The fact that TCP added *in vivo* as well as *in vitro* prevented the oxidative decline of α-ketoglutarate is, for the moment, unexplained. The data obtained support, in part, the view of Squibb(6) that animals receiving high dosages of vit. A showed a significant decrease in liver proteins.

Summary. The rates of oxidation of several Krebs cycle acids by rat liver homogenates were similarly affected by either a vit. A deficiency or a vit. A excess. In both conditions the initial increases of about 40% were followed by marked respiratory declines. Tri-o-cresyl phosphate *in vivo* or *in vitro* prevented the initial increase with subsequent decline in respiration of livers from abnormal vit. A-nurtured rats. However, this chemical in the diet (0.1%) reduced the liver vit. A level by 50%, decreased liver protein and markedly increased liver fat.

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Sodium Mobilization in the Perfused Rat Tail Artery.* (29613)

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Closed circuit perfusion of the rat tail with a medium in which sodium is reduced and replaced by sucrose produces a decline in the resistance of the vascular bed(1). In such a system, continuous monitoring with Na^+ and K^+ glass electrodes indicates that sodium is added to the medium from regions of the tail tissue not accessible to inulin. In contrast, when potassium or choline are the replacements for sodium, resistance of the vascular bed does not decline, and little, if any, sodium is added to the perfusing medium. This relationship between mobilization of sodium and peripheral vascular resistance suggests that vascular smooth muscle cells themselves are directly involved in the exchange. If so, this supports the view that the transcellular distribution of sodium is a determinant of vascular smooth muscle tension. Accordingly, in the present experiment, sodium and potassium distribution in the rat tail artery was measured by conventional chemical techniques following perfusion with low sodium solutions in which lactose, potassium chloride, or choline chloride served as substitutes. As anticipated, a differential mobilization of sodium was observed.

Methods. Male albino rats of an inbred Wistar strain weighing 300 g or more, in 4 groups of at least 8 animals each, and anesthetized with a pentobarbitone-phenobarbitone combination(2) were used. The ventral tail artery and a companion vein were cannulated and the tail then perfused at 0.65 ml/min and 37°C. The venous effluent was discarded. The system was first allowed to run freely for 3 minutes using a basal solution of the following composition in mM/

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TABLE I. The Effects of 20 Minute Perfusion of Rat Tail with Media in Which 30 mEq/Liter of NaCl Was Replaced by an Equivalent Amount of Lactose, Potassium Chloride, or Choline Chloride.

	Control Group 1	Lactose Group 2	KCl Group 3	Choline chloride Group 4
Effluent perfusate				
[Na], mEq/liter	147.7 ± 1.1	122.7 ± .4*	122.6 ± .6 *	121.4 ± .8 *
[K], "	4.92 ± .14	4.94 ± .08	32.4 ± .32*	5.30 ± .20
Caudal artery				
Total water, ml/kg fat-free wet wt	685.1 ± 6.7	689.7 ± 5.4	694.7 ± 4.7	688.5 ± 4.4
Total Na, mEq/kg " " "	105.6 ± 1.6	88.9 ± 1.8*	90.3 ± 2.4 *	96.2 ± 2.4 *†
Total K, mEq/kg " " "	63.44 ± 3.1	68.97 ± 1.6	90.81 ± 2.7 *	65.20 ± 2.7
e.c.f.v., ml/kg " " "	389.1 ±16.3	377.4 ± 9.5	360.4 ± 7.7	377.4 ± 8.1
Na_i, mEq/kg " " "	50.4 ± 3.3	44.4 ± 1.7	47.8 ± 2.4	52.1 ± 1.9 †
K_i, mEq/kg " " "	61.52 ± 3.1	67.11 ± 1.6	79.12 ± 2.80*	63.19 ± 2.70
No. of rats	8	8	8	8

± = standard error. * $p < .02$ compared with Group 1. † $p < .02$ compared with Group 2.

liter: NaCl, 115.0; KCl, 5.0; $NaHCO_3$, 25.0; NaH_2PO_4, 1.2; $CaCl_2$, 2.1; $MgSO_4$, 1.2; dextrose, 11.0; calcium disodium versenate, 0.026. To this was added 4% Plasdone (polyvinyl pyrrolidine) as plasma colloid substitute. The base of the tail was then ligated and the perfusate changed for one modified by addition of 400 mg% inulin (about 8 mM). This was then perfused without interruption for 30 minutes, the time necessary for inulin equilibration in this system.

