Hemodynamic Patterns in Essential Hypertension

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IT HAS been uniformly accepted that in essential hypertension the increase in peripheral resistance was responsible for the high blood pressure.[1] This assertion was the result of ingenious indirect estimations based upon the anatomic conditions of the vessels,[2-5] the perfusion of organs[6-9] or on the measurement of blood flow through a limb,[10, 11] the skin,[12] or the kidney.[13] The finding of a decreased arteriolar lumen, increased resistance to perfusion of organs from cadavers of hypertensive patients and normal or low blood flows in restricted areas were considered as evidence of a generalized increase in peripheral resistance.[14, 15]

Later measurements of cardiac output by different methods[16-25] gave support to this conclusion, since normal values were obtained but only very small series of patients were studied. For a long time only a few authors[26, 27] would disagree with the generalized idea of normal cardiac output-increased peripheral resistance hemodynamic pattern of essential hypertension.

It was during the last 10 years that several workers found that some hypertensive patients have increased cardiac output while peripheral resistance remained within normal limits.[28-31] Nevertheless this "new" hemodynamic pattern was held as "false diastolic hypertension"[32] with a better prognosis than the "old" pattern of the "true classic hypertension."[33]

It has not been settled yet if these different patterns of hemodynamic behavior correspond to particular stages of the disease or to different clinical entities maintaining this pattern uniformly during the whole course of the disease.

The difficulty to establish the hemodynamic course in essential hypertension is certainly responsible for our lack of knowledge of the influence that this important factor has in the natural history and pathogenesis of the disease.

In this paper we emphasize the hemodynamic pattern of labile hypertension, a frequent clinical initiation of essential hypertension leading or not to fixed forms of the disease.[34-39]

Our results in the labile group were compared with those in the normotensive controls and in the fixed hypertensive group with mild and severe forms of the disease.

This type of crossed study cannot substitute for a longitudinal study carried on in each patient along his different stages and will not answer with certainty the question of the hemodynamics in essential hypertension. However this cross study gives some hints that we deem valuable for the understanding of the disease.

Material and Methods

Blood pressure figures of 150 systolic and 90 mm. Hg diastolic recorded from an intraarterial needle were considered the upper normal limits. All patients studied had no treatment, or it had been discontinued for at least 2 weeks before performing the hemodynamic study. We classified as labile hypertension those patients who had three or more records of normal blood pressure while under our care for hypertension without drug treatment.

All the patients were submitted to a careful clinical history, physical examination, blood counts, sedimentation rate, blood glucose, urea

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and electrolytes, urinalysis, electrocardiogram, chest x-ray, excretory urogram, and, when considered necessary, aortography, perirenal pneumogram, catecholamine urine excretion, blood gases, and pH. Patients with clinical evidence of heart failure were not included in this series. Only two patients had urea levels above normal values, both had malignant hypertension and were included in this study.

Hemodynamic determinations were performed in 37 patients with essential hypertension—17 labile and 20 fixed—these were in-lying or outpatients of the Instituto de Investigaciones Médicas. Twenty hospitalized normotensive patients without cardiovascular, renal, blood, or metabolic disease were taken as controls.

The procedures to which the patients were going to be submitted were explained to them several days before they were carried out. Patients had a light breakfast, no sedation, and were recumbent with two indwelling needles, one in the right brachial artery and one in a vein of the left arm. After 30 minutes rest arm-tongue time was determined with Decholin and arterial blood pressure was recorded with a Statham P23Db transducer in a Twin-Viso recorder. Thereafter and with a 30-minute interval two determinations of cardiac output with Evans-blue dye-dilution technic were carried out, according to the Stewart-Hamilton method.[40] Following a nearly instantaneous injection of the dye into the vein, arterial samples were collected into centrifuge tubes every 2 seconds. A hand-driven rack was employed, and a 10-minute arterial blood sample was used for blood volume estimation.[41]

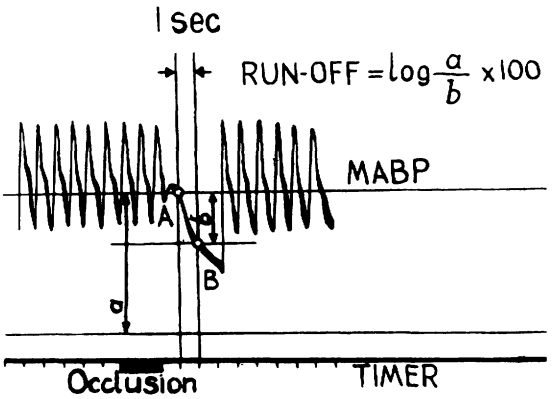

Figure 1

Graphic determination of the run-off index. MABP, mean arterial blood pressure; point A, intersection of the pressure decay line and the mean pressure; point B, intersection of the pressure decay line and the 1 second distal to point A vertical line; segment a, mean arterial blood pressure; segment b, difference between the mean arterial pressure and the pressure at B.

