Metabolic and Mechanical Properties of Aortas from Aldosterone-Salt Hypertensive Rats

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SUMMARY. Aortas from aldosterone-salt treated hypertensive rats and vehicle-infused normotensive controls were compared with respect to mechanical properties, metabolism, and energy turnover. Passive wall stress at any given circumference was slightly higher in aortas from the hypertensive rats, whereas active isometric force normalized to cross-sectional area was similar in vessels from the two groups at their respective optimal circumference for active tension development [hypertensive rats: \( n = 14 \), 19.73 ± 1.98; controls: \( n = 13 \), 22.57 ± 2.13 mN/mm²]. Metabolic parameters were measured with the aortas held at optimal circumference for active tension development, the optimal length for tension development \( n = 6 \), 5.67 ± 0.17 and \( n = 7 \), 5.29 ± 0.18 mm for control and aldosterone-salt groups, respectively. Basal oxygen consumption rate was elevated significantly in aortas from the hypertensive rats \( \left( n = 14 \right), 0.457 ± 0.026 \) vs. \( \left( n = 13 \right), 0.267 ± 0.028 \) \( \mu \text{mol/min per g}; P < 0.001 \). Under resting conditions, lactate production rate was similar in aortas from the two groups [hypertensive rats: \( n = 20 \), 0.129 ± 0.010; controls: \( n = 21 \), 0.112 ± 0.008 \( \mu \text{mol/min per g} \)]. Upon activation with added KCl, the rate of oxygen consumption and lactate production increased with tension development in both groups, but the stimulated rate of oxygen consumption was higher in hypertensives compared to controls \( \left( n = 14 \right), 0.580 ± 0.031 \) vs. \( \left( n = 13 \right), 0.441 ± 0.049 \) \( \mu \text{mol/min per g}; P < 0.025 \). The stimulated rates of lactate production were similar in the two groups [hypertensive rats: \( n = 20 \), 0.172 ± 0.009; controls: \( n = 21 \), 0.118 ± 0.009]. Despite the elevated oxygen consumption rate in hypertensives, metabolic tension cost in vessels from these rats was not significantly different from controls [hypertensive rats: \( n = 9 \), 0.049 ± 0.011; controls: \( n = 8 \), 0.047 ± 0.009 \( \mu \text{mol adenosine triphosphate/min per g per mN/mm²} \)]. These results indicate that the elevated oxidative metabolism in hypertensives is probably not due to inefficient energy utilization by the contractile system. Similarly, enhanced sodium-potassium transport does not appear to account for the elevated oxygen consumption rate, since the increase in energy utilization is significantly greater than that estimated to support the additional transport activity in these vessels. The elevation in oxygen consumption rate in the hypertensives is not the result of nonspecific effects of the aldosterone treatment, unrelated to the hypertension, since oxygen consumption rate in vessels from aldosterone-treated normotensive rats (no salt) \( \left( n = 4 \right), 0.233 ± 0.024 \) \( \mu \text{mol/min per g} \) was not elevated. Our results indicate that, unlike the spontaneously hypertensive rat model, in the aldosterone-salt model of hypertension, vascular oxidative metabolism and energy turnover is substantially elevated compared to aortas from normotensive controls. (Circ Res 55: 349–357, 1984)

It has been recognized for some time that structural changes in the vessel wall are important in the development and maintenance of both experimental hypertension and the hypertensive state in man (Folkow, 1978). Recently, these structural alterations have been defined more precisely in terms of the cellular mechanisms responsible for the vessel wall hypertrophy which is thought to occur in response to an increase in arterial wall stress. Vascular smooth muscle hypertrophy and/or hyperplasia appears to be responsible for the increase in cellular mass, whereas enhanced synthesis of connective tissue results in an increase in extracellular components (Wolinsky, 1970; Mulvany and Halpern, 1977; Brecher et al., 1978; Seidel, 1979; Olivetti et al., 1982; Owens and Schwartz, 1982). In addition, alterations in membrane ion permeability and active ion transport have been documented in a number of experimental hypertensive models (Jones, 1974; Friedman and Friedman, 1976; Friedman and Nakashima, 1978; Garwitz and Jones, 1982b; Overbeck and Grissette, 1982). Moreover, these functional changes are present prior to any detectable rise in blood pressure and, therefore, may play an important role in the pathogenesis of the hypertension (Jones and Hart, 1975; Garwitz and Jones, 1982b).

