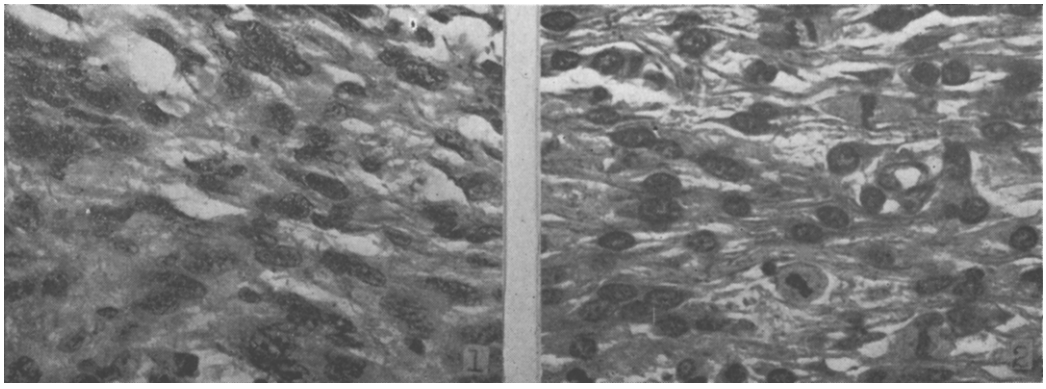

FIG. 1. ×335.
Connective Tissue Neoplasms Produced by Methylcholanthrene.

FIG. 2. × 450.
Description in text.

described in a recent communication,[4] was fed stilbestrol for the 280 days between the 34th and 314th days of the methylcholanthrene medication. On this 314th day, 500 mg of stilbestrol were implanted subfascially in the right upper quadrant of the ventral abdominal wall. The subsequent events and the clinical recovery of this animal have been reported.[5]

Methylcholanthrene was also administered in doses of 30 to 100 mg to 6 other mongrel dogs, 3 males (the 1st, 2nd, and 4th dogs previously described[4]) and 3 females, about 1½ to 3 years old and weighing 7 to 14 kg at the start of the experiments lasting 150 to 618 days, but without the production of neoplasms demonstrable at autopsy at or near the site of injection or in other locations.

Summary. Connective tissue neoplasms with the histologic characteristics of fibrosarcoma were produced in 2 dogs by the subfascial injection of methylcholanthrene.

NOTE: Dog 53 was presented at the March 5, 1943, meeting and dog 52 at the May 26, 1944, meeting of the Rocky Mountain Section of the Society for Experimental Biology and Medicine.

[4] Mulligan, R. M., PROC. SOC. EXP. BIOL. AND MED., 1943, **54**, 21.

[5] Mulligan, R. M., *Am. J. Path.*, 1944, **20**, 865.

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Effects of Fourneau 883 and Fourneau 933 on Late Renal Hypertension in the Rat.

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In a recent study of the effects of nembutal and yohimbine on the blood pressure of normal and hypertensive rats, Reed *et al.*[1] have shown that the blood pressure of *late* hypertensive animals is lowered by nembutal anesthesia and sympatholytic-adrenolytic doses of yohimbine, whereas the blood pressure of *normal* or *early* hypertensive animals is unaffected by these substances. These data were interpreted to signify a change in the mechanism of maintenance of renal hypertension in the animals used, the initial renal humoral disturbance which precipitates hypertension being superseded by neurovascular or other alterations which maintain blood pressure after the dis-

[1] Reed, Racheal K., Sapirstein, Leo A., Southard, F. D., Jr., and Ogden, Eric, *Am. J. Physiol.*, 1944, **141**, 707.

TABLE I.
Effects of F 883 and F 933 on Systolic Blood Pressure of Normal and Late Hypertensive Rats.

Description.	No.	Systolic pressure		
		Before inj.	After inj.	Diff.
	F 883 (5 mg per rat).			
Late Hypertensive	16	165	126	—39
Normal	8	117	115	— 2
	F 933 (10 mg per rat).			
Late Hypertensive	16	151	144	— 7
Normal	8	121	119	— 2

appearance of the original humoral imbalance.

The effects of the sympatholytic-adrenolytic drug yohimbine on late hypertension suggested that this state was maintained either through the sympathetic nervous system as a whole or through nervous involvement of the adrenal medulla alone. In the present investigation we have studied the effects of a purely adrenolytic substance, piperidino-methyl-benzo-dioxane (Fourneau 933) and a sympatholytic and adrenolytic drug, diethyl-amino-methyl-benzo-dioxane (Fourneau 883) on the blood pressures of late hypertensive animals. Evidence that in the doses used F933 is purely adrenolytic and that F883 has both adrenolytic and sympatholytic effects has been presented by Bacq and Fredericq[2,3] and others.

Methods. All hypertensive rats had been hypertensive (systolic pressure > 150) for at least 3 months before the effects of the 2 drugs were studied. Hypertension was induced by partial ligation of one renal artery according to the method of Wilson and Byrom.[4] Blood pressures were taken on unanesthetized animals by the tail plethysmograph method of Williams, Harrison, and Grollman.[5] Both substances were used on each hypertensive rat, an interval of one week being allowed after injection of the first before the effect of the second was determined. Normal controls were from the same stock and were of the same age and weight as the hypertensives. The drugs were made up just before injection in solutions containing 5 or 10 mg per cc. All injections were made intraperitoneally. Blood pressures were recorded immediately before and 30-45 minutes after the injection.

Findings. Fourneau 883 (sympatholytic and adrenolytic) at a dosage of 5 mg per rat lowered the blood pressure of late hypertensive rats to nearly normal levels. The maximum effect was observed in 30-120 minutes, and some effect persisted for 24 hours. Fourneau 883 was without effect on the blood pressure of normal animals.

Fourneau 933 (adrenolytic), at a dosage of 10 mg per rat, was without effect on the blood pressure of either hypertensive or normal rats.

The results are summarized in Table I.

Discussion. The lowering of blood pressure of late hypertensives by the sympatholytic and adrenolytic drugs yohimbine[1] and F883, and the failure of the adrenolytic drug F933 to exert any effect on the blood pressure of late hypertensive animals indicate that sympathetic activity rather than hyperfunction of the adrenal medulla is at fault in the mechanism which follows the renal mechanism in maintaining hypertension in the rat.

Summary and Conclusions. 1. The sympatholytic-adrenolytic drug F883 lowered the blood pressure of 16 late hypertensive rats to a nearly normal level. The blood pressure of normal rats was unaffected. 2. The adrenolytic drug F933 failed to lower the blood pressure of either late hypertensive or normal rats. 3. It is concluded that secondary hypertension of renal origin is mediated through the sympathetic nervous system rather than through the adrenals.

Our thanks are due to Dr. Eric Ogden for suggesting this experiment, and to Dr. George Emerson for supplying the two dioxane derivatives.

2 Bacq, Z. M., and Fredericq, H., *C. R. Soc. de biol.*, 1934, **117**, 806.

3 Bacq, Z. M., and Fredericq, H., *C. R. Soc. de biol.*, 1935, **118**, 183.

4 Wilson, C., and Byrom, F. B., *Lancet*, 1939, **1**, 136.

5 Williams, J. R., Jr., Harrison, T. R., and Grollman, A., *J. Clin. Invest.*, 1939, **18**, 373.