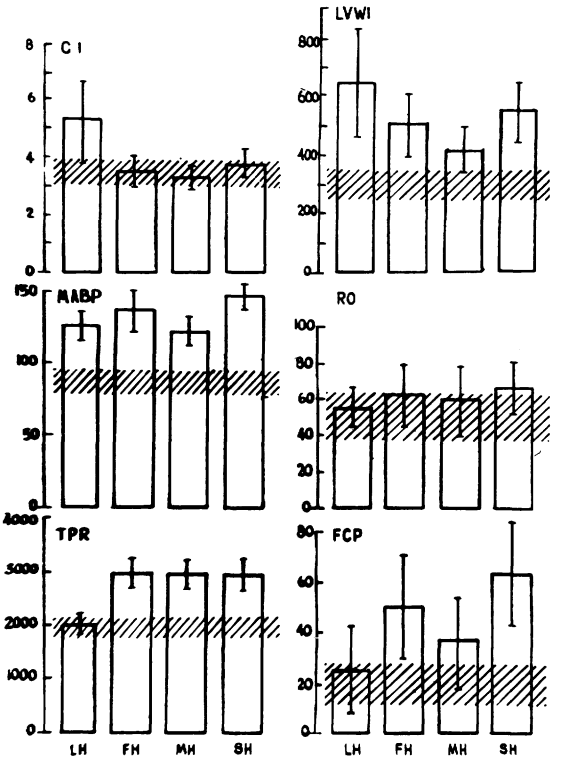

Figure 2

Hemodynamic patterns in different groups of hypertension. CI, cardiac index, L./min.M²; MABP, mean arterial blood pressure, mm. Hg; TPR, total peripheral resistance, dynes sec. cm.—⁵ M.²; LVWI, left ventricular work index, arbitrary units; RO, run-off index; FCP, flow cessation pressure, mm. Hg; LH, labile hypertension; FH, fixed hypertension; MH, mild fixed hypertension; SH, severe fixed hypertension. Shaded areas represent normal values, ± standard deviation. Vertical segments represent the range of values (± 1 standard deviation) for each group.

Cardiac output was calculated from dye-concentration values plotted on semilogarithmic paper and extrapolating the downward slope according to the Kinsman, Moore, and Hamilton procedure.[42] The results were reproducible, and the variance for 37 pairs of successive determinations (two standard deviations of the difference related to the mean cardiac output) was 10.8 per cent.

Circulatory arrest in the arm was induced by sudden insufflation of a pneumatic cuff to a pressure of 300 mm. Hg (fig. 1). This occlusion was maintained during 2 minutes while intraarterial pressure was continuously recorded. In this time-pressure curve the stabilized pressure (decay less than 4 mm. Hg per minute) was considered as the critical closing pressure[43, 44] or the flow

Table 1

Normotension

No.	Pt.	Sex, age	Wt.	Ht.	BSA	CI	BV	Pressure S	Pressure D	Pressure M	TPR	Pu	SV	RO	FCP
1	AL	F54	48.8	1.60	1.48	3.95	93.2	142	68	92.7	1877	56	105	48.5	29
						3.94	94.5	142	70	96.0	1950	56	104		
2	AP	F48	62.8	1.56	1.63	3.76	70.4	142	67	92.0	1955	74	83	43.3	23
						3.49	71.5	142	67	92.0	2091	76	75		
3	FC	M23	65.1	1.68	1.73	3.60	87.6	130	68	88.7	1972	76	82	33.1	12
4	NN	F20	41.7	1.54	1.35	4.02	81.3	120	65	83.3	1656	84	65	42.8	15
						3.98	80.8	120	65	83.3	1671	80	67		
5	RA	M25	57.1	1.64	1.62	3.69	97.0	118	70	86.0	1868	64	93	54.4	11
						3.64	97.1	114	69	84.0	1848	64	92		
6	SS	F31	64.7	1.57	1.64	4.00	72.4	120	64	82.7	1654	72	91	39.3	18
						3.96	74.7	116	68	84.0	1724	72	89		
7	RR	M34	86.1	1.78	2.04	3.44	102.0	126	89	101.3	2356	90	78	49.7	22
8	AV	F41	52.4	1.66	1.57	3.02	65.8	143	82	102.3	2605	72	66	40.7	15
						2.85	64.1	129	60	83.0	2310	68	66		
9	SS	M37	83.5	1.65	1.90	4.00	72.2	128	70	89.3	1784	65	117	37.7	20
						3.80	71.3	129	72	91.0	1900	65	111		
10	EE	M57	67.1	1.72	1.77	3.22	76.9	141	68	92.3	2290	64	89	85.9	10
11	MB	M74	74.7	1.63	1.79	3.55	74.6	132	63	86.0	1936	74	86	46.0	14
12	JC	M54	59.1	1.76	1.71	2.71	96.1	126	62	83.3	2460	72	64	59.1	15
13	AS	F64	76.6	1.57	1.76	3.22	59.5	132	58	82.7	2056	64	88	63.2	33
14	BF	F42	67.0	1.54	1.64	4.06	61.2	126	75	92.0	1702	92	72		
						4.14	60.6	120	57	78.0	1418	92	74		
15	RP	M27	61.2	1.67	1.68	2.80	91.5	114	67	82.7	2363	56	84	43.4	12
16	JG	M47	66.8	1.66	1.74	2.93	66.3	142	73	96.0	2617	68	75	37.6	24
						3.35	59.5	131	73	92.3	2201	68	86		
17	AP	M60	72.5	1.70	1.80	3.83	88.9	112	48	69.3	1447	64	118	40.3	27
18	LB	M69	55.5	1.60	1.56	4.09	116.0	150	65	95.0	1857	80	80	55.0	39
19	EE	M59	87.5	1.75	2.00	2.70	91.7	122	60	80.7	2392	64	84	48.9	14
20	ME	F55	59.8	1.45	1.49	3.24	68.3	125	78	92.7	2267	80	60	66.6	26
						3.47	64.0	125	78	92.7	2133	72	72		

