,13 Our experiments were designed to explore the effects of hypoxia on the relative and absolute distribution of regional blood flow.

Microspheres 50 μm in diameter were selected as the flow indicator because they are totally extracted in a single passage to a capillary bed and are too large to pass through anatomical shunts. Preliminary experiments had been carried out using 15-μm microspheres but results were nonreproducible. The particle distribution technique has been validated for the determination of cardiac output by other investigators.14,15 It is important to consider two possible problems with the microsphere method. First, what is the practical limit of cardiac output that can be measured with this method? If the particles are well mixed with blood, they should distribute in proportion to the blood flow distribution. The limiting factor would be the expected number of particles (not only the activity) in the tissue to be counted. When 100,000 particles were administered (the amount used for our determinations), 0.1% of cardiac output would represent 100 particles. Poisson statistics suggest that at that level the cardiac output can be measured with a precision of ±0.1% at 1 SD. The second question concerns the adequacy of mixing of microspheres when they are injected into the left ventricle.4 Preliminary experiments indicated that when microspheres were injected into the apical part or the inflow tract of the left ventricle, streaming was not a problem. In addition, if mixing had been a problem, the control distribution of cardiac output should have shown greater variation.

The validity of measuring absolute cardiac output by means of radioactive microspheres was evaluated by Archie et al.,4 who compared cardiac output measured by the microsphere reference sample method with either known pump cardiac output or cardiac output measured by indocyanine green dye. They found that there were good correlations of r = 0.94 and r = 0.90, respectively.8 We collected brachial artery blood as a reference sample over 30 seconds and found that more than 99% of total microspheres arrived within this 30-second period.

The reproducibility of the method is demonstrated in the small standard deviation during the control state for each dog, both in terms of the regional distribution of cardiac output and in the absolute value of blood flow in each organ. If significant streaming had occurred as expected, the deviations found in organ distribution in the control state would have been significantly greater. The standard deviations found in these experiments in the control state are comparable to those found by Kaihara et al.,17 who injected the particles into the left atria of dogs.

As in experiments by others,14,15 we observed that arterial blood pressure and heart rate increased under the influence of hypoxia. Cardiac output increased 15% above the control value under mild hypoxia, and 65% under severe hypoxia (Table 1).

The coronary circulation was dramatically affected by hypoxia. The percent of cardiac output supplied to the myocardium increased by only 15% under mild hypoxia, but under severe hypoxia it increased by 130%. The absolute coronary blood flow increased by 37% under mild hypoxia but under severe hypoxia increased by 285%. Myocardial oxygen consumption, calculated as the product of coronary blood flow and coronary arteriovenous oxygen difference, increased from 7.6 ml/min per 100 g under control conditions to 11.7 ml/min per 100 g during 5% O₂ hypoxia in spite of the decrease in oxygen extraction. Sarnoff et al.18 found
that when the left ventricular work was increased by raising
the cardiac output, the oxygen consumption of myocardium
increased only slightly in normoxia, hence the cardiac
efficiency rose strikingly. In contrast, when left ventricular
work was increased by raising the mean aortic pressure, 
oxygen consumption increased in parallel with left ventricu-
lar work, hence cardiac efficiency was unaltered. Sarnoff et
al.28 concluded that myocardial oxygen consumption was not
related directly to overall left ventricular work but more
closely to the magnitude and the duration of the left
ventricular systolic pressure pulse. Our results revealed a
comparable increase in heart rate and cardiac output with
10% oxygen, accompanied by a modest increase in aortic
pressure. With the more severe stimulus of 5% oxygen,
cardiac output increased to a far greater extent than heart
rate, and aortic pressure rose only modestly. The calculated
oxygen consumption compared to cardiac work revealed an
increase in cardiac efficiency compared to the control group.
These data suggest that even under the conditions of
moderate and marked hypoxia cardiac efficiency increases
as it does in normoxia with increases in volume work.

Eckenhoff et al.28 reported results different from our own;
specifically, that in the hypoxic dog left ventricular cardiac
work decreased and oxygen consumption remained relatively
constant; hence cardiac efficiency decreased.21 In their
experiments cardiac output decreased with hypoxia, whereas
in ours cardiac output increased. This may account for this
discrepancy.

Hypoxia per se seems to have relatively little effect on the
hepatic circulation.22 Fischer et al.22 found that in mild
hypoxia hepatic blood flow increased, but severe hypoxia
(less than 40% oxygen saturation) resulted in a decrease of
blood flow. These authors suggested that adrenergic stimu-
lation is induced by hypoxia. The microsphere method used
in our experiments measured only the hepatic arterial
portion of liver blood flow. In these experiments, hepatic
artery flow increased whether measured as the fraction of
cardiac output received or the absolute blood flow under the
circumstances of both mild and severe hypoxia. Portal blood
flow could not be measured directly by the microsphere
method. However, it was calculated indirectly by summing
the total arterial perfusion to the stomach, duodenum,
jejenum, ileum, colon, pancreas, and spleen, because these
organs drain into the portal circulation. These values
expressed as total splanchic blood flow in Tables 2 and 3,
were essentially unchanged by mild hypoxia but increased
slightly during severe hypoxia, although the percent of
cardiac output distributed to this area diminished slightly.

