ABSTRACT

The effect of intra-arterial and intravenous epinephrine on skeletal muscle blood flow and metabolism were studied in the human forearm following complete suppression of the circulation to forearm skin by epinephrine iontophoresis. Epinephrine by either route of administration increased blood flow, O₂ consumption and CO₂ production, and decreased arteriovenous differences of O₂ and CO₂ across the forearm. The increments in blood flow did not correlate with the increments in O₂ consumption or CO₂ production. In the intact forearm intravenous epinephrine increased deep forearm venous PO₂ but not venous PCO₂. Hypocapnia, induced by voluntary hyperventilation, did not alter the response of forearm blood flow to intravenous epinephrine. These results show that the vasodilator response of skeletal muscle vessels to epinephrine is not dependent on decrease in PO₂ or increase in PCO₂ in the environment of the high resistance vessels. They also suggest that the calorigenic effect of the hormone is not a dominant factor in its vasodilator effect in skeletal muscle.

ADDITIONAL KEY WORDS
epinephrine iontophoresis
autoregulation of blood flow
intravenous epinephrine
skeletal muscle oxygen consumption
hyperventilation
hypocapnia
β receptors
intra-arterial epinephrine

The possibility that the dilator response of blood vessels of skeletal muscle to small doses of epinephrine given intravenously or intra-arterially may be partly or entirely secondary to the metabolic effects of this hormone has been repeatedly considered (1-10). Most of this experimental work has dealt with a possible relationship between the vasodilator and the glycogenolytic effects of epinephrine. There is at present considerable evidence suggesting that the vasodilation in skeletal muscle in response to epinephrine is not causally related to its glycogenolytic effect (6-10). In contrast, a possible relationship between the circulatory response to epinephrine and its other prominent metabolic effect, e.g. the calorigenic effect, has received less attention. Recently, Lundholm and Svedmyr (11) found that intravenous infusion of epinephrine caused increase in O₂ consumption and in CO₂ production of human forearm skeletal muscle. They suggested that the vasodilator effect of epinephrine might be related in part to increased CO₂ production of skeletal muscle. Several studies of the effect of epinephrine on O₂ consumption of skeletal muscle in anesthetized animals are available but the results are contradictory (12, 13). The reasons for many of these contradictions were summarized by Baltzan et al. (9) in relation to the metabolic effects of epinephrine in general.

In the present investigation, the effects of
intravenous and intra-arterial epinephrine on O$_2$ consumption and CO$_2$ production of human forearm skeletal muscle were studied in relation to the vasodilator effect of the hormone.

**Methods**

Experiments were performed on 20 young, healthy, male volunteers. All subjects were studied in the postabsorptive state while lying recumbent on a table in an air-conditioned laboratory (room temperature 23 to 24°C). Experiments on the same subject were done at least 3 weeks apart and none of the subjects was used for the same type of experiment more than once. All subjects gave their informed consent to the studies.

The effect of epinephrine on the metabolism and blood flow of forearm skeletal muscle was studied following complete suppression of the circulation to forearm skin by epinephrine iontophoresis. The technique of epinephrine iontophoresis was similar to that used by Cooper et al. (14) with the important exceptions that the current intensity was higher (20 ma) and the duration of iontophoresis was longer (20 to 25 min). As described elsewhere (15), these modifications result in more complete suppression of the cutaneous circulation.

Epinephrine iontophoresis was carried out in 22 experiments. In 4 of these, epinephrine infusion was not given because iontophoresis resulted in incomplete suppression of skin blood flow or because there was absorption of epinephrine into the systemic circulation. Epinephrine iontophoresis was considered complete when the skin was uniformly blanched and remained so after release of 3 min of arterial occlusion.