Abbreviations for tables 1 to 4: Pt., patient; Wt., weight, Kg.; Ht., height, m; BSA, body surface area $M.^2$; CI, cardiac index, L./min. $M.^2$ BSA; BV, blood volume, L./Kg. body weight; Pressure, S, D, M, brachial arterial pressure, systolic, diastolic and mean pressures, mm. Hg; TPR, total peripheral resistance, dyne sec. $cm.^{-5}$. $M.^2$ BSA; Pu, pulse rate, beats/min.; SV stroke volume, ml.; RO, run-off index; FCP, flow cessation pressure, mm. Hg.

cessation pressure, as we prefer to call it. Prior to this estimation of flow-cessation pressure three trials of sudden circulatory arrest were performed with a similar procedure but lasting only 4 seconds. The continuous arterial pressure recording of this procedure allowed to calculate the "run-off index" with the following graphical analysis: the intersected point of the pressure decay line and the mean pressure (point A) was determined. A vertical line was then drawn 1 second distal to this point. The intersection of this line and the pressure slope is called point B. The index is calculated as logarithm of the ratio of the mean pressure (point A) to the difference between pressure at A and at B.[45]

Results

Three groups were considered (1) 20 normotensive subjects (12 men and eight women) with an average age of 46 ±16 years and an average globular volume of 41.6 ±5.9 per cent, were taken as controls; (2) a second group of 17 labile hypertensive patients (11 men and six women) with an average age of 49.0 ±12.0 years and a globular volume of 43.6 ±6.1 per cent, and (3) a third group of 20 patients with fixed hypertension (16 men and four women), with an average age of 52.7 ±13.0 years and a hematocrit value of 44.4 ±4.1 per cent. Within this last group we considered two subgroups: (3a) 10 patients with mild hypertension, i.e., diastolic blood pressure below 110 mm. Hg and (3b) 10 patients with severe hypertension, i.e., with dias-

tolic blood presure of 110 mm. Hg or above (tables 1 to 4).

No significant difference was found in the ages of the three groups. Sex distribution was not significantly different. No difference in globular volume was found. Body weight, height, and surface area were within normal limits in the normotensive and the labile hypertensive patients. Fixed hypertensive subjects were slightly overweight, and surface area was therefore also slightly larger.

The eyegrounds showed a normal picture or mild hypertensive retinopathy except in the severe fixed hypertensive group, in which two patients had grade-IV and four had grade-III hypertensive retinopathy (Keith, Wagener, and Barker classification).

Arterial Blood Pressure

The mean arterial blood pressure of the normotensive group was 87.7 ±7.1 mm. Hg (fig. 2); it was 124.3 ±11.4 in labile hypertensive and 137.0 ±15.5 mm. Hg in fixed hypertensive patients; the difference between labile and fixed hypertensive patients was significant ($p < 0.01$). Mean pressure in mild fixed hypertensive subjects was 125.6 ±9.2 and 148.4 ±11.7 in the severe cases. No significant difference was found between mild and labile, but between labile and severe fixed hypertensive subjects the blood pressure difference was highly significant ($p < 0.001$).

Cardiac Index

Mean value of cardiac index in the control group was 3.49 ±0.46 ml./min.M²; in the fixed hypertensive group it was 3.52 ±0.55, and in the labile patients it was 5.26 ±1.43 ml./min. M². No significant difference was found between fixed hypertensive and normal sub-

