

Hemodynamic Alterations in the Young Spontaneously Hypertensive Rat: Elevated Total Systemic and Hindquarter Vascular Resistance¹ (38169)

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(Introduced by J. P. LaRocca)

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In the established phase of hypertension of the spontaneously hypertensive rat (SHR), cardiac output is normal and total peripheral resistance is elevated (1-3). Tobia *et al.* (1) extended information on the hemodynamic characteristics of the SHR by measuring regional blood flow in the hindlimb and mesenteric circulations. Since blood flow through the iliac and superior mesenteric arteries is unaltered in the mature SHR (5-8 mo) in the face of normal cardiac output, their findings suggest that the rise in hindlimb or mesenteric vascular resistance is proportionate to the increase in total peripheral resistance, and that the hemodynamics of these regional vasculatures resemble that of the total systemic circulation. Similar regional and whole body hemodynamics exist in chronic renal hypertensive dogs, and in this connection cardiac output (4) and limb blood flow are normal (5), suggesting that the hemodynamic pattern of the limb circulation reflects that of the whole body. In contrast to these findings in chronic renal hypertension, Overbeck (6) reported that in early renal hypertension (less than 4 weeks duration) the hemodynamic state of the limb vasculature may not reflect total body hemodynamics since limb blood flow is normal in the presence of elevated cardiac output (4). In light of the proposal that a hyperdynamic circula-

tion (elevated cardiac output and heart rate) may exist early in the development of hypertension (3), the present study was carried out to determine whether a differing hemodynamic pattern exists between the hindquarter vasculature and the total systemic circulation in the young SHR (2-3 mo of age).

Methods. Spontaneously hypertensive rats (SHR) of the Japanese strain of Wistar rats (7) and their normotensive genetic predecessors, Wistar Kyoto (WKY), were raised in our laboratories. The SHR was inbred through brother-sister mating, whereas WKY was bred randomly. Male rats aged 2-3 mo were used throughout this study. All rats were housed on sawdust bedding in plastic cages (19" × 10½" × 8½" deep) in groups of 4. Each plastic cage was covered with an Econolid air filter (Maryland Plastics). Fresh air replaced room air approximately every 10 min, and room temperature was maintained at about 70°F.

Electromagnetic measurement of abdominal aortic blood flow. Blood flow was measured in 19 WKY and 15 SHR. Rats were anesthetized with pentobarbital sodium (50 mg/kg, ip) and body temperature was maintained at 36°-38°C with a YSI temperature controller (Yellow Springs Instrument Co., Model 73A). An incision was made in the lower abdomen, and the abdominal aorta was carefully isolated from surrounding tissue for a distance of 1-2 cm proximal to its bifurcation. A noncannulat-

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ing flow probe (Carolina Medical Electronics) of 0.75 mm internal diameter was placed on the vessel, and zero flow baseline was determined by mechanically occluding the vessel proximal to the flow probe. The electromagnetic flowmeter was connected to a Grass Model 7D polygraph on which all recordings were made. Arterial blood pressure was monitored from the cannulated (PE60) left carotid artery with a Statham P23DC pressure transducer. Pulsatile and mean abdominal aorta blood flow (ml/min) and mean carotid arterial blood pressure (mmHg) were determined during the study. Hindquarter regional resistance (mmHg·min/ml) was calculated by dividing mean abdominal aorta blood flow into mean carotid arterial blood pressure. The flow probe was calibrated *in situ* and *in vitro* by perfusing whole blood at various flow rates through the vessel, and details of this procedure have been published (1).

Electromagnetic measurement of ascending aortic blood flow in open-chest rats. Ascending aortic blood flow was determined in 8 WKY and 8 SHR open-chest preparations in order to estimate whether cardiac output is altered in the young SHR. Prior to opening the chest rats were artificially ventilated (room air 60–70 beats/min; Harvard Rodent Respirator) via the cannulated trachea. After thoracotomy and exposure of the ascending aorta, an electromagnetic flow probe (2 mm diameter) was positioned on the vessel. Pulsatile and mean aortic flow and mean carotid arterial blood pressure were measured during the experiment, and total peripheral resistance was calculated by dividing mean ascending aortic flow into mean blood pressure. The aortic flow probe was calibrated *in situ* by perfusing whole blood obtained from donor rats. Zero flow was approximated from the diastolic interval, and confirmed at the end of the experiment. Data (means \pm standard error) were analyzed for statistical significance by Student's *t* test.

Results. There was no difference in body weight (grams) between the SHR (217 \pm 7) and WKY (224 \pm 7), whereas heart rate (beats/min) was significantly ($P < .05$) increased in the SHR (440 \pm 7) com-

TABLE I. Hindquarter Hemodynamics in Young Spontaneously Hypertensive and Wistar Kyoto Normotensive Rats.