Since the major components of total forearm blood flow are represented by cutaneous and skeletal muscle flows (14), the plethysmographically measured forearm blood flow following epinephrine iontophoresis was considered to represent muscle blood flow entirely. Forearm blood flow was measured by venous occlusion plethysmography using a plethysmograph filled with water whose temperature was maintained thermostatically at 33 to 34°C. The circulation to the hand was arrested by infusing a sphygmomanometer cuff around the wrist to a pressure well above the subject’s systolic arterial blood pressure. Arterial blood was obtained from an 18-gauge Courand needle placed into the brachial artery of the opposite arm. Arterial blood pressure was measured with a Statham P23-Db strain gauge connected to the Courand needle via polyethylene tubing. Mean arterial blood pressure was obtained by electronic damping. Forearm vascular resistance was calculated as the ratio of mean arterial blood pressure divided by forearm blood flow. Venous blood was obtained from a polyethylene catheter placed into a deep forearm vein in a retrograde direction so that its tip lay within the portion of the forearm contained in the plethysmograph. The oxygen and carbon dioxide contents of blood samples were determined by the method of Van Slyke and Neill (16).

Expired air CO$_2$ concentration was monitored continuously with a Liston-Becker infrared CO$_2$ analyzer.

Epinephrine was administered by a Harvard constant infusion pump either intravenously at a rate of 10 µg/min or into the brachial artery at a rate of 0.1 µg/min. These dose levels were selected because in the intact forearm they give consistent and approximately equal increases in blood flow (17). Intra-arterial infusions were given into the brachial artery of the experimental arm through a Riley needle placed into the vessel at the upper part of the bicipital groove. For intravenous infusion, epinephrine was dissolved in 0.9% NaCl solution to give a concentration of 1 µg/ml; for intra-arterial infusions a concentration of 0.05 µg/ml was used.

The experimental design was as follows: After control measurements of forearm blood flow and two or three sets of arterial and venous blood samples were obtained, the infusion of epinephrine was begun while blood flow measurements were continued. After the blood flow and blood pressure became stable two or three more sets of arterial and venous blood samples interspersed with blood flow determination were obtained. The O$_2$ consumption and CO$_2$ production of forearm skeletal muscle were calculated from the blood flow and the corresponding arteriovenous differences by application of the Fick principle. In the experiments reported, the requirements from the application of the Fick principle, namely constant arterial and venous concentrations and constant blood flow, were met.

In view of the observation by Lundholm and Svedmyr (11) that epinephrine infusion caused an increase in arterial and deep forearm venous blood Pco$_2$, and their suggestion that this might be causally related to the associated vasodilation, the response to intravenous infusions of epinephrine was compared before and during hypocapnia induced by voluntary hyperventilation. We thought it unlikely that epinephrine iontophoresis would give complete suppression of skin blood flow for a sufficiently long period to perform these studies. For this reason we carried out these experiments in the intact forearm without epinephrine iontophoresis. Epinephrine was infused at a rate of 10 µg/min iv for 10 min during normal breathing and the infusion was repeated during
voluntary hyperventilation. This infusion of epinephrine was begun 4 min following the onset of voluntary hyperventilation. Hyperventilation was maintained throughout the infusion at a level designed to maintain blood Pco₂ at the preinfusion level. The two infusions were separated by a 15- to 20-min rest period and they were given randomly. Arterial and deep forearm venous blood samples were obtained during normal breathing before the infusion of epinephrine and 3.5 min following the onset of hyperventilation. The Pco₂, Pco₂, and pH of blood samples were determined within a few minutes following their collection with O₂ and CO₂ electrodes (18) and a Metrohm pH meter at 37°C. Venous blood gas tension and pH were corrected to the temperature of the blood at the time of collection as described elsewhere (19). Venous blood temperature was measured with a thermistor inserted into the venous catheter.

Results

Intra-arterial infusion of 0.1 μg/min of epinephrine in 9 subjects produced an initial, large but transient increase in forearm muscle blood flow followed by a less pronounced sustained increase in flow (Fig. 1). In the steady state, the O₂ difference between arterial and deep forearm venous blood decreased as did the CO₂ difference between deep forearm venous and arterial blood; the calculated rates of oxygen uptake and carbon dioxide production increased significantly. This response was typical of all studies (Table 1). There was no significant change in the O₂ or CO₂ concentrations in arterial blood.

