

changed by addition of choline. In one of 4 experiments betaine caused a significant acceleration of abscission but in the other experiments only a small effect was observed.

These results with betaine and choline additions are not unexpected since most enzyme systems are quite specific in their action. The slight effect of betaine can be explained by the greater molecular similarity of betaine to methionine. In addition, betaine, like methionine, occurs naturally in plants. Additional experiments concerning enzymes in abscission are needed to characterize an overall mechanism of the phenomenon of abscission.

Summary. Methionine (presumably as a methyl donor) accelerates floral abscission in tobacco. IAA retards abscission. When the two factors are added to developing ovaries in combination, in general the effect is one of

diminishing the effect of either when added alone. However, high concentrations of IAA completely overcome the accelerating effect of methionine.

1. Laibach, F., *Ber. deut. Ges.*, 1933, v51, 336.
2. Osborne, D., *Nature*, 1955, v176, 1161.
3. van Overbeek, J., Blondeau, R., Horne, V., *Am. J. Botany*, 1955, v42, 205.
4. Hotta, Y., Ota, T., *Bot. Mag., Tokyo*, 1956, v69, 126.
5. Yager, R. E., Muir, R. M., *Science*, v127, 82.
6. Lee, E., *Ann. Bot., Lond.*, 1911, v25, 51.
7. Ordin, L., Cleland, R., Bonner, J., *Proc. Nat. Acad. Sci.*, 1955, v41, 1023.
8. Byerrum, R., Sato, C., *Proc. Plant Physiol. Meetings*, 1956, v31, 37.
9. Facey, V., *New Phytol.*, 1950, v49, 103.

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Effects of Adrenalectomy and Aldosterone on Proximal and Distal Tubular Sodium Reabsorption.* (24338)

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Aldosterone is generally believed to be the most important of sodium regulating hormones, but its site of action is still controversial. Recently, Barger, Berlin, and Tulenko (1) demonstrated direct renal effect of aldosterone, but the precise renal site of action of the hormone has remained unknown. Our technic of stop-flow analysis(2,3) has been used to localize which site of sodium reabsorption is influenced by adrenalectomy and aldosterone.

Principle of stop flow analysis. By administration of an osmotic diuretic (mannitol) to the dog, very high rates of urine flow can be established. If during this period the ureter is clamped, intratubular pressure rises to equal net filtration pressure, at which point glomeru-

lar filtration ceases(2). During this period of stopped ureteral flow, the concentration of any substance in the intratubular fluid column will be changed along the nephron, depending upon how the individual segments handle this substance. The mannitol retards water reabsorption and provides a menstruum against which electrolyte concentrations may be changed. Upon release of occlusion, these concentration patterns are obtained in approximately 0.5 ml serial urine samples which segment this pattern into an ordered array, best pictured on a graph if concentration of each sample is plotted against accumulative urine volume. An elevation in p-aminohippurate (PAH) concentration in the pattern signals a proximal position, and a depression in the sodium pattern delineates a distal area (2,3).

Methods. Five experiments were performed on mongrel dogs weighing 11-20 kg, adrenalect-

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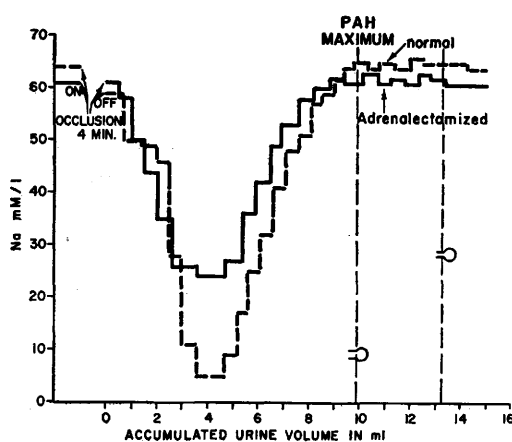


FIG. 1. Comparison of distal tubular sodium reabsorption during ureteral occlusion in a normal and in an adrenalectomized dog.

tomized through a single mid-line abdominal incision. Cortisone acetate, 100 mg intramuscularly, was given at time of operation and on the day preceding it. Thereafter, dosage of cortisone acetate was gradually lessened, final maintenance dosage varying from 10-25 mg/day. Dogs were given a normal diet supplemented with 100 mM of sodium/day. No animals were employed until at least one week after adrenalectomy. Two hours before stop-flow procedure, 3 dogs were given their normal maintenance dose of cortisone acetate intramuscularly, whereas all steroid therapy had been discontinued 2 days previously in the other 2 dogs. The animals were anesthetized with 30 mg/kg of sodium pentobarbital injected intraperitoneally. Through a small flank incision one ureter was catheterized with polyethylene tubing pushed up into the renal pelvis. A constant intravenous infusion was supplied at 10 ml/min. Infusions contained 15-20% mannitol plus PAH and creatinine dissolved in Ringer's solution. When urine flow stabilized at some high level (5-13 ml/min), several occlusions (2½-4 min) were performed after which 10-40 µg aldosterone was given intravenously. Serial occlusions were then performed at intervals of approximately 45 minutes.