An increased rate of active ion transport and enhanced biosynthesis activity in vascular tissue in association with the hypertensive state would be expected to place additional metabolic demands on the smooth muscle cell. However, little is known about the metabolism and energetics of vascular smooth muscle under these conditions. Daly and Gurpide (1959) first reported that vascular oxidative
metabolism was increased significantly in aortas from the DOCA (deoxycorticosterone acetate)-salt hypertensive rat model. Daly (1976) later demonstrated that both the oxidative and glycolytic utilization of glucose were elevated in aorta from renal hypertensive rats. A major drawback of these studies was that the mechanical state of the vascular smooth muscle studied was not controlled, and therefore it was impossible to distinguish between metabolic changes associated with increased energy utilization for contraction or other cellular functions.

In a recent study, Arner and Hellstrand (1981) examined the metabolism of vascular tissue from the spontaneously hypertensive rat (SHR) model under carefully controlled mechanical conditions, and, overall, the resting rate of energy metabolism of the SHR aorta was increased by approximately 13% compared to Wistar-Kyoto controls. Arner and Uvelius (1982) have also presented morphological data under similar conditions and concluded that the increased metabolic rate in SHR could be accounted for by an increased smooth muscle cell content. Thus, one may question the link between the reported increases in ion pumping and synthetic activity and metabolism, or, perhaps, the adequacy of the Wistar-Kyoto rat for comparison to the SHR in studies of metabolism.

The objectives of the present study were to characterize the mechanics, metabolism, and energetics of vascular smooth muscle from the aldosterone-salt hypertensive rat. This model of mineralocorticoid-dependent hypertension is particularly suitable, in that the hypertension is produced readily with the administration of physiological doses of aldosterone (Garwitz and Jones, 1982a). This overcomes the problems inherent in using pharmacological doses of other mineralocorticoids, e.g., deoxycorticosterone acetate, which may induce metabolic changes unrelated to the hypertensinogenic action of these hormones. These changes may effectively mask more subtle changes in cellular function associated with the development of the hypertension. Furthermore, by replacing the saline drinking fluid with water, normotensive animals with elevated levels of aldosterone similar to the hypertensives can be produced. These animals serve to control for nonspecific effects of the aldosterone itself.

Our results indicate that oxidative metabolism is substantially elevated in aortas from the hypertensive animals, compared to their age-matched, normotensive controls. However, the mechanical parameters and the economy of force maintenance were not significantly altered in this model of experimental hypertension.

**Methods**

**Animals and Tissues**

The aldosterone-hypertensive rat model has been presented in detail elsewhere (Garwitz and Jones, 1982a, 1982b). Briefly, the left kidney was removed from anesthetized male Sprague-Dawley rats (150-200 g body weight). An osmotic minipump (Alza) containing aldosterone (Sigma) dissolved in polyethylene glycol, or vehicle only for the control group, was implanted subcutaneously in the animals. Control rats (C) were given a 1% (wt/vol) NaCl solution to drink, whereas the aldosterone-treated animals (A) received a supplement of KCl (0.3% wt/vol) in the NaCl solution to aid in the maintenance of body weight. Systolic blood pressure was measured using a tail cuff technique.

On the morning of the experiment, the rats were decapitated and the thoracic aortas were quickly removed. Aortas were cleaned of adventitia and adherent fat, and then were cut transversely into three segments, each approximately 5-6 mm long and weighing 5-6 mg. One segment was mounted isometrically between a movable and fixed stainless steel wire (0.7 mm diameter) in the chamber for simultaneous measurement of force and oxygen consumption. The remaining two segments were cannulated on glass rods of comparable dimensions such that they were held isometrically for experiments to measure lactate production. At the end of each experiment, the segments were removed, cut open longitudinally, and muscle dimensions were then measured (segment length and circumference) by microscopy, using an ocular scale. The tissues were then blotted gently and weighed.