The effect of intravenous infusion of 10 μg/min of epinephrine on forearm muscle metabolism and blood flow was studied in 9 subjects. Three of these were rejected because, during the period of observation, blood flow or blood concentrations of O₂ and CO₂ were variable, thus invalidating application of the Fick principle (20). The time course of blood flow through the forearm muscle was similar to that seen during intra-arterial infusions of
### TABLE 1

**Effects of Intra-Arterial Infusion of Epinephrine (0.1 µg/min) on Forearm Muscle Blood Flow and Metabolism**

<table>
<thead>
<tr>
<th></th>
<th>C</th>
<th>E</th>
<th>D</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forearm muscle blood flow (ml/min per 100 ml forearm)</td>
<td>1.53 ± 0.08</td>
<td>3.07 ± 0.27</td>
<td>1.53 ± 0.25</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>aO₂ (ml/100 ml)</td>
<td>19.11 ± 0.40</td>
<td>18.63 ± 0.26</td>
<td>-0.47 ± 0.26</td>
<td>n.s.</td>
</tr>
<tr>
<td>a-VO₂ (ml/100 ml)</td>
<td>10.2 ± 0.56</td>
<td>7.08 ± 0.74</td>
<td>-3.12 ± 0.40</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>aCO₂ (ml/100 ml)</td>
<td>47.07 ± 0.97</td>
<td>46.83 ± 1.01</td>
<td>-0.24 ± 0.20</td>
<td>n.s.</td>
</tr>
<tr>
<td>v-aCO₂ (ml/100 ml)</td>
<td>6.53 ± 0.45</td>
<td>4.81 ± 0.55</td>
<td>-1.71 ± 0.32</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>VO₂ (ml/min per 100 ml forearm)</td>
<td>0.155 ± 0.01</td>
<td>0.203 ± 0.01</td>
<td>0.047 ± 0.007</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>VCO₂ (ml/min per 100 ml forearm)</td>
<td>0.099 ± 0.008</td>
<td>0.138 ± 0.01</td>
<td>0.039 ± 0.006</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

aO₂ = arterial blood oxygen content; a-VO₂ = arterial deep forearm venous oxygen difference; aCO₂ = arterial blood CO₂ content; v-aCO₂ = deep forearm venous-arterial CO₂ difference; VO₂ = forearm muscle oxygen consumption; VCO₂ = forearm muscle CO₂ production; C = control; E = epinephrine infusion; D = difference between C and E. P refers to comparison of mean D to zero by the t-test; n.s. = not significant. All values are mean ± SE obtained from 9 experiments on 9 subjects.

### TABLE 2

**Effects of Intravenous Infusion of Epinephrine (10 µg/min) on Forearm Muscle Blood Flow and Metabolism**

<table>
<thead>
<tr>
<th></th>
<th>C</th>
<th>E</th>
<th>D</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forearm muscle blood flow (ml/min per 100 ml forearm)</td>
<td>1.81 ± 0.16</td>
<td>4.40 ± 0.55</td>
<td>2.58 ± 0.47</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>aO₂ (ml/100 ml)</td>
<td>18.60 ± 0.56</td>
<td>18.97 ± 0.45</td>
<td>0.37 ± 0.16</td>
<td>n.s.</td>
</tr>
<tr>
<td>a-VO₂ (ml/100 ml)</td>
<td>8.01 ± 0.33</td>
<td>5.12 ± 0.56</td>
<td>-2.89 ± 0.48</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>aCO₂ (ml/100 ml)</td>
<td>48.78 ± 1.29</td>
<td>46.94 ± 1.12</td>
<td>-1.84 ± 0.52</td>
<td>&lt; 0.02</td>
</tr>
<tr>
<td>v-aCO₂ (ml/100 ml)</td>
<td>5.27 ± 0.56</td>
<td>4.98 ± 0.54</td>
<td>-0.29 ± 0.35</td>
<td>n.s.</td>
</tr>
<tr>
<td>VO₂ (ml/min per 100 ml forearm)</td>
<td>0.143 ± 0.008</td>
<td>0.214 ± 0.024</td>
<td>0.071 ± 0.020</td>
<td>&lt; 0.02</td>
</tr>
<tr>
<td>VCO₂ (ml/min per 100 ml forearm)</td>
<td>0.096 ± 0.013</td>
<td>0.220 ± 0.035</td>
<td>0.124 ± 0.027</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

RQ

Abbreviations as in Table 1. All values are mean ± SE obtained from 6 experiments on 6 subjects.

