central portion of the visual field can be received. Apart from these spots, the dual beams were crossed in the arteriole, causing unpaired single spot B. The lung surface can hardly be seen because the other part was non-illuminated.

Since the shot noise contains infinitely many waves having various frequencies, it cannot be filtered off by means of the electric filters. We have investigated a method of reducing the shot noise from the photomultiplier due to the reflecting light, so as to permit measurements of flow velocity in a backward scattering mode and found that the covering of the lung surface alienated the interface which reflected the incident beams strongly, far apart from the probing area. The high water content in the disc reduced the reflection at the rear surface of the disc. The reflection at the lung surface became weaker, probably because of the water trapped in the space between the rear surface of the disc and the tissue surface. Due to these advantages, the time-shared histograms in the covered lung surface showed a clear deviation in response to the cardiac cycle, in a sharp contrast to those in the non-covered lung surface.

Riva et al.[8,9] reported measurements of the retinal blood flow by means of the laser Doppler method in a backward reflection mode. Since, in their measurements, the laser beams proceed a long distance within the lens having a long focal length, the transparent tissue probably plays the function of alienating effectively the probing area from the interface between the air and tissues. As to the measurements in the other usual organs including the lung, the surface of the organs must be artificially covered in order to avoid undesirable shot noise due to the surface.

Although the blood flow in the arteriole of frog lung is briefly reported to be pulsatile[10], its quantitative measurements have not yet been reported. The present study shows that the flow velocity in the pulmonary arteriole begins to increase in an early phase of the cardiac cycle. This is probably due to the close situation of the lung to the heart. The N_2O uptake method[11] reveals that the blood flow of human pulmonary capillaries fluctuates strongly in response to cardiac events. The systolic flow attains 5 times as much as the diastolic flow. The blood flow velocity fluctuations, observed in the bullfrog, due to cardiac events, reach 25% of the mean value in the pulmonary arteriole, whose pulsatility is generally greater than in the capillary. The blood flow of pulmonary capillaries in the bullfrog is probably much smoother, and gas exchanges in the bullfrog could be made at a more continuous rate than in the human lung.

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Brain catecholamines and organ weight of mice genetically selected for high and low blood pressure[1]

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Summary. Statistically significant differences were found between the high and low genetically selected blood pressure lines for systolic blood pressure, norepinephrine content of whole brain, absolute heart weight, heart to b.wt ratio, kidney weight, kidney to b.wt ratio, and adrenal to b.wt ratio.

The physiological basis of the elevated blood pressure level in essential hypertension in man is for the most part unknown. There now exists a number of animal colonies in which selective breeding has provided animals with elevated blood pressures which may serve as animal models for human hypertension. There are currently 7 potential animal models among rodents, 6 rat colonies[2-7] and 1 mouse colony[8]. In each of these colonies the physiological basis for the elevated pressures is under investigation. This report describes some of the physiological and biochemical characteristics of the high and low blood pressure lines of mice compared to a random bred control.

Materials and methods. The 'high' and 'low' blood pressure lines used in this study were the result of 17 to 19 generations of selective breeding in a selection program designated BPI. Selection was begun in a base population derived from an 8-way cross among 8 inbred strains (LP/J, SJL/J, BALB/cJ, C57BL/6J, 129/J, CBA/F, RF/J and BDP/J) and was continued within closed lines. A concurrent control line propagated by random mating was maintained throughout the selection program. The development of these lines and the technique of indirectly measuring systolic blood pressure was described in a previous paper[8]. Briefly, systolic blood pressures were determined by occluding the flow of blood at the base of the tail and sensing the return of a pulse distal to the cuff when the pressure in the cuff was decreased (NarcoBio Systems Physiograph). The cuff width used was 25 mm, which work by Henry et al.[9] has shown to underestimate systolic blood pressure, and the diameter was 6 mm which is the appropriate size for mice over 23 g. The mice were restrained but unanesthetized and maintained at 37.5 °C during measurement. 5 readings were taken on each of 3 days during a period of 3–5 weeks when the mice were 100–150 days of age. In the 17–19 generation of selection the systolic blood pressure differed by 40–54 mm Hg between the high and low line.