**Solutions**

The physiological saline solution (PSS) had the following composition (mm): Na⁺, 146.2; K⁺, 5.0; Mg²⁺, 1.2; Ca²⁺, 2.5; Cl⁻, 143.9; HCO₃⁻, 13.5; H₂PO₄⁻, 1.2; and glucose, 11.4. Ca²⁺-free PSS was similar to PSS with the exclusion of CaCl₂ and the addition of 0.2 mm ethylene-glycol-bis (β-amino-ethyl ether)-N,N’-tetraacetic acid (EGTA). Solutions were gassed with mixture containing 5% CO₂ to obtain a pH of 7.4 at 37°C. Ethylenediaminetetraacetic acid (EDTA), 0.026 mm, was added to the solutions to remove heavy metal ion impurities. The solutions used in the oxygen chambers were first passed through Millipore sterilizing filters (0.45 μm) to remove any bacterial contaminants. Depolarization-induced contractions were elicited by the addition of KCl (approximately 45 μl) from a concentrate (2 mM) to increment the bath KCl concentration by 50 mm.

**Oxygen Consumption**

Simultaneous measurements of the rate of oxygen consumption (Jo₂) and force were made in a chamber similar to the one described previously in detail (Paul, 1983). The volume of the chambers used was between 1.6 and 3.0 ml. Clark-type polarographic electrodes (Yellow Springs Instrument no. 5331) with 650-μm platinum tip diameter were used. Numerous precautions were taken to reduce oxygen consumption in the absence of the arterial segment (background) to a minimum. These consisted of filtering the solutions used in the chamber to reduce bacterial Jo₂, the use of small tip electrodes to reduce self-consumption of O₂, and development of machinable glass and ceramic parts so that only non-O₂-absorbable or-consuming surfaces were present. In spite of these adjustments, a background Jo₂ of (n = 13), 1.15 ± 0.14 nmol/min for controls and (n = 14), 1.22 ± 0.13 nmol/min for the aldosterone group was present. These rates were shown to be quite constant over the period of measurement and are comparable to previously published values (Paul and Peterson, 1975), although, due to the small size of the tissues used...
in the present study, background rates are a larger fraction of the tissue O₂ consumption than in previous studies.

Lactate Production

To obtain a precision similar to that of the continuously measured O₂ consumption, parallel measurements of lactate elimination were made on two additional segments from the same aorta. These segments were cannulated on glass rods of comparable dimensions so that the vessels were held isometrically throughout the experiments. The segments were then placed in test tubes in 1.5 ml of PSS gassed with 95% O₂/5% CO₂, then transferred as required to additional tubes to change solutions. In this manner, the entire content of the tubes could be assayed for lactate. Lactate was measured using a linked enzymatic assay (Lundholm et al., 1963).

Mechanical Measurements

Isometric measurements of force were made with a Kistler-Morse transducer (compliance = 0.1 μm/mN). Vessel wall thickness was calculated according to T = wet weight/1.06 · C · L, and cross-sectional area as A = 2 × wet weight/1.06 · C, where 1.06 g/cm³ is used as an estimate of tissue density. L is segment length, and C is vessel circumference. The vessel circumference used to calculate wall thickness was the value measured in the cut-open vessel. Since the vessel has a tendency to resume its original circular orientation after being cut open, the artery must be under a slight tension to obtain this measurement. We found that circumferences measured in this manner were similar to values of optimal circumference for active tension development (lo), calculated from the active stress-circumference curves on these vessels [C: (n = 13), 5.65 ± 0.05 vs. (n = 6), 5.67 ± 0.17 mm; A: (n = 14), 5.21 ± 0.08 vs. (n = 7), 5.29 ± 0.18 mm].

Force-length curves were generated by means of the following protocol: after a 2-hour preequilibration in PSS under a preload of approximately 9 mN/mm segment length, two conditioning contractures were elicited by exposing the tissues to 50 mM KC1. The vessels then were relaxed and shortened to the length where resting tension on the vessel was reduced to zero, then stretched by 0.25 mm. Resting tension was measured after 5 minutes of accommodation at the new length. The muscles were then stimulated with 50 mM KCl, and active tension was recorded. After washout of KCl and a relaxation period of about 15 minutes, the vessels were stretched to a new length and the protocol was repeated.