Epinephrine, consisting of a large initial increase in flow and a less pronounced sustained increase. During the period of sustained increase in flow arteriovenous differences of oxygen decreased while arteriovenous differences of carbon dioxide remained unchanged. As with intra-arterial infusions, there were significant increases in oxygen consumption and
METABOLIC AND VASODILATOR EFFECTS OF EPINEPHRINE

INCREASE IN FOREARM MUSCLE O₂ CONSUMPTION (ml/min per 100 ml FOREARM)

INCREASE IN FOREARM MUSCLE CO₂ PRODUCTION (ml/min per 100 ml FOREARM)

FIGURE 2
Relationship between the increments in O₂ consumption and CO₂ production of the forearm in response to intravenous epinephrine and the corresponding increments in blood flow.

carbon dioxide production rates (Table 2). Arterial blood O₂ content did not change during infusion of epinephrine but the CO₂ content of arterial blood diminished significantly. Comparison of the results of the effect of intra-arterial and intravenous infusion of epinephrine showed that the increases in blood flow and in O₂ consumption were not significantly different but the increase in CO₂ production of forearm muscle was significantly greater during intravenous than during intra-arterial infusion of epinephrine. There are two possible reasons for this difference. A gradually diminishing arterial CO₂ content might have resulted in overestimation of the CO₂ production rate during intravenous infusion of epinephrine (20). Examination of the data did not disclose a consistent downward trend in the concentration of CO₂ in arterial blood during the period of observation. It is possible, however, that a slow change could have remained undetected because of the small number of blood samples obtained. A more likely possibility is that during intravenous infusion of epinephrine glycogenolysis increased, the concentration of lactic acid in arterial blood increased, greater buffering of lactic acid by forearm muscle took place, and hence, greater increase in CO₂ release occurred than in the experiments in which epinephrine was given intra-arterially; in those, the arterial blood
concentration of lactic acid remains unchanged.

Correlation between the increments in forearm muscle blood flow and the increments in O2 consumption or CO2 production by forearm muscle was not significant for either the intravenous or intra-arterial infusions of epinephrine (Figs. 2 and 3).

During intravenous infusion of epinephrine, blood flow to the intact forearm showed the well known large transient and the smaller sustained increase in blood flow which were similar to those seen with intravenous and intra-arterial infusions in the forearm during iontophoresis. There was a significant increase in deep forearm venous blood PO2, but no change in deep venous blood PCO2 or pH (Table 3). Hyperventilation-induced hypocapnia produced an increase in forearm blood flow and a decrease in forearm vascular resistance accompanied by increased deep venous blood PO2. Infusion of epinephrine during hypocapnia produced increases in blood flow and decreases in vascular resistance which were not significantly different from those seen during normal breathing (Table 3).

Discussion

The present findings confirm the observation that epinephrine increases the O2 consumption and CO2 production of human forearm skeletal muscle. Since this effect was observed both during intravenous and intra-arterial epinephrine infusions it must be due to a local effect of the hormone. Studies by others (21, 22) showed that β-adrenergic receptor blockade inhibits the increase in total body O2 consumption in response to catechola-
TABLE 3
Comparison of Effects of Intravenous Infusion of Epinephrine on Forearm Blood Flow and Blood Gas Tension before and during Hyperventilation