Mice were sacrificed by cervical dislocation. Brains were rapidly removed and placed on ice before weighing. Individual brains were added to 1 ml 0.1 N $HClO_4$ containing 5×10^{-4} M $NaHSO_3$ and homogenized by sonification using

a Branson 350 sonifier at a setting of 2 for 10 sec. After centrifuging the homogenates at 18,000×g for 20 min, 0.5 ml of the clear supernatant were transferred to 1.5 ml microcentrifuge tubes (Beckman) containing 25 mg acid-washed alumina[10], 0.9 ml 0.5 M tris, pH 8.5, and 22 µl of 5.55×10^{-5} M 3,4-dihydroxybenzylamine (DHBA) as internal standard. The tubes were shaken gently for ca. 10 min at room temperature. The alumina was allowed to settle and the supernatant fluid was aspirated off. The alumina was washed 3 times with distilled water. Catecholamines were desorbed from the alumina with 100 µl of 0.1 M $HClO_4$ containing 5×10^{-4} M $NaHSO_3$. Samples were injected onto Waters CX/Coracil as previously described[11,12] and catecholamines detected by electrochemical oxidation. Standards were prepared containing norepinephrine (NE), dopamine (DA) and DHBA using an LC25 electrochemical detector (Bioanalytical Systems, Inc., West Lafayette, Ind). Catecholamine concentration was estimated by comparing the NE:DHBA or DA:DHBA ratio with the NE:DHBA or DA:DHBA ratio of a known standard.

The heart was removed from mice killed by cervical dislocation and trimmed of attached tissue, rinsed of blood, blotted and weighed on a Mettler balance. The other organs were also trimmed of connecting tissue and weighed individually.

Results and discussion. The table lists the means and SE for the high, low and random lines for each of the traits.

Catecholamines. Norepinephrine content of a whole brain was significantly lower in the high line in comparison to both the low and random bred lines. The norepinephrine content of the low line was also significantly higher than that of the random bred. The level of norepinephrine was consequently inversely related to blood pressure levels in these 3 lines. Since the sympathetic nervous system plays a role in regulating the tone of the vasculature and the central noradrenergic system appears to be involved in blood pressure regulation many investigators have attempted to relate catecholamine metabolism to hypertension. Plasma norepinephrine is known to be slightly elevated in certain patients with essential hypertension. The elevated blood pressure in the Spontaneously Hypertensive rat (SHR) and the New Zealand genetically hypertensive (GH) rats are probably of a neurogenic origin and the catecholamine metabolism of the SHR has been most extensively studied. Whole brain norepinephrine content was found to be lower in the SHR strain compared to normotensive Wistar stocks[13], which is in agreement with our work in the mouse. Brainstem norepinephrine was reported to be significantly lower in the normotensive by Yamori et al.[14] and Sjoerdsma[15]. Ozaki et al.[16], however, found no difference between brainstem norepinephrine between SHR and Wistar over a wide range of ages studied. In the GH rat, norepinephrine level was significantly higher than in controls in the forebrain and cerebellum[17]. Comparable studies in our lines are now in progress.

Heart weight. In an earlier study Elias et al.[18] examined the heart to b.wt ratio (H/B) of a small number of mice 11-23 months old and reported significant differences between BPI high and low mice. We have reexamined this relationship in these 2 lines and the randombred controls in a total of 249 mice aged up to 20 months. The effect of age on heart weight, b.wt and H/B was examined in a 3-way analysis of variance with age, line and sex main effects for mice arbitrarily grouped 300-399, 400-499 and 500-599 days of age. No age main effect was discernible nor were any of the interactions involving age statistically significant. The data were then reanalyzed combining ages and these data are presented in the table.

