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RENAL EXCRETION OF POTASSIUM IN THE SHEEP

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SUMMARY

1. Observations were made on the daily intake and excretion of potassium and sodium in sheep housed in metabolism cages and fed once daily.

2. The diet of chaffed hay and crushed oats provided 400–600 m-moles K and 50–60 m-moles Na daily. About 90 % of the K was excreted in the urine, and over 90 % of the Na was found in the faeces.

3. In two groups of three experiments on each of three sheep, the urinary responses to intra-ruminal dosing just before feeding of (i) 1 l. distilled water, (ii) 1 l. 0·25 N-KCl, and (iii) 1 l. 0·125 N-NaCl, were studied. In the first group, urine was collected via the urine/faeces separator of the metabolism cage, whereas for part of the experiments in the second group it was collected by an indwelling bladder catheter.

4. In a third group of experiments with the same sheep, the effects on urinary excretion of K and Na of intra-ruminal dosing with (i) 1 l. distilled water, (ii) 1 l. 0·25 N-K acetate, and (iii) 1 l. 0·25 N-Na acetate were investigated. During part of these experiments urine was again collected via an indwelling bladder catheter. With chloride, 82 % of the additional potassium was excreted in urine in the 24 hr after dosing, but with acetate only 65 %. For sodium, the corresponding figures were 12–40 % with chloride and 43 % with acetate.

5. In most experiments, the administration of K salts produced a marked kaliuresis and, in spite of the low sodium intake, a natriuresis as well, which did not usually coincide with maximum K excretion. No adequately tested explanation appears to exist for the natriuresis observed in response to treatment with K salts.

INTRODUCTION

Herbivorous animals such as cattle and sheep normally have diets higher in potassium and lower in sodium than those of man or dogs, but until the recent publication of English (1966) there was little detailed information

on the excretion of dietary potassium by sheep maintained under controlled conditions. Anderson & Pickering (1962) reported the effects on renal electrolyte excretion of intravenous loads of KCl in the cow.

The present study was initiated to investigate the excretion of dietary potassium, and to study the renal response to sudden increases in the K^+ load presented to the digestive system of the sheep. A preliminary account of this work has been given as a demonstration to the Physiological Society (Dewhurst & Harrison, 1966) and in a lecture which has now been published (Keynes & Harrison, 1967).

METHODS

Sheep. Clun Forest ewes, aged 1½–2 yr and weighing 40–50 kg, were transferred from the Institute's farm to the sheep observation house 3–4 weeks before surgical preparation. The normal maintenance ration was 1000 g chaffed hay, largely cocksfoot or cocksfoot and lucerne, and 200 g oats given daily as one feed between 8.45 and 9.15 a.m. Water was allowed *ad libitum* and there was free access to a mineral salt lick except when the animals were under experiment.

Surgical preparation. A permanent rumen fistula was established in each sheep using a modification of Jarrett's (1948) type of cannula moulded in polyvinyl chloride (Welvic M 10/18, I.C.I. Ltd.). Surgery was performed under general anaesthesia (see Harrison, 1964) with aseptic precautions; at least 1 month was allowed after operation before any experimental observations were made.

Experimental procedure. The sheep were placed in metabolism cages in which urine and faeces could be collected separately with negligible cross-contamination of the samples. They continued to receive the same daily ration, but from a well-mixed bulk supply which was sufficient to last for the period of observation, and were usually fed at 9.30 a.m. when the faeces and urine containers were changed and the previous day's food and water consumption measured. Four litres of distilled water were allowed each day and part always remained unconsumed at the end of each 24 hr period. Sheep were allowed between 2 and 5 days to become accustomed to existence in a metabolism cage before observations were begun.

Collection of urine. For collection periods longer than 1 hr urine was drained into a covered polythene receiver beneath the urine-faeces separator of the metabolism cage; these samples therefore depended on voluntary micturition. At the start of each experiment the urine separator was washed with glass-distilled water, and the polythene receivers were always rinsed several times with glass-distilled water and then dried before use. The separators were rinsed with glass-distilled water during an experiment if debris accumulated on them.

