These positive reactions in locally sensitized monkey skin sites differ from positive reactions in man as the recipient for the Prausnitz Kustner reaction. In man a positive result consists of a button-like wheal without pseudopods and a surrounding areola. In the monkey the wheal shows marked pseudopodia formation and no surrounding areola. Instead there is a vague blueish tinge about the wheal which photographs fail to record.

Conclusion. The skin of the monkey *(Macacus rhesus)* is suitable for local passive sensitization to ragweed pollen extract by the intradermal injection of either serum from a sensitized guinea pig or serum from a human case of ragweed hay fever.

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Vaso-Pressor Action of Extracts of Plasma of Normal Dogs and Dogs with Experimentally Produced Hypertension.

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Marked chronic hypertension may be produced in dogs by compressing the renal arteries by means of silver clamps until moderate ischemia occurs (Goldblatt, Lynch, Hanzal and Summerville[1]). Nervous impulses originating in the kidneys do not appear to participate in the genesis of this hypertension, for if the renal nerves are severed, clamping the renal artery is still effective in causing hypertension (Page[2]). It is not unreasonable, therefore, to suppose that a pressor substance is liberated by the kidneys as a result of ischemia which might be responsible for the hypertension. The object of this investigation is to ascertain, by means of a method with which we had previously had experience (Page[3]) whether this hypothesis could be supported with experimental evidence.

Carotid loops were prepared in dogs for measurement of arterial pressure by the Van Leersum method. After a control period of 2 months during which blood pressure was measured daily, silver clamps were placed on the renal arteries according to the method of Goldblatt, Lynch, Hanzal and Summerville.[1] Amytal injected intraperitoneally (60 mg. per kg.) was employed as anesthetic.

[1] Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, *J. Exp. Med.*, 1934, **59**, 347.

[2] Page, I. H., *Am. J. Physiol.*, 1935, **112**, 166.

[3] Page, I. H., *J. Exp. Med.*, 1935, **61**, 67.

Within 3 days the arterial pressure rose, often as high as 260 to 300 mm. of Hg. Blood (60 cc.) was taken by puncture of the femoral artery before and after the production of hypertension. Heparin was used as anticoagulant. Alcoholic extracts of the plasma were prepared as previously described.[3] The pressor effect of the extracts was ascertained by intravenous injection into cats (2.5-3.5 kg.) anesthetized with ethyl urethane (6 cc. of a 25% solution per kilo). Blood pressure was recorded by means of a mercury manometer with a cannula in the carotid artery. Both vagus nerves were cut. The same volume of warm salt solution as that of the extract was always injected before the extract to be tested was injected. From one to 5 weeks after production of hypertension in 3 of the dogs, the hypophysis was removed (Page and Sweet[4]). Arterial pressure fell to normal. Blood samples were again obtained and extracts prepared and assayed for pressor activity.

Results. Extracts of dog's blood appear to differ slightly from those of human blood in that the pressor response when injected into cats is usually smaller. Both are characterized by the fact that the pressor response is dependent on the functional intactness of the central nervous system, for if the animal is pithed the extracts are inactive. Typical examples of results derived from study of the injection of extracts into 18 cats are presented (Table I).

If the same volume of warm salt solution as that of the extract produced a rise of more than 2-4 mm. of Hg. the experiment was abandoned, consequently the rises in arterial pressure recorded in the table are not volume effects.

These data show that rise in the cat's blood pressure is as liable to occur from extracts of plasma from dogs with normal blood pressure as those with marked hypertension. Hypophysectomy, although reducing the arterial pressure, did not alter the character of the response to the plasma extracts as assayed by this method.

The curves of the pressor action of plasma extracts resemble those obtained from human blood (Figs. 1 and 2). In Fig. 1 marked pressor action is shown by extracts of plasma of a dog rendered hypertensive compared with plasma from the same dog when arterial pressure was normal. The reverse is shown in Fig. 2, that is, extract from plasma of a dog with normal blood pressure was the more active. Since responses to the same extract are so irregular, not only in different animals but in the same animal at different periods in the experiment, it was necessary to test many extracts

[4] Page, I. H., and Sweet, J. E., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 260.

TABLE I.

Response of Cat's Blood Pressure to Injection of Extracts of Plasma from Dogs with Normal and Elevated Blood Pressure.

Cat No.	Dog No.	Dog's blood Pressure, mm. of Hg.	Volume of Extract	Equivalent amt. of plasma	Rise in cat's blood pressure, mm. of Hg.	
219	87	110	5	10	44	
219	87	110	5	10	36	
220	87	110	5	10	14	
220	87	280	5.5	11	14	
220	87	210	5	10	14	
226	87	210	5	10	6	
227	87	210	5	10	18	
214	86	140	5	10	0	
214	86	140	5	10	0	
214	86	230	5	10	16	
214	86	230	5	10	22	
218	86	204	5	10	8	
218	86	204	5	10	4	
218	86	204	5	10	6	
226	86	240	5	10	0	
218	84	116	5	10	2	
218	84	116	8.5	17	4	
218	84	200	5	10	8	
218	84	200	9	18	10	
229	84	210	10	22.5	0	
229	84	140	10	24.5	0	
229	84	160	10	22.0	sl. fall	Hypophysectomy
221	82	150	5	10	10	
221	82	218		2	10	
221	82	218	2.5	5	42	
221	82	150	4.8	9.6	2	
222	82	278	5	10	—2	
222	82	278	5	10	14	After cocaine sensitization
130	82	110	9	26	4	Hypophysectomy
215	83	240	5	5	16	
222	83	114	5.5	11	2	
222	83	212	5	5	2	
223	83	114	5	5	8	
223	83	212	5	5	12	
224	83	114	2.4	4.8	10	
224	83	212	2.0	4.0	12	
231	83	200	6	16	6	Hypophysectomy

on different animals. Such data have been secured. They demonstrate no correlation between the height of the blood pressure of the animal from which plasma was obtained and the pressor response in cats.