Table 2

Labile Hypertension

No.	Pt.	Sex, age	Wt.	Ht.	BSA	CI	BV	Pressure S	Pressure D	Pressure M	TPR	Pu	SV	RO	FCP
1	SF	M54	82.0	1.76	1.97	6.90	90.0	162	91	114.7	1670	64	215	74.4	21
2	LB	M46	68.0	1.62	1.72	4.67	84.0	170	96	120.6	2140	70	115	68.1	82
						4.52	80.0	162	92	115.0	2032	70	111		
3	DG	F40	55.4	1.56	1.54	3.96	79.5	180	94	122.6	2480	80	76	43.3	17
						4.10	80.6	180	95	123.3	2458	80	77		
4	PF	M56	83.0	1.75	1.97	3.83	62.2	156	100	118.7	2459	75	101	56.4	25
						3.66	63.3	165	107	126.0	2777	75	95		
5	TV	F54	70.5	1.59	1.73	4.43	82.4	179	104	129.0	2327	84	91	63.8	35
						4.13	80.7	164	90	114.7	2223	68	105		
6	DC	F49	69.0	1.50	1.62	4.89	78.1	208	109	142.0	2340	68	117	54.3	48
						4.81	82.1	209	107	143.0	2386	68	114		
7	MS	F25	48.3	1.55	1.44	4.46	90.9	190	118	132.0	2361	80	80		
						4.77	86.3	176	104	128.0	2145	85	81		
8	CI	M53	68.0	1.81	1.86	4.80	81.8	196	100	132.0	2194	80	120	40.5	22
						4.27	83.0	184	98	126.0	2322	78	102		
9	TL	M50	78.5	1.66	1.87	5.70	78.5	172	90	117.0	1640	65	164	51.7	14
						5.40	78.9	162	90	114.0	1688	65	155		
10	AR	M49	71.2	1.63	1.76	8.61	93.8	180	90	120.0	1101	50	306	63.7	28
11	JB	M20	92.4	1.70	2.20	6.68	85.2	175	90	118.3	1417	64	230	49.0	23
12	TG	M46	68.5	1.70	1.78	7.85	90.5	218	115	149.3	1529	78	178	53.6	16
						8.25	91.6	220	108	145.3	1402	80	183		
13	MA	F53	72.5	1.56	1.71	4.11	82.5	164	91	115.3	2243	64	110	39.6	6
						3.92	79.5	169	91	117.0	2389	64	105		
14	MM	M49	78.5	1.66	1.86	4.65	81.1	175	91	112.0	1927	60	144	52.3	20
15	LM	M61	50.5	1.60	1.50	4.93	84.0	168	90	116.0	1882	76	97	55.7	11
						4.79	86.1	168	90	116.0	1878	76	94		
16	PR	F60	73.1	1.55	1.72	5.23	74.3	240	104	149.3	2284	54	167	59.5	25
						5.13	72.3	240	100	146.7	2290	52	169		
17	LV	M69	55.4	1.61	1.56	4.37	96.0	170	93	118.7	2171	86	79		

Table 3

Mild Fixed Hypertension

No.	Pt.	Sex, age	Wt.	Ht.	BSA	CI	BV	Pressure S	Pressure D	Pressure M	TPR	Pu	SV	RO	FCP
1	LF	M62	82.0	1.68	1.92	3.54	68.0	181	105	131.7	2980	70	97	65.3	49
						3.22	70.0	178	100	126.0	3139	70	88		
2	VG	F19	50.0	1.56	1.47	3.83	90.0	152	100	117.3	2455	115	49	30.9	10
						3.50	91.0	158	104	122.0	2793	115	44		
3	PG	M55	79.0	1.65	1.85	3.80	58.3	155	95	115.0	2423	72	97	84.5	40
						3.62	60.6	160	103	122.0	2620	74	93		
4	MP	F74	91.1	1.51	1.86	2.73	50.2	169	90	116.3	3408	56	91	61.6	38
						2.93	56.3	183	90	120.0	3376	60	91		
5	MH	M49	91.7	1.61	1.94	3.38	62.0	175	93	120.3	2848	70	94	51.3	50
						3.29	62.7	173	92	119.0	2894	70	91		
6	JR	M48	68.1	1.67	1.76	3.64	97.8	230	110	150.0	3283	54	119	49.3	15
						3.72	97.0	225	102	143.0	3072	52	126		
7	CP	M72	83.5	1.76	2.06	2.24	82.0	184	94	124.0	4410	70	66		
8	CG	M39	75.0	1.61	1.78	3.05	61.5	200	105	136.7	3587	56	97	54.6	25
						3.33	62.0	190	100	130.0	3220	60	96		
9	MS	F51	76.5	1.54	1.74	3.76	72.7	170	98	122.0	2592	90	73	49.4	26
						3.73	69.0	162	90	114.0	2444	84	77		
10	LV	M72	60.2	1.57	1.59	3.10	67.0	180	105	130.0	3345	52	95	92.0	66

jects, but in labile patients values were significantly higher than in controls ($p < 0.001$) and fixed hypertensive patients ($p < 0.001$). Eighty-two per cent of labile patients and only 15 per cent of the fixed exceeded our normal range (tables 5 and 6).

Within the fixed hypertensive group the severe subgroup had a cardiac index (3.86 ±0.46) significantly higher ($p < 0.02$) than the mild subgroup (3.29 ± 0.48). The cardiac index of the severe fixed hypertensive group was significantly higher ($p < 0.05$) than that of the controls.