For collection periods of 1 hr, urine was continuously drained from the urinary bladder by an indwelling bladder catheter. A latex or plastic 14 FG Foley catheter with 5 ml. bulb was introduced into the bladder under epidural anaesthesia in the afternoon of the day before the experimental observations. For the induction of epidural anaesthesia, a small amount of 2% xylocaine (Xylocaine hydrochloride with adrenaline, Astra-Hewlett Ltd.) was injected subcutaneously over the region of the sacro-coccygeal junction before the introduction of a Wilfred Harris needle through the sacro-coccygeal space. Three to eight millilitres of 2% procaine (Procaine hydrochloride B.P. in normal saline, Evans Medical Ltd.) were injected to produce paralysis of the tail and sufficient loss of sensation in the perineo-vulval region to overcome the normal reaction to manipulation in this region. On a few occasions, slight motor paralysis of the hind limbs was produced but the animals rested quietly in the cage until recovery occurred. A modified Cusco vaginal speculum was

used, and the urethral orifice could be clearly seen for catheterization when illuminated by a headlamp. The tip of the catheter was lubricated with sterile K–Y jelly (Johnson and Johnson Ltd.) and, after inflation of the bulb with sterile water, the external end was lightly tied to the fleece above the right hock. During an experiment the catheter was connected to a length of polythene tubing from which urine drained into a measuring cylinder.

Collection of faeces. Faeces were collected for 24 hr periods in the polythene receiver of the metabolism cage and weighed with an accuracy of $\pm 0{\cdot}5$ g on a single pan Mettler balance (Model K 5). A representative aliquot of each sample was obtained and stored at $-20°$ C in a small screw-topped polythene bottle until analysed for wet, dry and ash weights and electrolyte content.

Analytical. Urinary electrolytes were estimated in duplicate. If duplicates differed by more than 2 % the estimation was repeated. Sodium and potassium were estimated by means of an EEL flame photometer (Model A) calibrated with mixed Na/K standards to read 1 m-equiv/l. Na^+ and K^+ respectively for full-scale deflexion. Chloride was estimated by electrometric titration (Sanderson, 1952).

Osmolality was determined by freezing-point depression using an Advanced Instruments Inc. osmometer (Massachusetts, U.S.A.).

Faecal electrolytes were estimated in triplicate on 10–20 g aliquots after allowing the deep-frozen samples to thaw completely in the closed container. The aliquots were dried at 100° C for dry weight determination and ashed for not less than 24 hr at 650–750° C. The ashed specimens were dissolved in 6 ml. 0·1 N-HNO_3 and made up to 50 ml. with de-ionized water. The supernatants were further diluted for estimation of Na and K as with urine.

A small but unmeasured amount of evaporation was to be expected in urine and faeces samples collected in the urine–faeces separator of the metabolism cage. Because of the slight underestimation of faecal water, faecal electrolytes were calculated on a dry-weight basis (m-equiv/kg). Urinary electrolyte concentrations (m-equiv/l.) are likely to be slightly greater than actually secreted by the kidney but neither of these errors affected the estimation of the daily output of electrolytes in urine and faeces.

Several representative samples of the bulk food used in the preliminary experiments were taken during each experiment and analysed for wet, dry and ash weights and electrolyte content as described for faeces.

RESULTS

Preliminary observations

Intake and daily excretion of potassium and sodium. When fed the maintenance ration of 1000 g chaffed hay and 200 g crushed oats, the sheep were receiving 400–600 m-moles of potassium and 50–60 m-moles of sodium daily. Urinary potassium excretion accounted for approximately 90 % of the total K recovered in urine and faeces, whereas faecal sodium represented over 90 % of the total Na recovered in urine and faeces. Data on the daily output of electrolytes in urine and faeces are given in Table 1. All periods of observation extended over 5 days or longer. The urinary [K^+] varied from 350 to 800 m-equiv/l.; [Na^+] from 0·3 to 30 m-equiv/l.; and [Cl^-] from 100 to 300 m-equiv/l. The dry matter (D.M.) content of faeces ranged from 36·6 to 45·4 %; K content from 40 to 180 m-equiv/kg D.M. and Na content from 20 to 100 m-equiv/kg D.M.

