INCREASED EFFECT OF EXTRARENAL PRESSOR FACTORS FOLLOWING REMOVAL OF KIDNEYS

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Not long ago the view of the renal factor in hypertension was that, in response to interference with renal circulation or damage to the kidneys, the renal tissue would begin to produce increased amounts of rennin which would enter the blood stream and react with the α_2-globulin of the plasma to create hypertension which has a powerful vasoconstrictor action.

This view encountered serious difficulties because a number of fundamental clinical and experimental studies showed that in the chronic stage of hypertensive disease, and in experimental renal hypertension, the amount of rennin in the blood of human patients or of animals was normal, and that removal from animals of one ischemic kidney, which appeared to be the source of rennin, did not reduce the arterial pressure [7, 8, 11, 14].

It then followed that increasing the constituents of the rennin-hypertension system in the blood did not play any part in maintaining the raised arterial pressure during the chronic stage of hypertension. At the same time, there was no doubt that interference with renal circulation and damage to renal tissue played an important part in the pathogenesis of hypertension, because removing clamps and restoring the circulation to an ischemic kidney in animals, or transplanting a normal kidney into subjects suffering from malignant hypertension, led to a reduction in the arterial pressure [5, 6, 10]. Damage to the renal circulation, produced either reflexly or surgically, and damage to renal tissue lead to an increase in arterial pressure, not through the rennin-hypertension system, but in some other way [3].

Grol'man [1], and Floyer [6] and Ledingham [9], consider that in addition to their excretory function, kidneys have a "metabolic" or "incretory" function, which plays an important part in the healthy organism in maintaining the arterial pressure at its normal level. When there is damage to the renal circulation, renal metabolism is depressed, and arterial pressure increased. The most powerful argument in favor of this idea is the development of hypertension in animals from which both kidneys have been removed. This kind of hypertension develops in animals in which the excretory function of the kidneys has been taken over by an artificial kidney or by peritoneal dialysis, when the life of the animal may be prolonged for 1-3 months. If during this period the kidney whose ureter is sutured to the inferior vena cava is left in the body, although it can perform no excretory function, it will nevertheless completely prevent the development of the hypertension normally associated with nephrectomy [1].

For this reason, postnephrectomy hypertension is, at present, thought to result from the absence of renal metabolism. The great resemblance between this condition and that due to renal hypertension has led to the view that the disturbance of renal metabolism plays an important part in increasing arterial pressure [5, 6, 9]. However, the essential feature of renal metabolism and the means by which the "renal deprivation factor" increases arterial pressure remain unexplained. V. V. Parin and F. Z. Meerson [2] have suggested that the metabolic antihypertensive function of the kidneys restrains the action of the principal extrarenal pressor factors (adrenalin, noradrenalin, vasopressin and mineral corticoids), and so makes possible the maintenance of normal arterial pressure. In the absence of kidneys, the action of the pressor factors listed may be increased despite the fact that their concentration in the blood has not changed, so that the arterial pressure is also increased.

To test this hypothesis, S. M. Shenderov [3] carried out a number of investigations in V. V. Parin's laboratory, and used small or moderate doses of the pressor factors.

In the present investigation we have compared the pressor response to moderate doses of adrenalin and pituitrin in normal animals and those from whom the kidneys have been removed.

METHOD

In rabbits, the arterial pressure was recorded from the carotid artery by a mercury manometer. After the

Pressor Responses to Adrenalin in Animals with and without Kidneys

Adrenalin						Pituitrin			
Increase in arterial pressure in mm Hg						Increase in arterial pressure in mm Hq			
Controls			Kidney removed			Controls		Kidney removed	
Number of experiment	1γ	2γ	Number of experiment	1γ	2γ	Number of experiment	0.3 units	Number of experiment	0.3 units
1	3	46	1a	10	20	1	14	1a	32
2	8	20	2a	68	78	2	18	2a	35
3	16	8	3a	14	42	3	12	3a	36
4	8	26	4a	28	34	4	25	4a	28
5	28	54	5a	44	58	5	20	5a	56
6	18	22	6a	18	42	6	8	6a	26
7	28	25	7a	46	28	7	4	7a	34
8	14	22	8a	44	52	8	32	8a	40
9	16	32	9a	40	54	9	26	9a	28
10	24	32	10a	28	48	10	27	10a	36
11	22	26	11a	30	38				
12	8	34							
13	16	36							
14	22	28							
15	22	28							
Average	16,8	29,2		39,5	54,4	18,3		35	

pressure in the jugular vein had been stabilized, the animals were given, first, an injection of 1 γ, and then five minutes later, a second injection of 2 γ per kg, of adrenalin.