The bronchial circulation showed a marked response to
severe hypoxia with an increase of 96% in absolute blood
flow. Under mild hypoxic conditions, however, there was no
significant change in blood flow compared to control
circumstances. These changes in bronchial blood flow are
interesting in these acute experiments because they may be
related to certain pathological states associated with severe
hypoxia. Under circumstances of bronchiectasis or congeni-
tal diseases resulting in severe hypoxia, bronchial blood flow
can increase so that 20% of the cardiac output will flow
through these vessels.24 It is interesting that under these
experimental circumstances, 10% oxygen did not result in
any increase in bronchial blood flow while 5% oxygen
caused a marked increase after only 20 minutes of equilibr-
ation.

The response of renal blood flow to hypoxia has been
found to vary, depending on the method used to measure
flow and the degrees of hypoxia.22 Korner22 reported that
hypoxia induced renal arterial constriction in the rabbit. Our
findings indicated that the renal fraction of cardiac output
was reduced by 10% in mild hypoxia and by 25% in severe
hypoxia while absolute blood flow remained unchanged in
mild hypoxia and was only slightly increased in severe
hypoxia.

The diaphragm showed a marked increase in blood flow,
comparing control and hypoxic conditions with an increase of
19% during exposure to 10% oxygen, an increase of
450% with 5% oxygen. The intercostal muscle, on the other
hand showed only a 30% increase in absolute blood flow
under 10% hypoxia and a 129% increase under 5% hypoxia,
suggesting that there may be some reflex mechanism to in-
crease blood flow to the diaphragm under these circum-
stances. It is possible that some of these increases in blood
flow were the result of reflex attempts at breathing, since
the dogs were not curarized. However, it is safe to assume
that the intercostal muscles also play a very significant role
under these circumstances and should show a parallel
marked increase in blood flow which was not found.

Bone blood flow has been measured previously using the
isotope clearance method, and values of 2.5–13.2 ml/min
per 100 g of bone were obtained.23 In these experiments,
blood flow to rib and femur using the microsphere technique
was 5.2 to 6 ml/min per 100 g for rib and 2.1 ml/min per 100 g
for femur. Although percent cardiac output to the bone
decreased under hypoxic conditions, there were no signifi-
cant changes in blood flow.

This study supports the contention that arterial oxygen
content plays a very important role in determining the
regional distribution of cardiac output.

Acknowledgments

We express appreciation for the advice of Dr. Solberg Permutt and Dr.
Juey Kong Young, and for the technical assistance of Katherine Harrison.

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Regulation of Myosin ATPase by Thyroxine/Banerjee et al.

Enzymatic Properties of Native and N-Ethylmaleimide-Modified Cardiac Myosin from Normal and Thyrotoxic Rabbits

Surath K. Banerjee, Ph.D., Irwin L. Flink, Ph.D., and Eugene Morkin, M.D.

Summary: Cardiac myosin from thyrotoxic animals (myosin-T) exhibits elevated Ca++-ATPase activity which is resistant to further stimulation by sulphydryl modification. In the present study, we have compared the enzymatic properties of myosin-T with those of myosin from euthyroid rabbits (myosin-N) and the derivatives of myosin-T and myosin-N formed by blocking the most rapidly reacting class of thiols (SH, thiols) with N-ethylmaleimide (NEM). Va, the Ca++-ATPase of myosin-T was about 250% greater than myosin-N and was nearly the same as NEM-modified myosin-N. Values for the apparent Km of myosin-T and NEM-modified myosin-N were 200% greater than the values for unmodified myosin-N. 

Thyroid Hormone administration causes development of hypertrophy and accumulation of myofibrillar proteins in the heart. The speed of myocardial contraction is increased in thyrotoxic animals, and there are reports of increased myosin ATPase activity. In contrast, depressed contractility and reduced myofibrillar, actomyosin, and myosin ATPase activities have been found in hypothyroidism induced by pressure overload. Thus certain adaptative responses in the contractile properties of the heart may be meditated by changes in myosin ATPase activity.

Recently we have found that the elevated Ca++-ATPase activity of cardiac myosin prepared from thyrotoxic animals (myosin-T) is resistant to further stimulation by sulphydryl modification. Similar results have been obtained by other investigators. In the present study we have characterized certain of the enzymatic properties of myosin-T and compared these with the properties of cardiac myosin prepared from euthyroid animals (myosin-N). We have also studied the enzymatic properties of myosin-N and myosin-T after blocking the most rapidly reacting class of thiols, the so-called SH, thiols, with N-ethylmaleimide (NEM).
The effect of hypoxia on the regional distribution of cardiac output in the dog.
H Adachi, W Strauss, H Ochi and H N Wagner, Jr

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