in a type-specific Group A strain so that its antigen agglutinates not only in several Group A serums, but also to a lesser degree in sera of Group C. This change has occurred as the result of transforming cultures of the S-phase of the type-specific culture to its corresponding R-phase and subsequently reconverting the latter to an S phase. It would thus appear that the R-phase culture, like the diphtheroid, may be the seat for reorganizations of antigenic constitution.

Both may be viewed as having something in common in respect of their proclivity for reorganization of biologic characters. The two mechanisms appear to differ in degree however, since passing through the diphtheroid state may lead to a frank recombination of characters that finds expression in a group-transformation. Further evidence for similarity between the diphtheroid and the R-culture-phase will be given fuller consideration in a subsequent publication.

The reorganizational significance of special cell-types and culture-phases was first pointed out in 1920,[2] and the special bearing of such variability phenomena on the origin of group and specific agglutinogens was indicated in 1926.[3] In 1931,[4] the same variation principles found application to the much discussed filtrable forms of bacteria—the G types, whose filtrability and marked variability have recently been confirmed by Haddow.[5]

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A Pressor Substance is Not Present in the Perfusate of Ischemic Kidneys.

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The physiological mechanism by which increased arterial pressure is produced and maintained following the establishment of renal ischemia is unknown. There is, however, much evidence indicating that the kidney plays a specific rôle. There are several studies which seem to eliminate the possibility that reflex constriction of the peripheral vascular bed is responsible for the increased pressure observed. Since the rise in pressure may occur in the presence of one

2 Mellon, R. R., *J. Med. Res.*, 1920, **42**, 61.

3 Mellon, R. R., and Jost, E. L., *J. Immun.*, 1926, **11**, 139.

4 Hadley, P. B., Delves, E., and Klimek, J., *J. Inf. Dis.*, 1931, **48**, 1.

5 Haddow, A., *J. Inf. Dis.*, 1938, **63**, 129.

normal kidney, it seems reasonable to assume that some pressor agent may be released from the ischemic kidney in the course of an experimental hypertension. We have attempted to demonstrate such an agent in the perfusate of ischemic kidneys in hypertensive dogs.[1-5]

Two groups of dogs were used. In the first group perfusion was carried out within a few days after unilateral partial constriction of the renal artery, because we thought that any active pressor agent might be released in greatest quantity in the early stages of experimental hypertension, thereby producing increased arteriolar tonus, with subsequent maintenance of increased pressure as a result of "organic" changes in the arterioles. In the second group frank hypertension was allowed to develop.

In the first series of experiments elevation of blood pressure was produced by partially clamping the renal artery on one side and explanting the kidney into the flank. Four days later the explanted kidney was removed and perfused for a variable length of time with warm Locke's solution. The solution was perfused through the kidney several times during a period of 30 minutes in order that the total quantity of perfusate might be kept within utilizable limits. The coagulum which sometimes formed in the perfusate was removed to permit reperfusion of the fluid.

The renal perfusate was injected into the femoral vein of anesthetized dogs in which the carotid blood pressure level was recorded.

Systolic and diastolic pressures were determined in the unanesthetized state by means of the Hamilton recording optical manometer.

Results. First Group: In the first group of 4 animals the blood pressure ranged from 160 to 185 mm Hg when the kidney was perfused. A pressor agent was not found in the perfusate.

Second Group: Hypertension was produced after a control period of several weeks during which a definite blood pressure level was established. In 3 of these animals elevation of the pressure level had persisted for more than 3 months after unilateral constriction of the artery. In a fourth animal it was necessary to partially clamp the second artery in order to maintain a high blood pressure. In 2 other experiments[5] perfusion was carried out 11 and 16 days respectively after unilateral constriction of the renal artery.

1 Goldblatt, Lynch, Hanzal, and Summerville, *J. Exp. Med.*, 1934, **59**, 347.

2 Blalock and Levy, *Ann. Surg.*, 1937, **106**, 826.

3 Child and Glenn, PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 217.

4 Alpert, Alving, and Grimson, PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 1.

5 Williams and Grossman, *Am. J. Physiol.*, 1938, **123**, 364.

TABLE I.

Dog No.	Pre-operative blood pressure	Pre-perfusion blood pressure	Duration of hypertension	Amt of perfusate	Duration of perfusion	Amt of perfusate injected	Anesthesia assay animal	Change in blood pressure
	mm Hg.			cc	min.	cc		
1	140/105	195/110	5 mo.	150	30	70	Pentobarbital	Transient fall
2	150/90	210/112	4½ "	150	20	70	"	" "
3	120/70	200/104	1st operation, 2 mo. 2d operation, 14 days	200	20	100	"	" "
4	165/105	250/156	3 mo.	250	60	225	Ether	Slight transient rise—8 mm Hg.
5	142/85	192/112	11 days	250	60	225	"	Slight transient rise—6 mm Hg.
6	165/105	205/150	16 "	250	55	230	"	Transient rise—12 mm Hg.

The results of the second group of experiments are shown in Table I. Although a definite hypertension was present, a pressor agent was not present in the perfusate. (In order to obtain the 6 hypertensive dogs, the vessels of 10 dogs were clamped.) The slight transient rises observed in dogs 4, 5, and 6 were produced when the same quantity of Locke's solution was injected at the same rate.

Summary. We were unable to obtain a pressor substance in significant amounts from the ischemic kidney of hypertensive dogs by perfusing such kidneys for from 20 to 60 minutes with Locke's solution.

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Comparison of Intravaginal and Subcutaneous Tests for Estrone and Estradiol Monobenzoate.

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It was known from previous experiments[1, 2] that by administering estradiol monobenzoate intravaginally, cornification of ovariectomized rats' vaginæ could be induced with about 1/200th of the amount needed subcutaneously. It was also known that by the subcutaneous rat test, estradiol monobenzoate in oil is 5 to 10 times as potent as estrone in oil. It seemed of interest, therefore, to determine the relative potencies of these two substances as judged by the intravaginal method. For, it might be argued, that if estradiol monobenzoate appears more potent merely because of slower absorption and excretion following subcutaneous injection, the local test might find it no more potent than estrone. If, however, it is more potent because a greater growth-stimulating property is determined by its chemical structure the ratio (estradiol monobenzoate: estrone) might be expected to remain the same, or be even greater because fewer variables are involved in the local test.

[1] Lyons, W. R., and Templeton, H. J., PROC. SOC. EXP. BIOL. AND MED., 1936, **33**, 587.

[2] Yerby, L. D., *ibid.*, 1937, **36**, 496.