Five minutes after the second injection, 0.3 units per kg of pituitrin were injected. The magnitude of the pressor response was measured on a kymogram in mm Hg. These experiments were carried out on 15 control rabbits and on 11 animals from whom the kidneys had been removed 48 hours previously.

RESULTS

The initial arterial pressure varied between 90 and 120 mm Hg , and there were no significant differences between the two groups.

The pressor responses to adrenalin and pituitrin are shown in the table.

It can be seen from the table that in nephrectomized animals the response to adrenalin was much higher than in the controls. The difference was clearly shown by those receiving 1 γ of adrenalin.

In normal rabbits such an injection caused an average age increase of 16.8 mm, and in those without kidneys, the increase was 29.5 mm, so that nephrectomy increased pressor response by nearly twice. When 2 γ of adrenalin was given, the difference was less, though it was still considerably higher in the nephrectomized group.

The pressor response to pituitrin was also greater in the experimental group. In the controls the maximum average arterial pressure increase was 18.6 mm, and in the nephrectomized rabbits it was 35 mm. The difference was both qualitative and quantitative. In the control group the pressure rise took 3-4 minutes, after which the blood pressure returned gradually to normal, and in the operated group, immediately after the first pressure increase, which lasted 5-16 seconds, a decrease in pressure by 20-30 mm commenced. This fall was gradually replaced by a third phase in which the pressure increased

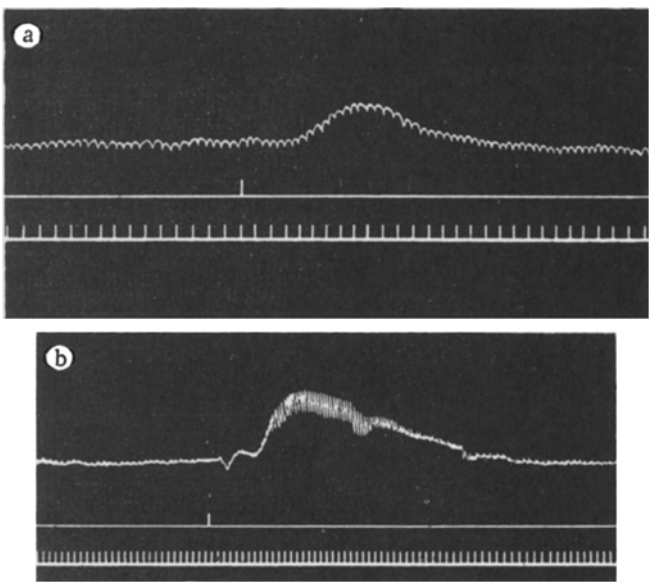

Fig. 1. Arterial pressure changes (pressor response) following intravenous injection of 1 γ adrenalin. a) Normal rabbit; b) nephrectomized rabbit. Curves, from above downward : arterial pressure, zero line, time marker (1 second).