Pneumographic records show that during the injection of extract, respiration may be markedly slowed and become shallow temporarily. Asphyxia might be responsible for part of the initial rise in pressure but against this hypothesis are the two facts that

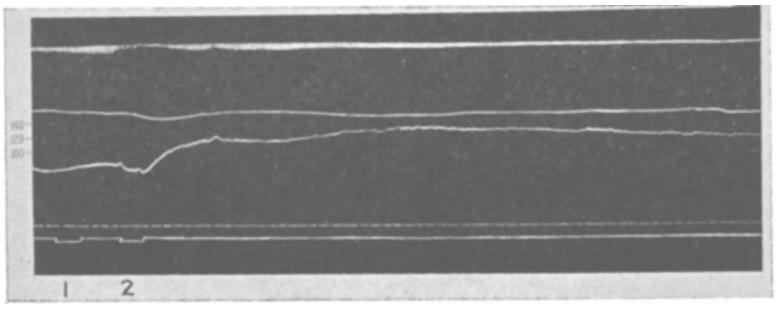

FIG. 1.

Effect of extract of plasma on arterial pressure of a cat. Uppermost line records respiration, second line down records the movements of the nictitating membrane, third line records arterial blood pressure, fourth line records time in 10-second intervals, and fifth line, the base line. 1. Salt solution 10 cc. 2. Extract (9 cc.) of 24 cc. of plasma from dog No. 61. Arterial pressure of this dog was 230 mm. of Hg.

there is no correlation between the inhibition of respiration and the rise in arterial pressure, and that removal of the adrenal glands does not prevent the rise. Then too, rise in pressure from asphyxia is ordinarily transient, while response from plasma extract is exceptionally prolonged (10 to 30 minutes).

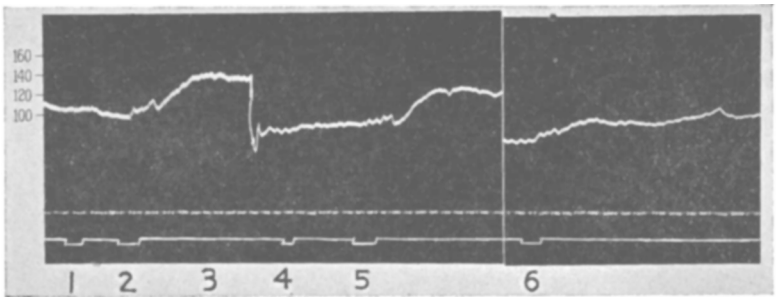

FIG. 2.

Effect of extract of plasma on arterial pressure of a cat. 1. Salt solution 5 cc. 2. Extract (5 cc.) of plasma of Dog No. 87; blood pressure 110 mm. of Hg. 3. Interval of 35 minutes. 4. Salt solution 5 cc. 5. Same as 2. 6. Extract (5 cc.) of 10 cc. plasma from dog No. 87 after renal artery was clamped. Blood pressure was 280 mm. of Hg.

These data do not support the hypothesis that hypertension produced by renal ischemia in dogs owes its genesis to circulation of peripherally acting pressor substances. They resemble those obtained by Page[3] from study of plasma from patients suffering from hypertension associated with nephritis or of the essential type. In such cases, extracts of plasma also did not differ significantly from

extracts of plasma from normal persons in their action on cat's blood pressure.

It is of interest to observe that hypophysectomy in 3 animals did not alter the pressor action of the plasma extracts. It may be inferred that the hypophysis does not secrete its pressor element into the blood stream when hypertension is produced by clamping the renal artery in amounts large enough to be detected by the method. As yet there is no evidence to decide how important an effect its secretion may have on vaso-motor centers in the brain. It seems safe to conclude that the pressor principle ordinarily separated from pituitary glands is not present in the blood in sufficient quantities to cause hypertension in dogs by action on the peripheral blood vessels.

These results, in agreement with those of Prinzmetal, Friedman and Rosenthal[5] obtained by transfusion of blood from normal to hypertensive dogs, suggest that some humoral substance is generated when the renal artery is constricted. While not itself directly pressor it causes abnormal constriction of blood vessels by some unknown mechanism.

Conclusion. Hypertension produced in dogs by means of compression of the renal artery has not been shown by the method employed to be caused by liberation of pressor substances into the blood stream which act directly on the peripheral blood vessels to cause vaso-constriction. Nor is the known pressor secretion of the pituitary gland present in amounts large enough to be detected by the method employed, in the blood of animals with hypertension. These conclusions are based on the following evidence: 1. Alcoholic extracts of plasma of dogs with hypertension when injected into anesthetized cats raises the cat's arterial pressure no more effectively than extracts from plasma of normal animals. 2. Removal of the hypophysis in animals with experimental hypertension does not alter the character of the pressor response to extracts of plasma.

5 Prinzmetal, M., Friedman, B., and Rosenthal, N., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 545.