Feeding behaviour. During the 24 hr between successive feeds most of the ration was eaten and only hard, possibly unpalatable, fragments of chaff

were left. Although complete records of the daily feeding cycle were not kept, the following general pattern was observed. When fed, the sheep ate the oats immediately and during the next 2–3 hr about half the hay was eaten. This was followed by a period of intermittent rumination which lasted until mid to late afternoon when there was another bout of eating. By nightfall only a small quantity of hay remained.

TABLE 1. Daily excretion of Na and K (mean values ±S.E.) in the urine and faeces of sheep receiving the maintenance ration

			K excretion (m-mole/day)			Na excretion (m-mole/day)		
Sheep	Month (1964)	No. of days	Urine	Faeces	% in urine	Urine	Faeces	% in urine
Fatima	April	11	369 ±10·2	39·9 ±5·2	90·2	3·6 ±1·3	25·5 ±2·4	12·4
Ada	April	12	373 ±7·7	53·0 ±7·7	87·5	3·0 ±1·4	37·4 ±2·3	7·4
Agnes	June	15	487 ±22·4	32·1 ±2·1	93·8	7·7 ±2·0	29·5 ±2·2	20·7
Fuchsia	August	5	506 ±18·5	43·7 ±4·1	92·1	0·7 ±0·0	15·5 ±1·1	4·3
Ada	August	5	558 ±23·8	45·3 ±8·4	92·5	0·9 ±0·4	28·2 ±2·1	3·1
Agnes	August	5	545 ± 23·1	45·0 ±3·4	92·4	0·4 ±0·1	23·4 ±2·1	1·7
Mean of means			473	43·2	91·4	2·7	26·6	8·3

The sheep usually drank during feeding and it was frequently noted that up to 1 l. of water might be drunk at one time. Since the D.M. of the food was approximately 90 % of its weight, it is calculated that the water consumed daily (2–3·5 l.) was sufficient to reduce the proportion of D.M. in the total intake to 23–31 %.

Collection of urine at intervals of 6 hr. In three experiments during which daily observations of urinary excretion were being made, the urine was collected at 6 hr intervals after feeding (i.e. at 3.30 p.m., 9.30 p.m., 3.30 a.m. and 9.30 a.m.) on the third day of experiment. The more frequent collection and disturbance of the sheep at unaccustomed times produced no obvious change in urine volume or electrolyte excretion.

The renal response to the administration of sodium and potassium salts by rumen fistula

Fairly large doses of Na and K salts were given by rumen fistula. In the first group of nine experiments (group I), three treatments were used: (i) 1 l. of distilled water (control), (ii) 1 l. 0·25 N-KCl, (iii) 1 l. 0·125 N-NaCl on each of three sheep ('Ada', 'Agnes' and 'Fuchsia'). Each dose was given by gravity drip into the rumen at 9.30 a.m. over a period of 15 min and

feeding was delayed until approximately 9.50 a.m. On the day of treatment the urine was collected at intervals of 6 hr.

Control administration of water. When compared with the voluntary drinking on the days before experimental treatment, drinking on the day of treatment was reduced in all three sheep. In two experiments the reduction was less than 1 l. and one sheep showed a rise in urine volume in the 24 hr following treatment. There was no marked change in electrolyte excretion.