<table>
<thead>
<tr>
<th></th>
<th>Normal breathing</th>
<th>Hyperventilation</th>
<th>( P_1 )</th>
<th>( P_2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forearm muscle blood flow (ml/min per 100 ml)</td>
<td>3.3 ± 0.3</td>
<td>5.9 ± 0.5</td>
<td>&lt; 0.001</td>
<td>5.0 ± 0.6</td>
</tr>
<tr>
<td>MABP (mm Hg)</td>
<td>90.1 ± 2.6</td>
<td>89.8 ± 1.4</td>
<td>n.s.</td>
<td>93.5 ± 1.3</td>
</tr>
<tr>
<td>Forearm vascular resistance (mm Hg/ml per min per 100 ml)</td>
<td>28.6 ± 1.9</td>
<td>15.8 ± 1.1</td>
<td>&lt; 0.001</td>
<td>20.9 ± 2.6</td>
</tr>
<tr>
<td>( P_{O_2} ) (mm Hg)</td>
<td>100.2 ± 2.2</td>
<td>99.2 ± 3.8</td>
<td>n.s.</td>
<td>117.4 ± 4.5</td>
</tr>
<tr>
<td>( P_{C0_2} ) (mm Hg)</td>
<td>40.5 ± 1.3</td>
<td>40.4 ± 1.3</td>
<td>n.s.</td>
<td>20.8 ± 0.9</td>
</tr>
<tr>
<td>( pH_a )</td>
<td>7.42 ± 0.013</td>
<td>7.43 ± 0.009</td>
<td>n.s.</td>
<td>7.68 ± 0.025</td>
</tr>
<tr>
<td>( P_{V0_2} ) (mm Hg)</td>
<td>44.9 ± 3.2</td>
<td>56.1 ± 5.1</td>
<td>&lt; 0.001</td>
<td>51.3 ± 5.9</td>
</tr>
<tr>
<td>( P_{VCO_2} ) (mm Hg)</td>
<td>48.9 ± 1.8</td>
<td>48.2 ± 1.3</td>
<td>n.s.</td>
<td>34.1 ± 2.6</td>
</tr>
<tr>
<td>pHv</td>
<td>7.38 ± 0.018</td>
<td>7.38 ± 0.013</td>
<td>n.s.</td>
<td>7.51 ± 0.019</td>
</tr>
</tbody>
</table>

MABP = mean arterial blood pressure; \( P_{O_2} \) = arterial blood oxygen tension; \( P_{CO_2} \) = arterial blood \( CO_2 \) tension; \( pH_a \) = arterial blood \( pH \); \( P_{V0_2} \) = deep forearm venous blood oxygen tension; \( P_{VCO_2} \) = deep forearm venous blood \( CO_2 \) tension; pHv = deep forearm venous blood \( pH \). \( P_1 \) refers to comparison of mean difference between C and E values during normal breathing to zero by means of \( t \)-test. \( P_2 \) refers to the same comparison made during hyperventilation to zero. \( P_3 \) refers to the same comparison made during normal breathing to those during hyperventilation. All values are mean ± se obtained from 8 experiments on 8 subjects.
mines and abolishes the increase in CO\textsubscript{2} production in the limbs of anesthetized dogs in response to isoproterenol (23). Therefore, it appears that the effect of epinephrine on O\textsubscript{2} consumption and CO\textsubscript{2} production of skeletal muscle are due to its β-adrenergic receptor stimulating effect.

Several reasons suggest that the increase in O\textsubscript{2} consumption and CO\textsubscript{2} production produced by epinephrine are not a major factor in the vasodilator effect of this hormone on skeletal muscle blood vessels. Neither the increase in CO\textsubscript{2} production nor the increase in O\textsubscript{2} consumption correlated with the increase in forearm muscle blood flow in the present experiments. (Measurements of blood O\textsubscript{2} and CO\textsubscript{2} were not made during the injection of epinephrine until a steady state of forearm blood flow occurred (see Fig. 1). If the vasodilator response to epinephrine is in part directly related to increased O\textsubscript{2} consumption and CO\textsubscript{2} production it might reasonably be expected that it must be accompanied by an increase in P\textsubscript{CO\textsubscript{2}} or decrease in P\textsubscript{O\textsubscript{2}} of the extracellular fluid which in turn would act on the smooth muscle of the high resistance vessels to produce vasodilation. In this study the P\textsubscript{CO\textsubscript{2}} of venous blood draining the forearm muscles did not change and its P\textsubscript{O\textsubscript{2}} increased during intravenous infusion of epinephrine. It may be argued that changes in venous blood gas tensions under these circumstances do not represent a reasonable estimate of the corresponding changes in the tensions of these gases in the extracellular fluid. This question is intimately connected with the possibility of different responses of nutritional (capillary) and nonnutritional muscle blood flow to epinephrine. If epinephrine increases nonnutritional blood flow to a greater extent than capillary blood flow it is possible that an increase in P\textsubscript{CO\textsubscript{2}} or a decrease in P\textsubscript{O\textsubscript{2}} of extracellular fluid could have occurred without being reflected in similar changes in venous blood. While some observers (24-26) found that epinephrine did not increase nutritional flow to skeletal muscle in man or in animals at a time when total flow to the muscle was increased, more recent studies yielded different results. Thus, Gosselin (27) found an increase in clearance of \textsuperscript{24}Na from muscle of anesthetized dogs in response to small concentrations of epinephrine and Coffman (28) found approximately equal percentage increases in clearance of Na \textsuperscript{131}I from human calf muscle and in calf blood flow measured plethysmographically. Furthermore, in the present study during hyperventilation-induced hypocapnia, which would reasonably be expected to be associated with lowering of the P\textsubscript{CO\textsubscript{2}} of extracellular fluid, the vasodilator response to intravenous epinephrine was not modified.