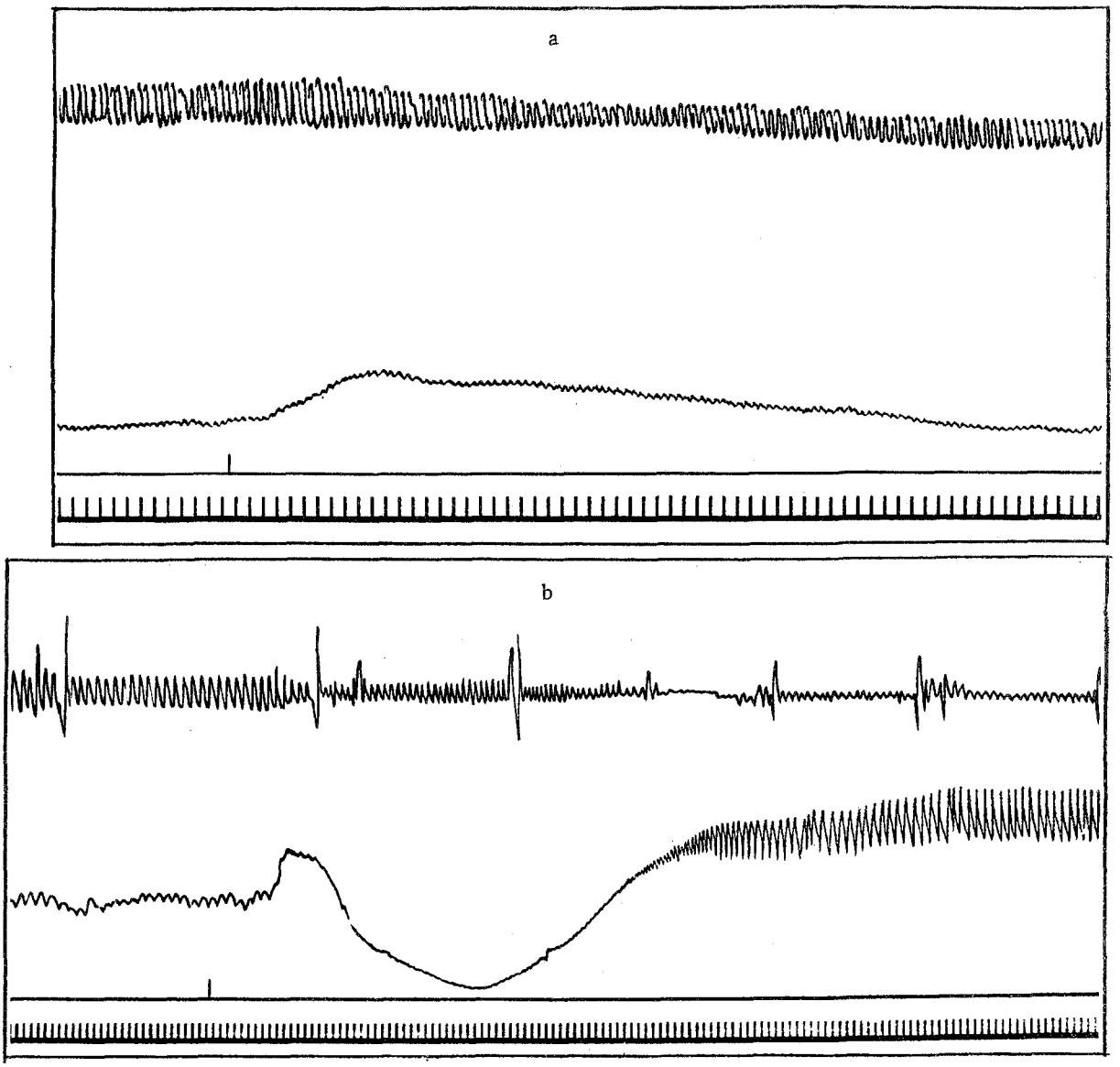

Fig. 2. Change in arterial pressure (pressor response) following intravenous injection of 0.3 units of pituitrin. a) Normal rabbit; b) nephrectomized rabbit. Curves as in Fig. 1.

to a higher level than the value reached immediately after the pituitrin injection.

The curves shown in Figs. 1 and 2 show the different pressor responses in the control of operated groups.

In considering the increased pressor response due to nephrectomy, it must be remembered that there may be two distinct reasons for the change. Firstly it may develop as a result of the elimination of a metabolic antihypertensive factor, whose destruction is responsible for the development of the hypertension due to nephrectomy, and secondly it may result from the elimination of the excretory function, which causes an accumulation in the body of nitrogen compounds, salts, and water.

The distinction between these two factors has been drawn by other investigations carried out in V. V. Parin's laboratory, where a wide range of pressor factors and experimental models, as well as peritoneal dialysis, have been used [3].

Thus, the condition of acute renal deprivation caused by bilateral nephrectomy causes a marked increase in the response to the extrarenal pressor factors, adrenalin and pituitrin.

SUMMARY

Experiments on rabbits have shown that the pressor effect of adrenalin and pituitrin increases considerably 48 hours after removal of both kidneys. This result confirms the authors' opinion that hypertension due to nephrectomy may be caused by an increased effect of extrarenal pressor factors without any change in their amount.

LITERATURE CITED

1. A. Grol'man, in: Hypertensive Disease [in Russian] (Moscow, 1953) p. 26.
2. V. V. Parin and F. Z. Meerson, An Outline of the Clinical Physiology of the Circulation [in Russian] (Moscow, 1960).
3. S. M. Shenderov, Zhurn. Patofiziol. i Éksper. Terapii (1960).
4. F. Braun-Menendez and A. C. Paladini, Circulation 17, 668 (1958).
5. P. M. Daniel, M. L. Prichard, and J. N. Ward-McQuaid, Clin. Sc. 13, 247 (1954).
6. M. A. Floyer, Clin. Sc. 14, 163 (1955).
7. F. W. Haynes, L. Dexter, and R. E. Seibel, Am. J. Physiol. 150, 198 (1947).
8. W. J. Kolff and I. H. Page, Am. J. Physiol 178, 531 (1955).
9. J. M. Ledingham, Brit. M. Bull. 13, 33 (1957).
10. J. P. Merrill et al., J. Am. M. A. 160, 277 (1956).
11. G. W. Pickering, Clin. Sc. 5, 229 (1945).
12. L. T. Skeggs and J. R. Kahn, Circulation 17, 658 (1958).
13. A. C. Taquini and J. C. Fasciolo, Medicina 9, 111 (1949).
14. A. C. Taquini, P. Blaquier, and A. C. Taquini, Jr., Circulation 17, 672 (1958).