Administration of KCl. In all three sheep there was an increase in urine volume and a marked rise in potassium excretion. The increase in K excretion appeared during the first and persisted throughout all four 6 hr

TABLE 2. Daily excretion of Na, K and Cl in the urine of sheep given 1 l. of 0·25 N-KCl by rumen fistula at the start of day 0. Urine was collected at 6 hr intervals on day 0 but at 9·30 a.m. only on days −2, −1 and +1 (group 1)

Sheep	Day	Water drunk (l.)	Urine volume (ml.)	Urine K (m-mole/day)	Urine Na (m-mole/day)	Urine Cl (m-mole/day)
Fuchsia	−2	2·9	960	522	0·8	214
	−1	3·2	1280	449	0·3	272
	0	2·5	1900	737	41·8	473
	+1	2·7	1130	538	0·8	258
Agnes	−2	2·9	1870	631	38·5	223
	−1	3·0	1800	561	16·6	209
	0	3·6	2910	708	109·3	418
Ada	−2	2·3	1100	523	1·2	257
	−1	2·6	1180	553	1·1	238
	0	2·9	2290	770	52·6	511
	+1	2·0	1090	516	0·9	177

periods following treatment. Sodium excretion on the day of treatment was considerably increased despite the fact that before treatment there appeared to be a net retention of sodium. Chloride excretion was elevated above control levels during the first three 6 hr periods. The data for these experiments are given in Table 2. The natriuretic response was not always synchronous with maximal urine flow nor with maximal potassium excretion.

Administration of NaCl. There was a slight increase in urine volume for each sheep; two animals showed a slight and one a more marked rise in sodium excretion. The natriuresis in response to 125 m-moles of NaCl was less than that observed after treatment with 250 m-moles KCl. In all experiments there was an increased excretion of chloride but no consistent change in potassium excretion (see Table 3).

Hourly observations on urinary excretion

To permit more detailed study of the responses described, the experiments were repeated with hourly sampling of urine by means of a urethral

catheter. To avoid, if possible, any effects of emotional disturbance on urinary function in the conscious sheep (see Andersson, 1955), catheterization was performed under epidural anaesthesia in the afternoon of the day before the experimental treatment (see p. 610). Using the same three sheep as in the previous experiments, the experimental protocol was modified so that hourly collections of urine were made during the hour before and for the 12 hr after treatment. The subsequent 12 hr specimen

TABLE 3. Daily excretion of Na, K and Cl in the urine of sheep given 1 l. of 0·125 N-NaCl by rumen fistula at the start of day 0. Urine was collected at 6 hr intervals on day 0 but at 9.30 a.m. only on days −2, −1 and +1 (group I)

Sheep	Day	Water drunk (l.)	Urine volume (ml.)	Urine K (m-mole/day)	Urine Na (m-mole/day)	Urine Cl (m-mole/day)
Fuchsia	−2	2·5	800	428	1·6	183
	−1	2·5	840	442	3·1	210
	0	2·6	960	495	8·1	243
Agnes	−2	3·5	1920	561	0·4	272
	−1	3·5	1790	569	0·4	226
	0	2·9	2200	423	7·7	314
	+1	3·4	1815	550	13·6	268
Ada	−2	2·5	1090	556	0·8	242
	−1	2·8	1310	638	0·3	260
	0	2·0	1430	547	37·8	390
	+1	2·5	1330	509	4·2	298

was collected after voluntary micturition with separation in the metabolism cage. Two groups of experiments were carried out. In the nine experiments of group II the treatments were as for group I, namely (i) 1 l. distilled water, (ii) 1 l. 0·25 N-KCl, (iii) 1 l. 0·125 N-NaCl. In the third group of ten experiments (group III) the treatments were: (i) 1 l. distilled water, (ii) 1 l. 0·25 N potassium acetate, (iii) 1 l. 0·25 N sodium acetate.

Pre-feeding diuresis. Hourly collections of urine were begun at 8.30 a.m. At 9.30 a.m. the feed box was removed for refilling and the electrolyte solutions given by fistula before the animals were fed. All three sheep often showed a marked increase in urine volume either between 8.30 and 9.30 a.m. or after the removal of the feed box. Though the urine collected during this time was of low osmolality and low electrolyte concentration, the hourly output of potassium was similar to the mean hourly excretion observed during the previous 48 hr.