These considerations suggest that the increase in blood flow during epinephrine infusion is not directly related to the increase in O\textsubscript{2} consumption or CO\textsubscript{2} production of skeletal muscle. There remains the possibility, however, that epinephrine-induced vasodilation may be secondary to the increase in metabolic rate and that it may be mediated by mechanisms other than a change in the P\textsubscript{O\textsubscript{2}}, P\textsubscript{CO\textsubscript{2}} or pH in the environment of the high resistance vessels. The exact mechanism by which increase in metabolism of skeletal muscle affects its blood flow is not clearly understood. Recent studies by Scott et al. (29) suggested that the mechanism involved is a release of vasodilator substances from the muscle into the extracellular fluid and venous blood. Their evidence suggests that the substance involved is not oxygen or hydrogen ion but it is likely to be adenosine triphosphate. The possibility that such a mechanism was responsible for the vasodilator response to epinephrine can be examined only indirectly. The classic case where an increase in skeletal muscle blood flow is secondary to increase in metabolism is contraction hyperemia (that occurs during a period of sustained contraction). In anesthetized dogs, there is an excellent linear correlation between oxygen consumption of muscle and its blood flow at rest and during contraction (30). Similarly, in the human forearm following epinephrine iontophoresis, we found an excellent linear relationship between the forearm muscle blood flow and its O\textsubscript{2} consumption or CO\textsubscript{2} production, at rest and during sustained contraction (15); the 95% confidence bands in
METABOLIC AND VASODILATOR EFFECTS OF EPINEPHRINE

Relationship between $O_2$ consumption and blood flow of forearm muscle (above) and between $CO_2$ production and blood flow of forearm muscle (below) before and during intravenous or intra-arterial epinephrine. The shaded areas represent the 95% confidence bands about the regression lines describing the relationships between $O_2$ consumption or $CO_2$ production and muscle blood flow at rest and during sustained contraction (15). Note that during epinephrine administration blood flow is higher for any given $O_2$ consumption or $CO_2$ production than during muscle contraction.

Figure 4 were obtained in that study. Superimposed on these graphs are the data of the present investigation. Note that the resting data agree closely with the results of the previous investigation indicating the comparability of these two studies. In contrast, most

Circulation Research, Vol. XXI, November 1967
of the data obtained during epinephrine infusion fall outside the 95% confidence bands, suggesting that the main mechanisms responsible for the epinephrine-induced vasodilation are different from those responsible for the increase in flow during muscular contraction. It must be emphasized that these comparisons constitute indirect evidence. Therefore, the possibility that a fraction of the vasodilator response to epinephrine might be due to its associated metabolic effects cannot be excluded with confidence.

The present data and the fact that epinephrine causes dilation of isolated small coronary arteries (31) and relaxation of isolated muscle strips from large arteries following α-adrenergic receptor blockade (32) suggest that the vasodilation accompanying epinephrine infusion is largely the result of a direct effect of the hormone on the smooth muscle of the high resistance vessels.

Our findings that the time-course and the magnitude of the increase in blood flow through the forearm muscle induced by epinephrine were similar following intravenous and intra-arterial infusion of the hormone add further support to the view expressed by previous workers (9, 10, 17, 28, 33) that there is no fundamental difference in the response of skeletal muscle blood vessels to intravenous or intra-arterial epinephrine.

References

20. ZIERLER, K. L.: Theory of the use of arteriovenous concentration differences for measur-


Relationship between the Metabolic and Vasodilator Effects of Epinephrine in Human Forearm Muscle
HERMES A. KONTOS, DAVID W. RICHARDSON and JOHN L. PATTERSON, Jr.

doi: 10.1161/01.RES.21.5.679

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1967 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/21/5/679

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/