Female mice were consistently smaller and had lighter hearts than their male counterparts in the same line and the H/B ratio was also smaller in the low and random females but the same in high males and females. Although absolute heart weight in males of the random line was as large or larger than that in the high line, random mice were considerably heavier resulting in a smaller H/B ratio.

There was no significant difference between the b.wts of the high and low mice but they were both significantly smaller than the randombreds. This is undoubtedly due to the effects of inbreeding depression since the 2 selected lines had inbreeding coefficients about 0.40-0.50 while the randombred had very little inbreeding.

In addition to confirming the findings of the earlier study, we have also found that the differences in H/B ratio between the high and low blood pressure lines are consi-

Characteristics of lines selected for high blood pressure, low blood pressure and the randombred line

Characteristic	Generation	Sex	High	Low	Random	Probability**
Systolic blood pressure (mm Hg)	18	♂	143.0 ± 2.0 (78)*	95.0 ± 2.0 (76)	115.0 ± 3.0 (27)	$p<0.001$
		♀	149.0 ± 2.0 (79)	96.0 ± 2.0 (75)	119.0 ± 3.0 (24)	
Norepinephrine content of whole brain (ng/g)	18–19	♂	386.0 ±26.0 (12)	505.0 ±38.0 (12)	435.0 ±20.0 (12)	$p<0.001$
Dopamine content of whole brain (ng/g)	18–19	♂	1130.0 ±97.0 (12)	1139.0 ±90.0 (12)	1122.00±62.00 (12)	$p>0.05$
Body weight (g)	17–18	♂	31.7 ± 0.6 (50)	31.0 ± 0.6 (40)	34.2 ± 1.0 (36)	$p<0.001$
		♀	27.8 ± 0.5 (52)	27.5 ± 0.6 (49)	30.0 ± 0.8 (42)	
Heart weight (mg)	17–18	♂	162.0 ± 3.1 (50)	130.0 ± 2.5 (40)	170.0 ± 5.0 (36)	$p<0.001$
		♀	146.0 ± 4.6 (52)	109.0 ± 3.0 (49)	128.0 ± 2.9 (42)	
Heart/body weight ratio (mg/g)	17–18	♂	5.17± 0.12 (50)	4.22± 0.07 (40)	5.04± 0.14 (36)	$p<0.001$
		♀	5.22± 0.12 (52)	3.96± 0.07 (49)	4.32± 0.09 (42)	
Right kidney weight (mg)	17–18	♂	272.0 ± 4.8 (49)	232.0 ± 7.4 (40)	277.0 ± 8.4 (35)	$p<0.001$
		♀	187.0 ± 4.6 (51)	174.0 ± 6.5 (49)	183.0 ± 4.6 (42)	
Left kidney weight (mg)	17–18	♂	266.0 ± 5.2 (42)	229.0 ± 7.3 (40)	272.0 ± 6.1 (36)	$p<0.001$
		♀	181.0 ± 4.3 (51)	171.0 ± 6.1 (49)	179.0 ± 4.8 (42)	
Combined kidney/body weight ratio (mg/g)	17–18	♂	17.1 ± 0.32 (49)	14.9 ± 0.35 (40)	16.3 ± 0.41 (36)	$p<0.001$
		♀	13.3 ± 0.22 (51)	12.5 ± 0.33 (49)	12.2 ± 0.26 (42)	
Right adrenal weight (mg)	17–18	♂	1.80± 0.10 (18)	1.49± 0.05 (20)	1.65± 0.09 (13)	$p>0.05$
		♀	1.90± 0.13 (18)	1.76± 0.11 (15)	1.60± 0.10 (31)	
Left adrenal weight (mg)	17–18	♂	1.68± 0.10 (18)	1.55± 0.06 (20)	1.69± 0.11 (13)	$p>0.05$
		♀	1.91± 0.15 (18)	1.58± 0.13 (15)	1.62± 0.11 (31)	
Combined adrenal/body weight (µg/g)	17–18	♂	110.0 ± 7.0 (18)	100.0 ± 5.0 (20)	98.0 ± 6.0 (13)	$p<0.05$
		♀	136.0 ± 8.0 (18)	119.0 ± 7.0 (15)	110.0 ± 6.0 (31)	

* Means ± SE (sample size). ** Probability associated with analysis of variance for the comparison between lines.

derably larger than previously found. The H/B ratio of the low line is 20% smaller than that of the high line rather than the 10% found by Elias et al.[18].