Control administration of water. Control experiments from groups II and III did not show any marked differences and typical experiments from each group are shown in the left hand sections of Figs. 1 and 2. After feeding there was always a delay of 1–3 hr before any significant rise in electrolyte excretion occurred. Where there had been a pre-feeding diuresis, urine volume and electrolyte excretion fell to near the mean level

for the preceding 48 hr. After the delay, potassium and chloride excretion rose and maximal K excretion occurred about 5–6 hr after treatment and feeding. Urine volume was variable but generally rose during the period of rising K excretion. When a rise in Na excretion occurred it accompanied

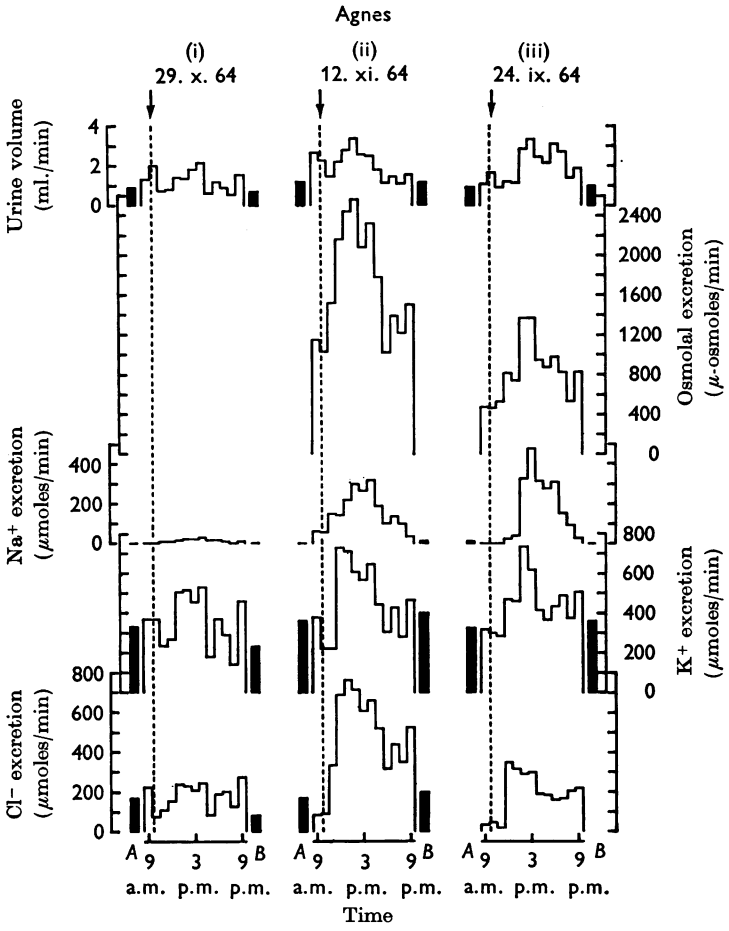

Fig. 1. Urinary excretion after administration by rumen fistula (at arrow) of (i) 1 l. water, (ii) 1 l. 0·25 N-KCl, and (iii) 1 l. 0·125 N-NaCl. Animal fed immediately after treatment. Urine collected at hourly intervals by bladder catheter for 1 hr before and 12 hr after treatment. *A* represents mean excretion during 48 hr preceding experiment and *B* represents mean excretion for period 12–24 hr after treatment.

high or rising K excretion. The data for 12 × 1 hr samples and the 12 hr overnight sample were used to calculate the 24 hr excretion data which were compared with the mean data for group I. The only important

difference was that the Na output in the experiments with bladder catheterization was higher than in the earlier group.