Results. Distal sodium reabsorption. The dashed curve in Fig. 1 is a typical sodium concentration pattern obtained during stop-flow in a normal non-adrenalectomized dog. The

sodium concentration of free flow diuretic urine collected immediately before occlusion is 63 mM/l. There is a fall in concentration as distal fluid enters the urine collector after release of occlusion. The lowest concentration reached, 5 mM/l, represents that sample acted upon by a maximum number of distal tubules during occlusion, *i.e.*, the best distal sample(3). As fluid from the loops and proximal tubules enters the collector, the sodium concentration rises and forms a plateau at the original free flow concentration. The summit of PAH concentration curve (not shown in Figure) indicates the best stop flow proximal sample to be at 10 ml on the horizontal scale(3). The sodium concentration pattern of the adrenalectomized dog, as indicated by the solid line, is in striking contrast to this normal pattern. Sodium concentrations of the free flow urine and proximal plateau are normal, but the lowest concentration achieved by the distal tubule is now 24 mM/l.

Ability of the normal dog to reduce distal sodium concentrations to extremely low levels during occlusion is one of the most constant findings in stop-flow analysis. In 59 normal occlusions the mean distal sodium concentration was 4.9 mM/l with standard deviation of 2.6 mM/l. In only 2 experiments did the distal value exceed 10 mM/l. In 5 adrenalectomized dogs (Table I), however, distal sodium concentrations ranged from 8 to 24 mM/l with a mean of 13.6 mM/l and standard deviation of 6 mM/l. Adrenalectomy has interfered with the ability of distal tubule to reduce sodium concentration during occlusion ($P = <.001$). Moreover, as time length of occlusion was increased in consecutive occlu-

TABLE I. Comparison of Sodium Concentrations during Ureteral Occlusion in Distal Tubules of 5 Adrenalectomized Dogs before and after Aldosterone.

| Distal sodium conc., mM/l | |
|---------------------------|--------------|
| Adrenalectomized control | Aldosterone* |
| 24 | 8 |
| 12 | 10 |
| 12 | 3 |
| 12 | 5 |
| 8 | 6 |

* 10-40 µg aldosterone given intrav. immediately after completion of control occlusion.

sions the distal sodium concentrations remained identical, *i.e.* the distal tubule was not capable of further lowering concentration even when allowed more time.

The effect of aldosterone on the adrenalectomized dogs is shown in Table I. In all dogs, distal sodium concentrations were normally lowered during occlusions performed approximately 2 hours after completion of control occlusion and intravenous injection of aldosterone. This ability of aldosterone to increase distal sodium reabsorption may have one of several explanations. As sodium is actively transported out of the distal tubule there is no doubt some passive diffusion with the concentration gradient back into the tubule. Aldosterone may either activate the enzyme systems responsible for active sodium transport outwards or, less likely, decrease passive diffusion inwards of sodium through changes in permeability characteristics of the tubular cells or membrane.

Proximal sodium reabsorption. As described above, sodium concentrations of the best proximal stop flow samples are equal to their respective free flow values in both the normal and adrenalectomized dogs. This indicates that during occlusion the proximal tubule could not change sodium concentration from its free flow value in the proximal tubule(3,4). As calculated by methods described previ-

ously(4), sodium concentration of proximal reabsorbate is equal to that of plasma in both normal and adrenalectomized animals, and is not changed detectably by administration of aldosterone. However, the data collected thus far do not conclusively indicate that the volume of proximal sodium and water reabsorbed is not affected by adrenalectomy and aldosterone. Such experiments are now in progress.

Summary. The technic of stop-flow analysis has been used to localize the site of renal sodium reabsorption which is affected by adrenalectomy and aldosterone. Following adrenalectomy, the distal tubule was not able to reduce sodium concentration to the low value achieved during stop-flow in normal dogs. Following aldosterone administration this distal reabsorptive capacity was restored. No conclusion could as yet be made regarding the effects of aldosterone on the proximal tubule.

1. Barger, A. C., Berlin, R. D., Tulenko, J. F., *Endocrin.*, 1958, v62, 804.
2. Malvin, R. L., Wilde, W. S., Sullivan, L. P., *Am. J. Physiol.*, 1958, v194, 135.
3. Wilde, W. S., Malvin, R. L., *ibid.*, 1958, v195, 153.
4. Malvin, R. L., Wilde, W. S., Vander, A. J., Sullivan, L. P., *ibid.*, in press.

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Contact Transmission of Poliomyelitis Virus Among Monkeys.* (24339)

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The problem of transmitting poliovirus from infected to normal animals is of interest and importance to humans because of its value as a model in the study of the natural transmission of the disease. As early as 1912, Levaditi and Danulesco(1) reported that normal Rhesus monkeys housed with infected monkeys did not develop poliomyelitis. Sabin

and Winsser(2) were not able to demonstrate any evidence of poliovirus in normal monkeys associated with other animals receiving type 2 virus orally. On the positive side, Faber and his colleagues(3) were able to detect lesions typical of poliomyelitis in two of the cranial nerve ganglia of uninoculated monkeys housed in the same room with infected animals. Howe and Bodian(4) isolated poliovirus from the stools of two chimpanzees which were

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