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Inability of Purified Renin to Reduce the Blood Pressure of Hypertensive Dogs.*

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Wakerlin and his associates^{1, 2} recently reported a striking reduction in the blood pressure of chronic, hypertensive dogs treated with daily injections of hog kidney extract over a period of 4 months. These authors believed the reduction in blood pressure to be closely related to a concomitant formation of an antirenin substance which they found in the blood of these animals.

They have not proved indubitably that the pressure reductions were due to the injection of the renin present in their renal extract, for this was comparatively crude, and contained many substances other than renin. These original observations have not yet been confirmed; furthermore, Winternitz and associates³ could not obtain a reduction in pressure in their dogs following prolonged administration of crude kidney extracts or highly purified renin.

In the following preliminary report, results are given of the changes (a) in the blood pressure of 3 chronic, hypertensive dogs subjected to a prolonged course of daily, intramuscular injections of purified renin and (b) changes in the ability of the blood plasma of these dogs to neutralize the pressor effect of renin.

Methods. Two of the three hypertensive dogs used in this study (Dogs 13 and 28) were made hypertensive by application of a Goldblatt clamp⁴ on the left renal artery and envelopment of the right kidney by cellophane.⁵ The third animal (Dog 30) was made hypertensive by removal of the right kidney and envelopment of the left by cellophane. All of the dogs had been hypertensive for at least 54 days before renin injections were started.

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¹ Johnson, C. A., and Wakerlin, G. F., *Proc. Soc. Exp. Biol. and Med.*, 1940, **44**, 277.

² Wakerlin, G. F., and Johnson, C. A., *J. A. M. A.*, 1941, **117**, 416.

³ Winternitz, M. C., Mylon, E., and Katzenstein, R., *Yale J. Biol. and Med.*, 1941, **13**, 789.

⁴ Goldblatt, Harry, Lynch, J., Ranzal, R. F., and Summerville, W. W., *J. Exp. Med.*, 1934, **59**, 347.

⁵ Page, I. H., *J. A. M. A.*, 1939, **113**, 2046.

One day before the daily injections of renin were begun, plasma was obtained from each dog and tested for its ability to neutralize the pressor effect of renin in the manner described by Wakerlin.² These assays were repeated 6, 12, and 16 weeks after the beginning of renin administration.

Purified renin (Fraction D) was prepared from fresh hog kidney cortex according to the method of Helmer and Page.⁶ Each dog received a daily, intramuscular injection of renin until he died (Dog 30), or until 4 months had elapsed. The dosage employed was equivalent to one gram of fresh kidney cortex per kilogram of body weight per day. Blood pressure recordings were taken thrice weekly by direct cannulation of the femoral artery.

Results. The continued daily injection of purified renin was not followed by a significant reduction in blood pressure (Table I). Dogs 18 and 28 had a reduction of 9 and 5% respectively after 123 days of daily renin injections. The blood pressure of Dog 30

TABLE I.
Effect of Daily Injections of Purified Renin upon Blood Pressure of Chronic Hypertensive Dogs.

Dog No.	Average arterial blood pressure (mm of Hg)					
	Before renin injections		During renin injections			
	Before hypertension*	After hypertension†	1st to 4th week‡	4th to 8th week‡	8th to 12th week‡	12th to 16th week‡
13	112	176	165	168	162	167
28	110	173	161	150	159	160
30§	124	163	176	190	226	

*Average blood pressure of week preceding the initial operation.

†Average blood pressure of 2 weeks preceding administration of daily renin injections.

‡Average blood pressure during 4-week interval.

§Died of uremia 74 days after daily renin injections were instituted.

TABLE II.
Pressor Effect of a Standard Renin Solution* when Injected into Anesthetized Nephrectomized Dogs Following Its Refrigeration with Plasma of Hypertensive Dogs Receiving Daily Injections of Renin.

Plasma used Dog No.	Maximum pressor response of nephrectomized dogs to refrigerated renin-plasma mixture			
	One day before renin injections commenced	During renin injections		
		End of 6th week	End of 12th week	End of 16th week
13	40	30	54	40
28	37	30	28	26
30	32	28		

*A single batch of purified renin, Fraction C, was used for test purposes. One cc of this solution was equivalent to 34.5 g of fresh hog kidney cortex.

⁶ Helmer, O. M., and Page, I. H., *J. Biol. Chem.*, 1939, **127**, 757.

actually increased during the renin administration (39% increase) although he died of uremia on the 74th day of treatment.

Following the prolonged administration of purified renin, the plasma of Dogs 13, 28, and 30 likewise showed no appreciable change in ability to neutralize the acute pressor effect of renin when refrigerated with it (Table II).

Discussion and Summary. The inability of prolonged administration of purified renin to change materially the blood pressure of the 3 hypertensive dogs reported herein does not necessarily refute the findings of Wakerlin, for he used a crude preparation of renin, and the reductions in pressure in his hypertensive dogs may have been due to some other factor present in his kidney extracts. The present observations indicate, however, that the prolonged administration of purified renin neither reduces the blood pressure of hypertensive dogs nor endows their plasma with the ability to inhibit the vasopressor response of renin.

13698

A Simplified Procedure for Preparing an Improved Pavlov Pouch.

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The classical operation for preparing an innervated pouch ("Pavlov Pouch") of a portion of the stomach^{1, 2} is difficult and time-consuming and there is some doubt whether the pouch retains its full vagus innervation.³ Modifications have been suggested which were designed to simplify the technic^{4, 5} or to preserve a larger proportion of the nerve supply.⁵⁻⁸ However, with one exception⁸

¹ Pavlov, I. P., *Ergebn. d. Physiol.*, 1902, **1**, 246.

² Pavlov, I. P., *The Work of the Digestive Glands*, 2nd ed., London, 1910.

³ Jemerin, Edw. E., and Hollander, Franklin, *Proc. Soc. Exp. Biol. and Med.*, 1938, **38**, 139.

⁴ Boldyreff, W. N., *Bull. Battle Creek Sanit. and Hosp. Clinic*, 1925, **20**, 206.

⁵ Neuwelt, F., Olson, W. H., and Neeheles, H., *Proc. Soc. Exp. Biol. and Med.*, 1940, **44**, 74.

⁶ Hollander, Franklin, and Jemerin, Edw. E., *Ibid.*, 1938, **39**, 87.

⁷ Cope, O., McMahon, C. E., Hagströmer, A., and Thompson, R. H., *Arch. Surg.*, 1940, **40**, 717.

⁸ Avrorov, P. P., and Schpuga, G. M., *Kub. Nauch. Medicin. Vestnic.*, 1940, **12-13**, 238.