Statistical Methods

Values are presented as the mean ± SEM. Significance was determined using Student's t-test, with a probability of less than 0.05 regarded as statistically significant.

Results

General Characteristics of the Aldosterone Hypertensive Rat Model

Aldosterone was infused into the rats at 0.25 μg/hr for a period of 4 weeks. This rate of aldosterone infusion was found previously to produce a consistent level of hypertension at plasma levels of aldosterone within the "stressed" physiological range (Garwitz and Jones, 1982a). As shown in Table 1, systolic blood pressure in the treated rats was elevated significantly after 4 weeks of aldosterone infusion. Body weights in the hypertensive group were somewhat lower than in controls, although the aldosterone-salt-treated animals did continue to gain weight throughout the study. Aortic wall thickness in these rats was increased significantly relative to the controls (Table 1) in spite of significantly lower body weights in the hypertensive rats. Arterial wall thickening is a characteristic response of the vessel wall to an elevation in pressure and presumably reflects an increased synthesis of both cellular and extracellular material (Olivetti et al., 1982).

Mechanical Properties

The resting wall stress-internal circumference relationship in aortas from control and hypertensive rats is shown in Figure 1. The curves are basically exponential in shape, with the curve for the aldosterone animals shifted slightly to the left compared to the control curve. Over the entire range of circumferences studied (4.75–6.25 mm), resting wall stress in aortas from the hypertensive rats was consistently higher than in control aortas. However, these increases were not statistically significant.

Active force development in response to 50 mM KCl was measured at predetermined lengths (see Methods) to determine the active wall stress-circumference relationship. This relationship in aortas from control and hypertensive rats is depicted in Figure 2. Wall stress values have been normalized to the maximum value for each vessel in order to reduce variability. Active stress development in vessels from the two groups was similar, although the curve for controls was somewhat broader than the curve for the hypertensive group. The optimal circumference for active tension development (lo) was smaller in the aldosterone-salt hypertensive rats than in the controls, although this difference was not statistically significant [C: (n = 6), 5.67 ± 0.17 vs. A: (n = 7), 5.29 ± 0.18 mm].

This protocol for measurement of active and passive force-length relations was chosen because it minimizes the manipulations of the tissue required for the generation of force-length relations. However, the above-described results may be influenced by the presence of basal tone. In a control series of experiments, the amount of relaxation in unstimulated preparations at lo, induced by a Ca++-free PSS (basal tone) expressed as a percent of the maximum active force was 4.0 ± 1.1% for aorta from control rats (n = 14) and 12 ± 2.2% for the aldosterone hypertensive aortas (n = 14). Therefore, resting tension, as measured above, was only slightly higher than true passive tension in these vessels. Corrections for basal tone would tend to reduce the small difference in active stress observed at lo (Table 2). In an additional control series, the passive tension as a function of length was measured in the presence and absence of Ca++. Again, basal tone was found...
Table 1

Effects of Aldosterone-NaCl Treatment on Body Weight, Systolic Blood Pressure, and Aortic Wall Thickness

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>n</th>
<th>Age (wks)</th>
<th>Body wt (g)</th>
<th>Systolic blood pressure (mm Hg)</th>
<th>Aortic wall thickness (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>16</td>
<td>10</td>
<td>326 ± 5</td>
<td>116 ± 3</td>
<td>135 ± 3</td>
</tr>
<tr>
<td>Aldosterone</td>
<td>16</td>
<td>10</td>
<td>252 ± 9*</td>
<td>194 ± 3*</td>
<td>173 ± 5*</td>
</tr>
</tbody>
</table>

* P < 0.001.

Metabolic Properties

Simultaneous measurements of oxygen consumption and force were made under isometric conditions, using aortas from control and hypertensive rats mounted at L0. A typical tracing from such experiments is shown in Figure 3. The response to 50 mM KCl in the aorta from both the control (A) and hypertensive (B) was an increase in both oxygen consumption and isometric force. Isometric force reached about 95% of its maximum value in approximately 15 minutes, whereas the rate of oxygen consumption rapidly increased to a maximum value and decreased to a steady state at a time comparable to that for active force. As shown in Figure 3, A and B, active force development in response to 50 mM KCl was similar in both the control and hypertensive. However, the basal levels of oxygen consumption were significantly different, with \( \dot{O}_2 \) in the aorta from the hypertensive elevated considerably compared to the basal rate in the control. An approximate doubling of the basal rate of oxygen consumption occurred in response to 50 mM KCl in the control aorta, whereas \( \dot{O}_2 \) increased by only 37% above basal in the aorta from the aldosterone-treated rat.

