anoxic anoxia or hemorrhage indicate that physiological activity is being measured by the use of colchicine blockade. Increased numbers of mitoses were evident before a real increase in either the hematocrit or reticulocyte percentage was detected in the circulating blood.

The ability of the bone marrow to produce erythrocytes depends on the size and activity of the *functional* marrow volume. The total volume of erythroid marrow cells may be estimated by histological examination. Determination of the rate of mitotic division by the colchicine technic provides an empirical measure of the functional activity of the marrow.

The mechanism by which colchicine arrests mitotic division is unknown. It is not believed that the number of mitotic figures is increased by the alkaloid. Brues(7) found no evidence of stimulation of mitosis by colchicine in regenerating rat liver nor did Mellgren (8) in the developing adrenal gland.

The work reported involved the sacrifice of the rat in order to obtain adequate marrow samples. Preliminary observations indicate that in animals as large as the rabbit, marrow samples obtained by the needle puncture following colchicine administration give essentially the same results as those observed in the rat. Such a modification provides a technic capable of wider application.

Summary. 1. The influence of colchicine on arrest of erythroid mitoses of intact rat marrow was measured quantitatively. 2. A comparison was made after colchicine injection of the erythroid mitotic percentage of normal rats and of those of erythropoietically stimulated animals. Fourteen normal rats showed a range of 2.5 to 4.8%, average 3.6%. Fifteen rats, 1 to 3 days after moderate hemorrhage, gave 3.8 to 12.0%, average 6.9%. Six rats exposed for 6 hours per day for 2 to 3 days (12 to 18 hours) to a barometric pressure of 300 mm Hg yielded 5.6 to 8.5%, average 7.0%. Mitotic percentage increase above normal was evident in the stimulated animals before an established reticulocyte response was observed.

The author wishes to thank Professor Wilfred M. Copenhaver of the Department of Anatomy for his guidance in the identification of mitotic cell types and Mr. John Hegmann for his technical assistance.

Received June 15, 1951. P.S.E.B.M., 1951, v77.

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Effect of Therapeutic Doses of Ephedrine on Renal Clearances in Normal Man.* (18841)

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(Introduced by H. W. Smith.)

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On the basis of unpublished observations of Chasis, Goldring, and Smith(1), Smith states that ephedrine has no or a negligible effect on the renal circulation; he reproduces only one experiment in which 35 mg of ephedrine injected intravenously caused a small and probably insignificant decrease in renal plasma flow (diodrast clearance) and filtration rate (inulin clearance), and concludes that the mode of action of adrenaline and

* This work was aided by a grant from The Commonwealth Fund.

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TABLE I. Effects of Therapeutic Doses of Ephedrine on Renal Hemodynamics in Man.

Subject	Dose, mg	Length of exp, min	Control values*			After ephedrine†			Change	
			Filtration rate, cc/min	Renal plasma flow, cc/min	Filtration fraction	Filtration rate, cc/min	Renal plasma flow, cc/min	Filtration fraction	Filtration rate, %	Renal plasma flow, %
Mc.‡	50	138	110	530	.21	109	498	.22	0	—6
V.	35	110	65	383	.17	70	399	.17	+ 7	+ 4
H.	50	119	149	580	.26	143	653	.22	— 4	+12
P.	75	110	148	797	.19	146	833	.18	— 1	+ 4
E.	50	180	111	695	.16	104	618	.17	— 6	—11
S.	50	139	85	542	.16	81	513	.16	— 4	— 5
W.§	75	205	140	580	.24	161	651	.25	+15	+12
K.‖	50	168	84	435	.19	81	415	.20	— 4	— 4

* Avg of 3 control periods.

† Avg of 4 to 8 periods.

‡ A brief period of syncope with hypotension accompanied by reduction in clearances occurred immediately after injection of ephedrine. This period was excluded.

§ EPAH = 94%. Renal A-V oxygen difference = 1.2 cc/100 cc. Both values remained constant.

‖ Ephedrine administered intramusc. except for K., in whom it was administered intravenously.

ephedrine is quite different.¶ Subsequently, Ranges and Bradley(2), in a hemodynamic study, reported that 50 to 75 mg of ephedrine administered intramuscularly caused a significant decrease in renal plasma flow (diodrast clearance) with no change in filtration rate (mannitol clearance). They drew their conclusions from observations on 6 subjects but present no data. They postulate that adrenaline and ephedrine act in a similar manner. The earlier report of Smith, with its contradictory results, is not mentioned.