Total Peripheral Resistance

Total peripheral resistance was calculated according to the equation

$$TPR = \frac{MBP \times 1332 \times 60}{CI}$$

where MBP means mean brachial pressure, 1,332 is a constant to convert units to cgs system, 60, to convert time from minutes to seconds, and CI, cardiac index.

In fixed hypertension TPR (3,128 ±495 dynes sec. cm.$^{-5}$M.^{2}) was significantly higher ($p < 0.001$) than in labile hypertension (2,013 ±420 dynes sec. cm.$^{-5}$M.^{2}) and in controls (2,037 ±326; $p < 0.001$). No difference was found between normal and labile hypertension nor was there any between mild and severe hypertension. Fixed hypertensive patients never had a normal total peripheral resistance. Two labile hypertensive patients had a very slight increase in resistance and, in one, this was less than the normal value.

Pulse and Stroke Volume

No difference was found in pulse among the groups. Stroke volume was significantly higher in labile (78.5 ±31.3 ml./M.^{2}) than in the fixed hypertensive (53.0 ±14.3) and the normal (49.7 ±7.8) groups. These differences were highly significant ($p < 0.001$). No significant difference was found between mild and severe hypertension.

Blood Volume

Blood volume values were found to be 81.4 ±15.9 ml./Kg. in normal subjects; 83.0 ±8.0 in labile hypertension, and 80.8 ±20.7 in fixed hypertension. The mean value for mild hypertension was 71.3 ±14.3, while in severe cases it was 90.3 ± 23.2; the difference was statistically significant ($p < 0.05$).

Good correlation was observed between blood volume and cardiac output in fixed hypertension ($r = 0.77$; $p < 0.001$) and in labile hypertension ($r = 0.82$; $p < 0.001$). A wide

scatter was found when blood volume and cardiac output were related in the control group ($r = 0.29$; $p < 0.2$).

No correlation was observed between total peripheral resistance and blood volume in the control group ($r = -0.28$; $p < 0.3$). An inverse correlation was observed in fixed hypertension ($r = -0.53$; $p < 0.01$) which was more significant in the labile group ($r = -0.84$; $p < 0.001$).

The ratio blood volume/cardiac output represents the time in which an amount of blood equal to the blood volume passes through a complete section of the cardiovascular system. This time is significantly lower in labile hypertension (38.4 ±6.8 sec.) than in control subjects (51.7 ±12.3 sec.) and in fixed hypertension (55.5 ±12.1 sec.) with a $p < 0.001$.

Useful Cardiac Work

Mean arterial pressure times cardiac index was taken as an index of left ventricular work expressed in arbitrary units (mm. Hg L./min. M.^{2}). The mean value for the control group was 306 ±141; for the fixed hypertensive group 496 ± 110, and for the labile patients 656 ±202. In this last group left ventricular work was significantly higher than in the control ($p < 0.001$) and the fixed hypertensive group ($p < 0.01$). Left ventricular work was also higher in fixed hypertension than in control subjects ($p < 0.001$).

Severe fixed hypertensives showed a mean value of 572 ± 84, significantly higher ($p < 0.001$) than that observed in mild cases (420 ±74).

Run-off Index and Flow Cessation Pressure

The run-off index informs about the resistance to blood flow in the arm (fig. 2). It was higher in the fixed hypertensive (62.5 ±16.7) than in control (49.2 ±12.7) group, with $p < 0.01$. No difference was found between normal and labile hypertensive groups (55.0 ±9.9). Within the fixed hypertensive group, although the run-off index was higher than in the normal, the difference was not significant for mild patients.

When control and fixed hypertension cases were plotted in a graph of run-off against total peripheral resistance, a low correlation was found ($r = 0.33$; $p < 0.05$). For the labile hypertension group this type of correlation was negative ($r = -0.30$) but not significant.

The flow cessation pressure was higher in the fixed group (49.4 ±23.5 mm. Hg) than in normal (20.0 ±8.0 mm. Hg; $p < 0.001$) and labile subjects (26.2 ±18.4 mm. Hg; $p < 0.01$). A significant difference was also found

Table 4

Severe Fixed Hypertension

No.	Pt.	Sex, age	Wt.	Ht.	BSA	CI	BV	Pressure S	Pressure D	Pressure M	TPR	Pu	SV	RO	FCP
1	RV	M46	76.7	1.77	1.93	3.75	70.0	230	120	156.7	3452	72	100	80.9	72
2	FF	M54	69.0	1.65	1.75	4.26	140.0	220	115	150.0	2814	55	135	38.4	44
						4.47	139.0	230	115	153.3	2747	52	150		
3	VP	M57	62.0	1.73	1.73	2.98	96.4	240	115	146.7	3944	100	52		
4	AE	M47	100.4	1.79	2.19	4.05	88.0	180	110	133.3	2628	76	117	73.9	75
						4.15	85.1	167	110	129.0	2503	76	119		
5	LA	F60	55.3	1.44	1.45	3.60	66.5	210	132	158.0	3510	96	54	67.3	40
						3.46	65.6	224	116	152.0	3389	98	51		
6	AG	M45	88.0	1.76	2.02	3.66	84.2	184	111	142.0	3126	66	112	65.5	43
7	AD	M45	84.0	1.66	1.91	3.58	76.3	204	114	144.0	3216	58	118	49.0	82
						3.52	76.1	202	112	142.0	3222	58	116		
8	TP	M60	78.8	1.73	1.92	4.74	113.0	200	107	138.0	2330	75	121	65.9	80
						4.42	114.0	212	116	148.0	2676	68	125		
9	JR	M52	55.2	1.71	1.64	3.93	97.0	206	119	148.0	2998	52	125	86.2	90
						3.83	96.3	190	104	132.0	2772	52	121		
10	IV	M48	98.0	1.72	2.10	4.25	74.5	250	144	179.3	3378	64	139	58.7	45
						4.09	74.6	238	132	167.3	3252	64	134		