The results from a series of such experiments are summarized in Table 2, along with parallel measurements of lactate production (\( \dot{L}_ac \)) in segments of aorta from the same animals used for the \( \dot{O}_2 \) meas-
TABLE 2
Basal and Stimulated Metabolism in Aortas from Control and Hypertensive Rats

<table>
<thead>
<tr>
<th>Metabolic Parameters</th>
<th>Control</th>
<th>Aldosterone-salt</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Basal (PSS)</td>
<td>KCl (50 mM)</td>
</tr>
<tr>
<td>$J_{O_2}$</td>
<td>0.267 ± 0.028 (13)</td>
<td>0.441 ± 0.049 (13)</td>
</tr>
<tr>
<td>$J_{ATP}$</td>
<td>0.112 ± 0.008 (21)</td>
<td>0.188 ± 0.009 (21)</td>
</tr>
<tr>
<td>$J_{ATP}$</td>
<td>1.43 ± 0.28 (8)</td>
<td>2.44 ± 0.11 (8)</td>
</tr>
<tr>
<td>$P_e$</td>
<td>31.88 ± 1.75 (13)</td>
<td>22.57 ± 2.13§ (13)</td>
</tr>
</tbody>
</table>

Metabolic parameters (± SEM) are given as µmol/min per g blotted weight; number of tissues used given in parentheses. $J_{O_2}$, rate of O$_2$ consumption; $J_{ATP}$, rates of lactate and ATP production, respectively. $J_{ATP}$ $\Delta$ = 6.42 $J_{O_2}$ + 1.25 $J_{ATP}$, calculated from tissues in which both $J_{O_2}$ and $J_{ATP}$ were measured on the same aorta; $P_e$, resting isometric force (basal) and § active isometric force (KCl, total-pasive) in mN/mm$^2$.

$^*$ $P < 0.001$.
$^†$ $P < 0.025$.

Under basal conditions (unstimulated vessels mounted isometrically at their respective $l_0$), $J_{O_2}$ in the aldosterone group was approximately 71% higher than in controls. It should be noted that the $J_{O_2}$ and $J_{ATP}$ values reported in this paper for the control vessels are similar to rates previously reported for rat aorta (Paul, 1983). Upon exposure to 50 mM KCl, $J_{O_2}$ increased significantly in vessels from both the control and hypertensive rats, with $J_{O_2}$ in the hypertensives elevated significantly relative to the stimulated rate of oxygen consumption in control aortas. Similarly $J_{ATP}$ increased significantly.
in both, upon exposure to 50 mM KCl. However, the rate of lactate production in aorta from the control and hypertensive animals was similar under both resting and stimulated conditions. As expected from these results, the calculated rate of ATP production \( (J_{\text{ATP}}) \) in aortas from the hypertensives was significantly higher than \( J_{\text{ATP}} \) in controls under both basal and stimulated conditions. This large difference in \( J_{\text{ATP}} \) was not reflected in the mechanical properties however. Active force development in response to 50 mM KCl, in contrast to \( J_{\text{ATP}} \), was comparable in aortas from control and hypertensive rats. Passive stress in control aortas at \( l_0 \) (5.7 mm) was higher than that in the aldosterone group at its respective \( l_0 \) (5.3 mm), as predicted from the passive stress-circumference curve in Figure 1.

The relationship between \( J_{\text{ATP}} \) and isometric force can be used to calculate the metabolic tension cost in aortas from the control and hypertensive rats. Metabolic tension cost refers to the rate of ATP utilization required for maintenance of active tension and is expressed normally in terms of ATP hydrolysis per unit muscle mass per unit force/cross-section area (Paul, 1980). As can be seen in Figure 4, there was no significant difference in metabolic tension cost (the slope of the lines) in aortas from the two groups. In this figure, a line is shown joining the two mean values measured under unstimulated and stimulated conditions in vessels from the two groups. The slope of this line was not used to calculate a mean value of tension cost, although it is similar in value. Rather, the tension cost values from each of eight experiments were averaged to obtain a more accurate mean value for each group.