	WKY	SHR
Mean arterial pressure (mmHg)	115 \pm 4 ^a	181 \pm 5 ^b
Abdominal aortic flow (ml/min)	8.8 \pm 0.5	8.2 \pm 0.5 ^c
Hindquarter Vascular resistance (mmHg·min/ml)	13.0 \pm 1.8	20.8 \pm 1.0 ^b

^a Mean \pm standard error of 19 WKY and 15 SHR.

^b Different from WKY with $P < .001$.

^c Not different from WKY with $P > .05$.

pared to WKY (394 \pm 9). The data in Table I indicate that abdominal aortic blood flow is unaltered in the SHR (8.2 \pm 0.5) compared to WKY (8.8 \pm 0.5), whereas hindquarter vascular resistance is elevated in the young SHR. There is no significant difference in ascending aortic flow between the SHR (24.6 \pm 1.1) and WKY (30.4 \pm 2.7), although mean arterial pressure and, thus, total peripheral resistance are increased (Table II).

Discussion. Some insight into the func-

TABLE II. Open-Chest Hemodynamics in Young Spontaneously Hypertensive and Wistar Kyoto Normotensive Rats.

	WKY	SHR
Mean arterial pressure prior to thoracotomy (mmHg)	109 \pm 3 ^a	154 \pm 3 ^b
Mean arterial pressure after thoracotomy (mmHg)	65 \pm 6	96 \pm 5 ^b
Ascending aortic flow (ml/min)	30.4 \pm 2.7	24.6 \pm 1.1 ^c
Total peripheral resistance (mmHg·min/ml)	2.14 \pm 0.1	3.93 \pm 0.2 ^b

^a Mean \pm standard error of 8 WKY and SHR each.

^b Different from WKY with $P < 0.005$.

^c Not significantly different from WKY with $P > .05$.

tional role of regional circulations in the development of hypertension may be gained by examining regional and whole body hemodynamics. For example, the proportional rise in vascular resistance in a regional territory may be greater than the percentage increase in total peripheral resistance if regional blood flow were decreased in the face of normal cardiac output. Such findings of a disproportionate increase in vascular resistance would identify a preferential regional site of abnormal control of vascular resistance in hypertension. In the present study the observations of unaltered hindquarter blood flow and cardiac output suggest that a proportionate increase in vascular resistance occurs in the total systemic and hindquarter circulations of the young SHR.

Previously we have examined cardiac output in the mature SHR (5–8 mo of age) and found unaltered cardiac output in the SHR compared to WKY normotensives (1), a finding which confirmed that of Iriuchijima (2) who reported that cardiac index was normal in the SHR (3–6 mo of age). We extended observations of the total systemic circulation to the hindlimb and mesenteric regional vasculatures and found similar regional and whole body hemodynamics in the mature SHR; normal cardiac output and regional flow and elevated total peripheral and regional resistances. The findings of normal blood flow and elevated vascular resistance in both the young and mature SHR suggest that the developmental and established phases of hypertension in the SHR are characterized by a similar hemodynamic pattern.

Elevated cardiac output has been determined in the ether anesthetized young SHR when compared to a normotensive Wistar (West Jersey Biol. Suppl.) control group (3). However, more recently cardiac output has been examined in the young SHR and in its normotensive genetic predecessor (WKY), and in this regard there was no significant difference between the 2 groups, although total peripheral resistance was increased in the SHR (8). Thus, our results of unaltered cardiac output and elevated total vascular resistance in the pentobarbital-

anesthetized young SHR relative to WKY, confirm those of Pfeffer *et al.* (8) and strengthen the contention that cardiac output is normal early in the development of hypertension in the SHR. These data highlight the importance of the hypothesis that an abnormality in vascular control, rather than cardiac output, is primarily responsible for the pathogenesis of hypertension. In light of the finding that the limb hemodynamic pattern does not reflect whole body hemodynamics in the early stages of renal hypertension (6), the data derived in the present study indicating a similar hemodynamic pattern between the hindquarter and total systemic circulation, suggest that early in the development of high blood pressure differing hemodynamics exist between genetic and renal hypertension. Whether these hemodynamic differences reflect different pathogenetic mechanisms in each of these experimental forms of hypertension remains to be determined.

Summary. Abdominal aortic blood flow and hindquarter vascular resistance were determined in young (2–3 mo) spontaneously hypertensive rats (SHR) and in age-matched Wistar Kyoto (WKY) normotensives. Abdominal aortic blood flow was similar in the 2 groups, whereas hindquarter vascular resistance was elevated in the SHR compared to WKY. Additionally, in the open-chest preparation there was no significant difference in ascending aortic blood flow between hypertensives and normotensives, while total peripheral resistance was increased in the SHR relative to WKY. These data suggest that early in the development of hypertension in the SHR the hemodynamic pattern of normal blood flow and elevated resistance exists in the hindquarter vasculature and the total systemic circulation.

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