Table 5

Mean Hemodynamic Data. Normotension, Labile Hypertension, and Fixed Hypertension

		Mean	± S.D.	P < NC vs. LH	NC vs. FH	LH vs. FH
Cardiac index	NC	3.49	0.46			
(L./min./M.^{2} BSA)	LH	5.26	1.43	0.001	NS	0.001
	FH	3.52	0.55			
Blood volume	NC	81.4	15.9			
(L./Kg. body weight)	LH	83.0	8.0	NS	NS	NS
	FH	80.8	20.8			
Mean arterial	NC	87.7	7.1			
pressure (MM. Hg)	LH	124.3	11.4	—	—	0.01
	FH	137.0	15.5			
Total peripheral	NC	2037	326			
resistance (dynes	LH	2013	420	NS	0.001	0.001
sec. cm.$^{-5}$ M.^{2} BSA)	FH	3128	495			
Blood volume × 60	NC	51.7	12.3			
Cardiac output,	LH	38.4	6.8	0.001	NS	0.001
(sec.)	FH	55.5	12.1			
Left ventricular	NC	306.2	47.8			
work index	LH	656.2	202.7	0.001	0.001	0.01
(arbitrary units)	FH	496.2	110.6			
Pulse rate	NC	71	10			
(beats/min.)	LH	70	11	NS	NS	NS
	FH	71	17			
Stroke index	NC	49.7	7.8			
(ml./M.^{2} BSA)	LH	78.5	31.3	0.001	NS	0.001
	FH	53.8	14.3			
Run-off index	NC	49.2	12.7			
	LH	55.0	9.9	NS	0.01	NS
	FH	62.5	16.7			
Flow cessation	NC	20.0	8.0			
pressure (mm. Hg)	LH	26.2	18.4	NS	0.001	0.01
	FH	49.4	23.5			

NC, normotensive control; LH, labile hypertension; FH, fixed hypertension; BSA, body surface area; S.D., standard deviation; NS, not significant.

between severe (63.4 ±20.0 mm. Hg) and mild cases (35.4 ± 18.9 mm. Hg; $p < 0.01$).

Discussion

The observation of high cardiac output in labile hypertension is similar to the findings of Stead[46] and Hickam[47] under the effect of anxiety. There is no reason to believe that our labile hypertensive patients were more anxious than the controls during the procedure, since no difference was found in heart rate and variation of cardiac output estimation with a 30-minute interval between both groups. Starr[48] and Wolf et al.[49] have also shown that in some cases of neurocirculatory asthenia and labile hypertension the cardiac output, estimated by the ballistocardiographic method, was increased while peripheral resistance was found to be normal or even low.

Eich et al.[33] made cardiac output determinations with Hamilton's dye-dilution technic in a large group of patients with labile hypertension; they found the high cardiac output-normal peripheral resistance hemodynamic pattern in 40 per cent of patients with an age below 50 and in 29 per cent of older patients. The greater incidence (82 per cent) of high cardiac output in our patients may be explained by the fact that the authors mentioned above included in their series labile hypertensive patients who were normotensive at the time of measurement and therefore they were obviously hemodynamically normal. Fejfar and Widimsky[50] mentioned high

cardiac output as a characteristic hemodynamic pattern of young patients with essential hypertension.

Total peripheral resistance values were referred to body surface area. The resistance calculated from the mean arterial pressure-cardiac output ratio may appear low in a patient of large size with normal cardiac index even with high blood pressure. Conversely, a small-sized patient with normal cardiac index may have increased calculated total peripheral resistance with normal pressures. Our labile hypertensive patients have total peripheral resistance within normal ranges, except two cases with a slight increase and one in whom it was found to be decreased.

Since the run-off index may be considered related to the resistance to blood flow in the forearm and hand,[45] the results seem to show that labile patients have normal upper limb vascular resistance and, therefore, increased blood flow.