Discussion

The mechanical characteristics of aortas from aldosterone-salt hypertensive rats were not fundamentally different from those of vessels from control normotensive rats. Passive wall stress-circumference curves for controls and hypertensives were similar in shape, although the curve for the hypertensive rats was shifted slightly to the left relative to the control curve, and passive wall stress at any given circumference was higher in aortas from hypertensives. These findings suggest that the 28% increase in vessel wall thickness in hypertensives may reflect an increase in extracellular components as well as an increase in collagen and elastin content. This increase in collagen and elastin content might be expected to elevate passive tension values in these vessels. Active wall stress in aortas from aldosterone-hypertensive rats was similar to controls. This suggests that force-generating capability in vessels from hypertensives was not different from that of the controls. This observation is in accord with similar recent findings in arteries from SHR and DOCA-salt hypertensive rats (Seidel, 1979; Warshaw et al., 1979; Arner and Hellstrand, 1981; Cox, 1982).
The present experiments on vascular metabolism indicate that basal oxygen consumption is elevated significantly (71%), in aortas from aldosterone hypertensive rats compared to controls. These findings confirm and extend the initial report by Daly and Gurpide (1959) of elevated oxidative metabolism in aortic slices from DOCA-salt hypertensive rats. Arner and Hellstrand (1981) also reported an increase in basal Jo₂ in aortas from spontaneously hypertensive rats. However, in the SHR, the observed change in basal oxygen consumption was much smaller (an increase of about 16% relative to the WKY control) than the increase we have measured in aortas from aldosterone hypertensive rats. Moreover, the increased metabolism in the SHR aorta could be accounted for by an increase of similar magnitude in the vascular smooth muscle cell content. This does not appear to be the case for the aldosterone hypertensive rat. An increase in the smooth muscle cellular mass of about 27% has been estimated in aorta from the aldosterone hypertensive rat. Garwitz and Jones (1982a) reported cell water values of 1.06 in aortas from aldosterone hypertensive rats compared to 0.79 kg cell H₂O/kg dry weight in aortas from controls. When expressed per wet weight, for comparison to the metabolic values used in this study, an increase of 27% is obtained (0.302 vs. 0.237 kg cell H₂O/kg wet weight). Clearly, this increase cannot explain the 71% increase in the basal Jo₂ which we have measured in vessels from these animals. Unlike the SHR, in the aldosterone model of hypertension, cellular oxidative metabolism is substantially elevated compared to that of normotensive controls, even when the increase in cellular mass is taken into account.

The nature of this increase in vascular oxidative metabolism or the stimulus for its development is not clearly understood at this time. This metabolic change conceivably could reflect a direct action of aldosterone on the vascular metabolic machinery, since specific mineralocorticoid receptor sites have been identified and characterized in aortic tissue preparations from the rat (Meyer and Nichols, 1981). However, the physiological effects of aldosterone binding to these vascular sites have not been clearly defined. In classically recognized mineralocorticoid target tissues, such as kidney and descending colon, aldosterone treatment increases oxidative metabolism, but the increase is thought to be secondary to a primary enhancement of active sodium transport (Reich and Scott, 1979). Active Na⁺-K⁺ transport is known to be increased significantly in arterial smooth muscle from the aldosterone hypertensive rat (Garwitz and Jones, 1982b). However, the increase in JₐNaCl in aortas from these animals measured in the present study appears to be significantly greater than the increase required to support the additional transport activity. Current evidence suggests that in vascular smooth muscle, 3 Na⁺ and 2 K⁺ are transported per cycle of the transport mechanism, and that this requires the hydrolysis of one ATP (Fleming, 1980). Using previously published data on Na⁺ fluxes in the rat (Garwitz and Jones, 1982b), an ATP utilization for the Na⁺-K⁺-ATPase of 0.128 μmol/min per g for the control animals and 0.266 μmol/min per g for the aldosterone hypertensive rats can be calculated, assuming similar stoichiometry. An additional 0.138 μmol ATP/min per g would therefore be required for active sodium transport in the hypertensives. In this study, an increase of 1.4 μmol ATP/min per g was calculated from the differences in basal metabolism in the eight tissues in which both Jo₂ and Juc were measured (Table 2). We believe this is the most precise estimate; however, if the group means for all tissues studied are used, a difference of 1.24 is obtained. Utilizing the measured values for tension costs, 0.076 μmol/min per g of this difference could be ascribed to the differences in basal tone. Thus, enhanced active Na⁺-K⁺ transport could account for only a small fraction of the increased energy utilization in aortas from the hypertensive rats. The amount of the increase attributable to increased cellular mass is approximately 0.5 μmol ATP/min per g. Therefore, the increased energy utilization observed in the aortas from the hypertensive rats would require some process(es) using 0.6–0.8 μmol ATP/min per g. For comparison, this additional ATP utilization is similar to that required for the maintenance of 70% of maximal active isometric force.