In view of the confusion on this matter, and because the importance of ephedrine as an agent for sustaining blood pressure in spinal anesthesia, etc., we have reinvestigated the renal response in normal subjects to therapeutic doses of this drug.

Methods. The subjects were 8 male convalescent patients from the wards of the Third Medical (New York University) Division of Bellevue Hospital without known cardiovascular or renal disease. The renal plasma flow was determined by the p-aminohippuric acid clearance (C_{PAH}) and the filtration rate by the inulin clearance (C_{IN}). Inulin was determined by Harrison's diphenylamine method as described by Goldring and Chasis(3), and PAH by the method of Smith, Finkelstein, Aliminosa, Crawford, and Graber(4). Pulse rate and blood pressure were measured every 10 minutes or oftener and the mean blood pressure calculated as one-third of the pulse pressure plus the auscultatory diastolic pressure, or measured directly by means of a calibrated mercury manometer connected to the brachial artery. After 3 control periods of 12 to 30 minutes each, 35 to 75 mg of ephedrine were injected intramuscularly and the overlying muscle massaged for 2 minutes; 35 mg were given intravenously to one subject. Clearance studies were continued for varying periods of time. The extraction ratio of PAH (E_{PAH}) and renal arterial-venous oxygen difference were measured in one subject at the mid-point of each clearance period by catheterization of the renal vein. Oxygen content was determined in duplicate by the method of Van Slyke and Neill(5).

¶ The records of this laboratory for 1938 show 7 experiments, 2 of which were complicated by pyrexial hyperemia. In the other 5, ephedrine was administered intrav. or intramusc. in doses of 30 and 45 mg, respectively. The diodrast and inulin clearances were unaffected in all.

2. Ranges, H. A., and Bradley, S. E., *J. Clin. Invest.*, 1943, v22, 687.

3. Goldring, W., and Chasis, H., *Hypertension and Hypertensive Disease,* New York, The Commonwealth Fund, 1944.

4. Smith, H. W., Finklestein, N., Aliminosa, L., Crawford, B., and Graber, M., *J. Clin. Invest.,* 1945, v24, 388.

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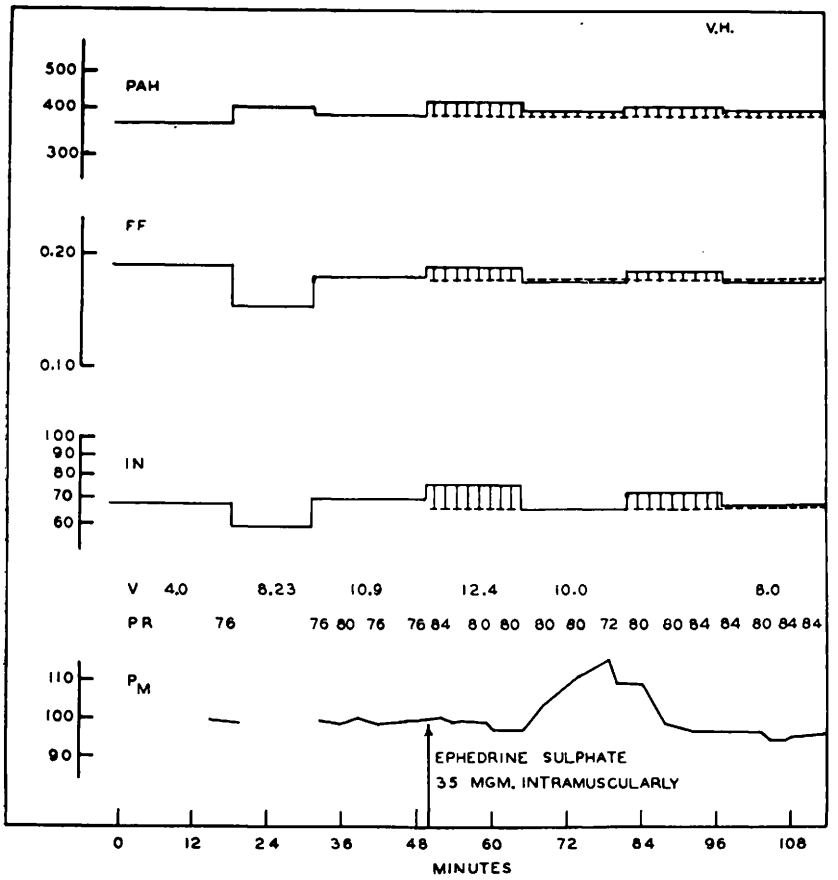

FIG. 1. Action of ephedrine on renal plasma flow (PAH or p-aminohippurate clearance in cc/min), filtration rate (IN or inulin clearance in cc/min), filtration fraction (FF or inulin/PAH clearance ratio), mean blood pressure (P_m in mm Hg), pulse rate (PR in beats/min) and urine flow (V in cc/min) in a normal subject.