Patients with labile hypertension have an increased cardiac output and they lack an adequate vasodilatation to maintain a normal blood pressure. The value of total peripheral resistance represents, for comparative purposes, the cross-section area—or the radius—of the most narrow part of the circulatory system. According to Laplace's law similar radius with different pressure will mean different tension. Therefore a hypertensive patient will have a higher vascular tension than normotensive, even if both have the same peripheral re-

Table 6

Mean Hemodynamic Data. Normotension, Mild Fixed Hypertension, and Severe Fixed Hypertension

		Mean	± S.D.	P < NC vs. MH	NC vs. SH	MH vs. SH
Cardiac index	NC	3.49	0.46			
(L/min./M² BSA)	MH	3.29	0.48	NS	0.05	0.02
	SH	3.86	0.46			
Blood volume	NC	81.4	15.9			
(L./min./M² BSA)	MH	71.3	14.8	NS	NS	0.05
	SH	90.3	23.2			
Mean arterial	NC	87.7	7.1			
Pressure (mm. Hg)	MH	125.6	9.2	—	—	—
	SH	148.4	11.7			
Total peripheral	NC	2037	326			
resistance (dynes	MH	3132	387	0.001	0.001	NS
sec. cm.$^{-5}$ M.² BSA)	SH	3124	448			
Blood volume × 60	NC	51.7	12.3			
Cardiac output,	MH	54.4	13.6	NS	NS	NS
(sec.)	SH	56.6	11.1			
Left ventricular	NC	306.2	47.8			
work index	MH	419.9	74.6	0.001	0.001	0.001
(arbitrary units)	SH	572.4	84.2			
Pulse rate	NC	71	10			
(beats/min.)	MH	71	19	NS	NS	NS
	SH	71	17			
Stroke index	NC	49.7	7.8			
ml./M.² BSA)	MH	48.7	11.5	NS	NS	NS
	SH	57.5	16.0			
Run-off index	NC	49.2	12.7			
	MH	59.9	18.8	NS	0.01	NS
	SH	65.0	15.0			
Flow cessation	NC	20.0	8.0			
pressure (mm. Hg)	MH	35.4	18.9	0.01	0.001	0.01
	SH	63.4	20.0			

Abbreviations as in table 5.

sistance. It must also be considered that the resistances in the systemic circulation are parallel circuits and total peripheral resistance may be normal if locally increased resistance areas are compensated by others adequately vasodilated.

While normotensive and fixed hypertensive patients have a direct correlation between total resistance and resistance in the arm, the labile patients show a trend to negative correlation. This finding suggests that in the last group the muscular vascular bed dilates passively buffering the increased resistance of other areas, accordingly to Brod et al.[51] A very good correlation was found between cardiac output and blood volume in patients with labile and fixed hypertension but this was absent in normotension.[52] This finding may be interpreted as demonstrating the influence of the capacity vascular bed on the development of the hemodynamic pattern in hypertension. The restricted capacity vascular bed would cause an increase in venous return and an increased cardiac output. An increase in the contractile energy of the myocardium may result in the same hemodynamic changes. The former view is supported in labile hypertension by the reverse correlation between blood volume and total peripheral resistance. The finding of normal flow cessation pressure, representing a normal capacity tone[43, 53] would suggest a primary myocardial effect.

The hemodynamic pattern of our fixed hypertensive patients was similar to that found by Bolomey et al.,[25] Werkö and Lagerlof,[28] Varnauskas,[29] Taylor,[30] and Rowe et al.[31] In a smaller number of cases cardiac index was higher than controls. Similarly, to Harris and Gibson[54] we did not find blood volumes lower than normal as Rochlin, Shohl and Cary did,[55] but we observed a reversed correlation between blood volume and total peripheral resistance. Such a relation may represent the adjustment of a restricted capacity vascular bed as seems to occur also in labile hypertension. This interpretation should fit with that of Floyer and Richardson[56] and Wilson[57] in experimental renal hypertension in which they thought that the behavior of the capacity vessels was more important than the constriction of arterioles.

When fixed hypertensive patients were grouped according to severity, the highest cardiac index was observed in those with higher diastolic pressure. Cardiac index was also higher in severe hypertension than in normotensive subjects. Curiously enough peripheral resistance was similar in both groups with mild and severe hypertension. This conclusion is different from that of Varnauskas[29] and Rowe et al.[31] who considered that more severe disease runs parallel to increased peripheral resistance. It is possible that this difference could be explained if some of the patients in these authors' series had left heart failure. Another difficult point to explain is that the blood volume was larger in severe than in mild hypertension. Although it is known that secondary hyperaldosteronism occurs more often in severe than in mild hypertension,[58, 59] a relation with the blood volume has not yet been established.

The run-off index as indirect expression of resistance to blood flow in the upper limb,[45] was not significantly different in mild hypertension and controls but in severe hypertension the run-off index was markedly increased. The normal run-off index with high blood pressure as seen in labile hypertension would represent an increased blood flow through the segment studied. These results agree with those obtained by Conway[60] but are different from those found by Brod et al.[51] and Abramson and Fierst,[16] who showed with a plethysmographic method that vascular resistance in the arm was either normal or low in the whole group of hypertensive patients. Our results in fixed severe hypertension are similar to those of Pickering[10] and Prinzmetal and Wilson,[11] who observed normal blood flow in the upper limb of their hypertensive subjects.