The results of the present study indicate that metabolic tension cost was similar in the aortas from control and hypertensive rats. This finding is similar to that reported for the SHR model (Arner and Hellstrand, 1981). Inefficient utilization of energy by the contractile system, therefore, is unlikely to be responsible for the elevated energy turnover in activated vessels from the hypertensives. It appears that other energy-consuming cellular process must be increased in the hypertensives to explain this phenomenon.

The complex interrelationships among the major parameters involved—elevated oxidative metabolism, aldosterone treatment, high salt intake, and the hypertension—are not readily resolvable. However, results with a second control animal utilized in these and previous experiments have shown that aldosterone infusion without an accompanying high intake of sodium does not result in either changes in ion transport (E. Garwitz McMahon and A. Jones, unpublished observations) or significant hypertension. The elevated Jo₂ in hypertensive rats is not simply an effect of aldosterone treatment per se, as Jo₂ in vessels from aldosterone-infused normotensive animals was not elevated.

Aortic lactate production in the control and hypertensive rats was not significantly different under both resting and stimulated conditions, although basal Juc was slightly higher in the aldosterone group. Basal Juc was elevated by 15% in the hyper-
tensives, which is less than the increase expected based on a 27% increase in cell mass derived from the increase in cell H2O/kg in the hypertensives. This would suggest that cellular J02 is actually slightly reduced in aortas from the hypertensives, compared to controls. There is strong evidence that, in vascular smooth muscle from a number of species, aerobic lactate production is specifically coupled to active Na+-K+ transport (Paul et al., 1979; Paul, 1983; Lynch and Paul, 1983). Paul and coworkers demonstrated that under conditions known to inhibit Na+-K+ transport (e.g., ouabain or the removal of external sodium), vascular lactate production is decreased whereas oxygen consumption and isometric force are both increased. Although a specific coupling of aerobic glycolysis to Na+-K+ transport was indicated in most species studied by Paul (1983), responses in rat vessels appeared to be an exception. Nonetheless, it was anticipated that the increased rate of sodium transport in aortas from the hypertensive rats might be accompanied by a concomitant increase in aerobic lactate production, if such a coupling exists in rat aorta. The absence of any detectable difference in J02 in control and hypertensives thus suggests that the energetics of active sodium transport in rat aorta are somewhat unique. Elevated basal rates of oxygen consumption in hypertensives indicate that Na+ transport in rat arterial smooth muscle might be more dependent on oxidative rather than glycolytic metabolism. Further study is required to characterize adequately the energetics of active Na+-K+ transport in rat arterial smooth muscle, and to delineate its role, if any, in the observed increase in basal J02 in the aortas from hypertensive rats.

Our results indicate that the basal energy flux in aortas from aldosterone-salt hypertensive rats is significantly elevated compared to controls. This is noteworthy, for this is not true in the spontaneously hypertensive rat model. In both models, however, the coupling between metabolism and mechanical activity appears to be unaffected by the hypertension. It may be of particular importance to our understanding of hypertension that the increases in J02, Na+-K+ transport and blood pressure itself are not simply related to the aldosterone treatment, but require concomitant salt loading. Questions as to the nature of the processes underlying this increased basal energy flux, its dependence on time and blood pressure, as well as its reversibility, need to be resolved before the significance of this phenomenon with respect to hypertension can be appreciated fully.

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