Heavier hearts in hypertensive rats have been reported in the SHR, the GH and the Milano stocks. For example, Takatsu and Kashii[19] found a progressive increase in heart weights with age in both the SHR and Wistar-Kyoto with the increase in the SHR more pronounced. The H/B in the SHR was significantly larger than the controls by 13 weeks. In the GH rat heart weights were not significantly heavier when compared to the controls for either young or old rats, but the hypertensive rats are significantly lighter, suggesting a H/B difference between the lines[20]. In the GH hypertensives cardiac hypertrophy occurs only in rats over 6 weeks of age who have greatly elevated pressures[3]. Heart weights were also heavier in the Milano hypertensive rats compared to normotensive controls[4]. Relatively larger hearts would be an expected outcome of sustained elevated blood pressure and this has been found to be true in the SHR, GH, Milano spontaneously hypertensive rat and now in the hypertensive mouse.

Kidney weight. No age effect was found in the 3-way analyses (age, line and sex) of variance for b.wt, right kidney weight and left kidney weight and combined kidney to b.wt ratio (K/B). The results of a subsequent 2-way analysis of variance for sex and line main effects for each variable are shown in the table. Statistically significant differences were found among lines and between sexes for each variable. There was also a significant interaction between lines and sexes caused by larger differences among the males of the 3 lines than among females. The K/B of the high line is about 10% larger than the low line.

Kidney enlargement in hypertensive animals has been reported by other investigators. In the SHR the kidneys are larger than Wistar/NIH controls by 15%[15] but apparently smaller in older SHR when compared to Kyoto Wistar normotensives[21]. Kidneys are also larger in salt hypertension in Sprague-Dawley and Wistar compared to Fisher rats[22]. Bianchi et al.[4] found larger kidneys in terms of absolute and relative weight in the Milano hypertensive rats. Larger kidneys in hypertensive animals may be due to structural alterations as suggested by Hall et al.[22]; kidney damage evidence by fibrotic tissue, distortion of glomeruli, dilation of tubules and the presence of colloid pools was reported by Smirk and Phelan[23] in the GH rats. Hormonal involvement may also be involved since kidney weight is a sensitive index of androgen activity[24] and testosterone has been shown to be directly related to blood pressure in the SWR/J mouse[25]. Whatever the mechanism, there seems to be a tendency toward larger kidneys in hypertensive animal models.

Adrenal weights. Statistically significant differences were found among the adrenal to b.wt ratios (A/B) of the 3 lines with the high line showing larger ratios than the lows and randombred lines. The A/B ratios in females were consistently larger than the males. The absolute adrenal weights were not significantly different among the 3 lines. Sjoerdsma[15] reported larger adrenals in the SHR when compared to Wistar/NIH normotensive rats. Bianchi et al.[4] found that the absolute adrenal weight was significantly heavier in the Milano hypertensive rat but the relative weight was about the same.

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Rhythmic variations in the activities of aldolase and isocitrate dehydrogenase in the heart muscle of the scorpion, *Heterometrus fulvipes* (C. Koch)

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Summary. The activity levels of aldolase and isocitrate dehydrogenase were assayed in the heart muscle of scorpion, *Heterometrus fulvipes*. The enzyme activities showed a circadian rhythmicity with a peak value at 20.00 h in the heart muscle.

Circadian rhythmicity in arachnid metabolism has received limited attention. Locomotor activity[2], neurosecretion[3], rate of heart beat[4], spontaneous electrical activity in the ventral nerve cord and segmental nerves[5], level of metabolites[6] and enzymes[7,8] had been shown to undergo regular circadian rhythmic changes in the scorpion, *Heterometrus fulvipes*.