Following this preliminary procedure, the perfusion, still with inulin, was either continued unchanged for a further 20 minutes (Group 1), or changed for one in which 30 mEq/liter of Na as NaCl was replaced isosmotically by lactose (Group 2), by an equivalent amount of KCl (Group 3), or by equivalent choline chloride (Group 4). Lactose rather than the more conventional sucrose was used in Group 2 to avoid interference by glucose in the inulin method. At the end of this time a length of about 13 cm of tail artery was excised in less than 2 minutes by stopwatch, then quickly dissected free of adventitia and placed in a pre-weighed, stoppered bottle for immediate weighing. Inulin, Na, and K in the tissue as well as in the venous effluent collected in the terminal minute of perfusion were analyzed by conventional methods modified for the small samples available here(2). Similar 3 and 8 minute runs were also carried out but are not described since equilibration was not equally advanced in all groups at these earlier periods.

Results. The results are presented in Table I. The primary chemical data show that although total water is the same in all groups and effluent [Na] is reduced equally in all test groups, the tissue lost more of its total Na when perfused with media in which Na was replaced by either lactose or by K than by choline. The tissue, of course, gained K in Group 3.

Since there was little difference between any of the test groups in the transcellular distribution of water as measured with inulin, the derived data for ionic partition show a withdrawal of Na from the cellular space in Group 2 in which lactose served as Na replacement, a similar but lesser withdrawal of cell Na in Group 3 with KCl as replacement, and no loss of cell Na in Group 4 where choline chloride was the substitute.

There was no change in total K or in its partition except for that induced in Group 3. Here, a substantial part of the added K found its way into the cellular space.

Discussion. The tail artery perfused with 3 conventional low sodium media loses sodium from the "cellular space" when lactose and, to a lesser degree, when potassium chloride are the substitutes. No such withdrawal occurs with choline chloride as replacement. (We here define "cellular space" as cells and those paracellular elements not permeated by inulin.) Other investigators have already

shown that much of the sodium burden in the cellular space of smooth muscle is rapidly exchangeable(3,4,5). It has not been shown before, however, that the mobilization of sodium depends so directly on the composition of the medium.

In previous experiments in which we monitored Na^+ and K^+ activity with glass electrodes during closed circuit perfusion of the rat tail with plasma, we obtained similar information. There too we found that sodium was readily and rapidly mobilized from the tail tissues when its concentration in the medium was reduced by substitution with sucrose but not by substitution with choline. Peripheral vascular resistance fell in the first but not in the second instance. Here, we have observed that at least some of the mobilized sodium comes from the artery itself; this supports the idea that the transcellular distribution of Na^+ is a determinant of vascular smooth muscle tension.

In our previous study with closed circuit perfusion of the rat tail no withdrawal of sodium from tail tissues was noted when potassium chloride replaced sodium chloride. Here, by contrast, open circuit perfusion resulted in some withdrawal of sodium from the cellular space of the tail artery. The two experiments are not comparable in degree, however, for when the system was closed, Na^+ concentration was reduced some 14 mEq/liter whereas here, in open circuit perfusion, Na^+ concentration was reduced some 25 mEq/liter. It is worth noting that a withdrawal of sodium from the cellular space was measured with sucrose or potassium which are thought to pass readily through the smooth muscle cell membrane but not with choline which is thought to be excluded(3).

Since it is thus a fact that sodium is mobilized and removed from the cellular space of a small artery to varying degrees by different types of sodium-substituted media, experiments which use a change in the sodium concentration of a perfusate as a test variable must obviously be interpreted with caution in terms of the resultant transcellular ionic equilibrium rather than in terms of the imposed change alone.

Summary. The content and distribution of Na, K, and water in the rat tail artery were determined after perfusion *in situ* for 20 minutes with media in which 30 mEq/liter of NaCl was replaced by equivalent amounts of lactose, KCl, or choline chloride. Inulin was used as index of the extracellular space. Equilibrium attained with choline chloride substitution could be explained entirely in terms of simple mixing in the free extracellular fluid. Equilibrium attained with lactose substitution involved a withdrawal of Na from the "cellular space." A similar but smaller loss of Na from the cellular space was also observed with KCl substitution but this was overshadowed by the progressive entry of K into this space. Thus the vascular tree contains, in a phase not accessible to inulin, a large pool of Na which is potentially capable of ready mobilization.

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