The flow cessation pressure was higher in fixed hypertension than in normotension and, furthermore, patients with severe hypertension had higher values than those of the mild group. Our results are similar to those of Ashton,[62] who considering the minimal plethysmographic occlusion pressure as the critical

closing pressure found higher values for hypertensive than for normal subjects. Since we think that there is not a real "closing" of the arteries and communication still persists with the veins through the capillaries, an increased flow cessation pressure must be interpreted as an increase of "capacity tone."[43, 53]

The observations discussed above would suggest that the evolution and the natural history of the hemodynamic pattern of hypertension is as follows:

1. A first stage with labile pressure reactions produced by transient increases in cardiac output. Autoregulation of blood flow through the kidney, splanchnic area, skin, and brain would be responsible for blood shifting to the muscles. The starting point could be a venoconstriction decreasing the amount of blood in the capacity system displacing it to the heart or an increase in the contractile force of the myocardium by shifting the cardiac performance to a sympathetic-like stimulated level. This type of reaction is explained by Brod[63] as an anticipation to muscular work and by Borst and Borst-de Geus as a mechanism to ensure the output of sodium.[64] Vasoactive drugs would cause a very similar hemodynamic pattern to the one described for this stage of hypertension as was shown for isoproterenol,[65] atropine,[65] and dopamine.[66] Ledingham and Cohen[67, 68] suggest the same pattern for the beginning of experimental renal hypertension.

2. The second stage with the development of permanent hypertension, normal cardiac output, and increased peripheral resistance must be explained by a resetting of the barostat or by a change in cardiac dynamics. The increased blood pressure of the first stage would cause a myogenic contraction of the arterioles as shown by Folkow.[69] As a consequence of this an additional increment in pressure would stimulate the barostatic mechanism already adjusted to a certain hypertensive level.[70] The final result of the barostat activity would be a reduction of the cardiac output to normal values. This reaction would positively diminish the "work of the heart," since this is proportional to the square of the cardiac output. The work of the left ventricle is remarkably higher in labile hypertension than in mild fixed hypertension and although myocardial efficiency is better in work against increased output than increased pressure[71] the mechanical work as such could be the leading regulating factor.

3. Finally, a third stage in severe hypertension, in which morphologic vascular changes and ischemia would cause the release of vasoactive and salt-retaining substances[58, 59] with a new increase in blood volume and cardiac output.

Summary

Hemodynamic studies, including cardiac output, arterial blood pressure, run-off index, flow cessation pressure, and blood volume, were performed in 20 normotensive control subjects, 17 labile hypertensive patients and 20 patients with fixed hypertension, 10 of them with a mild elevation of the diastolic pressure and 10 classified as severe because of a diastolic blood pressure above 110 mm. Hg.

In labile hypertension cardiac output was elevated, whereas blood volume, peripheral resistance, run-off index and flow cessation pressure were normal when blood pressure was high. This hemodynamic pattern was interpreted as due to an enhanced myocardial contractile energy or a restriction of the capacity vascular bed.

In mild fixed hypertension total peripheral resistance and flow cessation pressure were uniformly increased, but cardiac output and run-off index were normal. This pattern may be explained by the influence of flow autoregulation and the barostatic mechanism.

In severe fixed hypertension blood volume, cardiac output, and peripheral resistance were found to be high. Renal ischemia and secondary hyperaldosteronism may determine the development of this last stage of hypertension.

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Reports of Medical Cases, With a View of Illustrating the Symptoms and Cure of Diseases

By Richard Bright—1827

In this case we have the most unequivocal proof of the derangement of the kidney being connected with the extensive and sudden occurrence of anasarca:—there could indeed be no doubt of this, from the first moment that I had an opportunity of seeing the patient. The coagulable urine,—and the urine already containing the red particles of the blood in large abundance,—led me from the beginning to form my opinion as to the seat of the disease. Moreover, dissection showed no other adequate cause for the dropsical affection: and as during life no suspicion could be entertained that either the liver, the intestines, the heart, or the lungs were diseased, so the examination showed all these organs to be in a state of perfect health. I feel that it may be matter of doubt how far the employment of diuretics during such diseased tendency may have been instrumental in producing the peculiar appearance of the kidneys; but it is to be remembered that the particular symptom, the haematuria, which appears so immediately connected with this morbid state, has been observed to occur in a greater or less degree under all modes of treatment, and even before any treatment has been adopted in the sudden anasarca, and therefore we cannot in fairness ascribe the morbid appearance of the kidney to the remedies,—or at all events we must admit a certain high degree of disease to have existed in that organ from the commencement of the symptoms; but whether to the extent discovered in this case after death or not, we can never determine. —*Original Papers of Richard Bright on Renal Disease*. Edited by A. ARNOLD OSMAN. London, Oxford University Press, 1937, pp. 37-38.

Hemodynamic Patterns in Essential Hypertension

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