Results. The results are tabulated in Table I, with a typical experiment shown in Fig. 1. In one instance we observed an 11% reduction in renal plasma flow and a 6% reduction in filtration rate, but clearance changes were negligible in the other 7 subjects.

It is generally agreed that in respect to cardiodynamic effects, ephedrine resembles adrenaline(2) although its action is more irregular(6). In these experiments, ephedrine regularly caused a small increase in systolic and diastolic blood pressure. The blood pressure generally began to increase within a few minutes after the administration of the drug, reached its maximum value in about 15 minutes (range 5 to 34 minutes), remained at this level for approximately 15 to 30 minutes and then slowly declined towards the control value. The increase in mean pressure on one occasion exceeded 40 mm Hg, and seemed unrelated to the dose of ephedrine (Table II). The pulse rate also increased slightly, usually by less than 10 beats per minute, and often remained elevated for the duration of the experiment.

Because the average values of several clearance periods, as shown in Table I, could mask transitory changes in renal hemodynamics, the clearances obtained during the period of maximal ephedrine effect, as judged by blood pressure and pulse rate, are shown in

6. Starr, I., Gamble, C. J., Margolies, A., Donal, J. S., Jr., Joseph, N., and Eagle, E., *J. Clin. Invest.*, 1937, v16, 799.

TABLE II. Renal Clearances During Maximal Ephedrine Effect.

Subject	Control values* Filtration rate, cc/min	Control values* Renal plasma flow, cc/min	Period of maximal ephedrine effect† Filtration rate, cc/min	Period of maximal ephedrine effect† Renal plasma flow, cc/min	Change in mean blood pressure, mm Hg	Change in pulse rate per min
Mc.	110	530	114	542	+22	+12
V.	65	383	65	390	+10	+ 5
H.	149	580	144	620	+ 8	+ 4
P.	148	797	155	773	+14	0
E.	111	695	97	580	+26	0
S.	85	542	93	539	+16	+16
W.	140	580	127	616	+43	+ 9
K.	84	435	83	410	+21	+ 2

* Avg of 3 control periods.
† Value for single period of max ephedrine effect, as judged by increase in blood pressure and pulse rate.

Table II. Even these maximal effects show no consistent increase or decrease in renal plasma flow or filtration rate.

E_{PAH} and renal arterial-venous oxygen difference, measured in one subject (W.I.), remained constant at normal values of 94% and 1.2 cc/100 cc, respectively, throughout the course of the experiment, demonstrating that ephedrine does not inhibit tubular excretion of PAH or cause diversion of renal blood through arterial-venous channels.

Summary. Ephedrine in therapeutic doses (35 to 75 mg) administered intramuscularly to 7 subjects and intravenously to one failed to cause any consistent or significant change in renal plasma flow, filtration rate, PAH extraction ratio, or renal arterial-venous oxygen difference, despite an increase in mean blood pressure and pulse rate. These results are in agreement with the conclusion of Chasis, Goldring, and Smith(1) that, in marked contrast to adrenaline, ephedrine in therapeutic doses has no or a negligible effect on the renal circulation.

Received June 18, 1951. P.S.E.B.M., 1951, v77.

Potentiating Effect of Tetraethylammonium on Pressor Response to Epinephrine and Nor-Epinephrine.* (18842)

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The property of tetraethylammonium (TEA) of potentiating the pressor response to epinephrine and other pressor agents has been attributed(1) to the elimination of homeostatic blood pressure reflexes by this ganglionic blocking agent. In this connection, it is important to discover whether or not TEA has any direct potentiating effect on the action of epinephrine and it was the purpose of this investigation to attempt to shed some light on this aspect of the problem.

Methods. Twelve cats, weighing 2.23-5.57 kg, were anesthetized with ether after premedication with atropine sulphate 1.0 mg/kg. Both vagus nerves were divided and the spinal cord was then pithed in 10 animals after cervical laminectomy; in the remaining 2 animals the probe was passed through the orbit. The preparation was then left for an hour, body temperature being maintained constant by means of a warming device. Carotid blood pressure was recorded on a kymograph by

* This study was supported by a grant from Parke, Davis Co.

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