Administration of KCl (group II). A representative experiment of this group is shown in the middle section of Fig. 1. Peak values of excretion

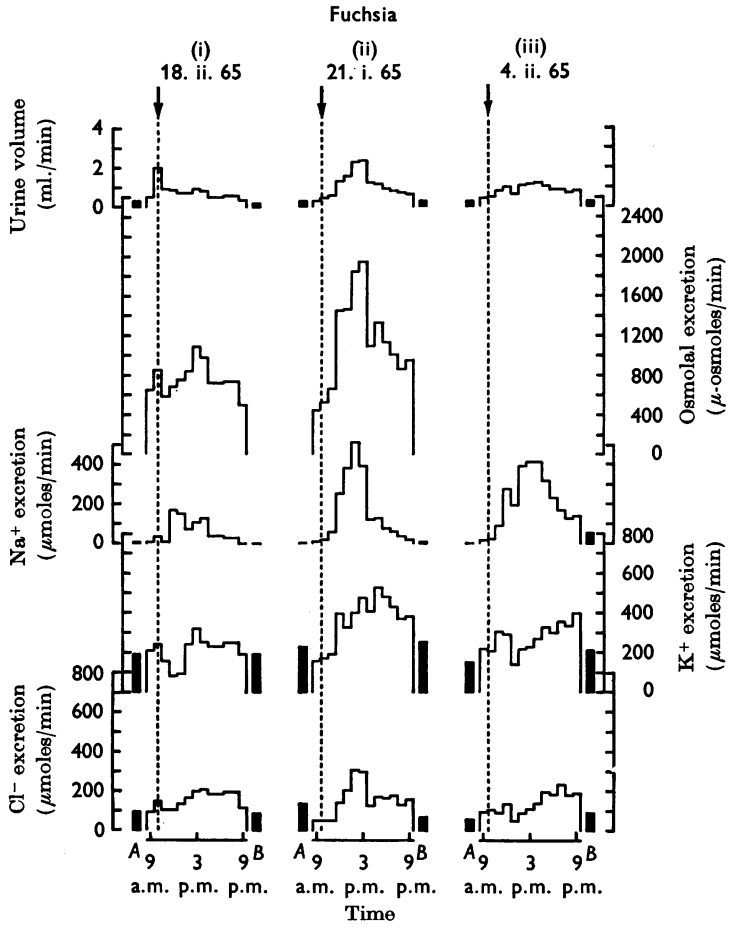

Fig. 2. Urinary excretion after administration by rumen fistula (at arrow) of (i) 1 l. water, (ii) 1 l. 0·25 N-K acetate, and (iii) 1 l. 0·25 N-Na acetate. Animal fed immediately after treatment. Urine collected at hourly intervals by bladder catheter for 1 hr before and 12 hr after treatment. *A* represents mean excretion during 48 hr preceding experiment and *B* represents mean excretion for period 12–24 hr after treatment.

were higher than in the control experiments and occurred after only 2–3 hr. There was a natriuresis which was maximal 1–2 hr after the peak of the kaliuresis and was not necessarily accompanied by increased urine

volume. Increased chloride excretion began earlier and reached higher levels than in the control experiments. The response to KCl administration did not differ appreciably from that seen in the experiments with 6 hr collections of urine by voluntary micturition.

Administration of NaCl (group II). A typical experiment for this group is shown in the right-hand section of Fig. 1. As in the water control experiments of this series, K excretion rose 2–3 hr after treatment. A natriuresis occurred slightly after the peak of the normal kaliuretic response to feeding. As with KCl there were no marked differences in the calculated 24 hr data between these experiments and those described earlier.

From the combined 24 hr data for both groups of experiments in which the chloride salts of Na and K were used (Table 4), it can be seen that after the administration, by rumen fistula, of 250 m-moles of KCl, approximately

TABLE 4. The 24 hr excretion (means ± S.E.) of Na, K and Cl in the urine of sheep given 1 l. of distilled water; or 1 l. of 0·25 N-KCl; or 1 l. of 0·125 N-NaCl; or 1 l. of 0·25 N-potassium acetate; or 1 l. 0·25 N-sodium acetate; by rumen fistula at the start of each experiment

Solution given...	Water	KCl	NaCl	K acetate	Na acetate
No. of experiments...	8	6	6	4	3
Na/24 hr (m-moles)	26·9*	82·5	49·3	75·0	137·5
	± 8·4	± 14·2	± 18·3	± 20·0	± 31·4
K/24 hr (m-moles)	454·8	690·0	509·8	528·4	406·0
	± 36·0	± 35·2	± 28·6	± 28·8	± 42·3
Cl/24 hr (m-moles)	228·3†	457·3	332·9†	192·3	188·7
	± 21·8	± 17·9	± 25·7	± 18·8	± 18·2

* Sodium excretion data in the water control experiments on three non-catheterized animals (group 1) have been omitted since they had a very much lower mean excretion of 2·0 ± 0·6.

† Chloride excretion data incomplete. The figures represent the mean of seven water control experiments and five NaCl experiments.

80 % of the additional K load and 90 % of the additional Cl load were eliminated in urine in the next 24 hr. There was also a marked increase in Na excretion. After the administration by rumen fistula of 125 m-moles of NaCl, approximately 40 % of the additional Na load and 80 % of the additional Cl load were eliminated in urine in the next 24 hr.

Administration of potassium acetate (group III). In comparison with the effect of intra-ruminal KCl, potassium acetate produced a more gradual rise in K excretion and its maximal effect was less. In the experiment on sheep 'Ada' there was no obvious increase in K excretion and the animal was disturbed by the presence of the catheter and did not ruminate. The experiment was therefore repeated when a K response similar to that in the other sheep was observed, but in neither experiment on 'Ada' was there a clearly defined natriuresis. In the experiments on 'Fuchsia' and 'Agnes' there was a definite natriuresis with maximal rates of excretion occurring

1–3 hr earlier than was observed after KCl administration, and preceding instead of following the peak of potassium excretion (see middle section of Fig. 2). There was no change in chloride excretion except in 'Fuchsia' where an increase coincided with the natriuresis.

In comparison with the effects of KCl administration, K given as the acetate appeared to be less completely eliminated in urine in the first 24 hr (see Table 4). There was a natriuresis in response to either salt. The chloride of KCl appeared to be almost completely eliminated in the urine in 24 hr whereas with acetate treatment there was no increase in chloride excretion.

Administration of sodium acetate (group III). The calculated daily output of electrolytes for the 24 hr after treatment are given in Table 4 and a representative experiment is shown in the right-hand section of Fig. 2.

Potassium and chloride excretion did not differ appreciably from that observed in the control experiments of this group. There was a moderate natriuresis in all three experiments.

A comparison of the 24 hr data for the administration of sodium as the chloride and acetate salt showed that chloride excretion in response to NaCl was increased to give nearly quantitative elimination in 24 hr, as was seen following KCl administration (see Table 4), whereas there was no rise in chloride excretion after sodium acetate.

DISCUSSION

The high K and low Na content of the diet used in these experiments is typical of many forages grown in the inland areas of this country under modern systems of pasture management. It was calculated that the daily water consumption was sufficient to reduce the D.M. intake of the food to 23–31 %, which is similar to the D.M. content of 21–25 % for fresh grass swards (Evans, 1961).

The finding that on this diet 90 % of the K recovered in urine and faeces was in urine confirms the findings of English (1966) who worked with sheep which were on a diet of lower K:Na ratio than in our experiments. In view of this it is perhaps not unexpected that at least 80 % of an additional load of potassium should also be excreted in urine. In the three experiments with KCl administration for which estimations of faecal electrolytes were made, there was no rise in faecal $[K^+]$ in the 48 hr after treatment.

The marked diuresis seen in many experiments before feeding was probably due to an inhibition of the release of anti-diuretic hormone (ADH) (see Andersson, 1955). Anderson (1961) observed a diuresis in cattle subjected to the discomfort of arterial puncture during continuous collection of urine by an indwelling urethral catheter and found that repeated

experiments on the same cows produced a form of conditioned diuresis associated with the preliminary procedure of clipping, swabbing and anaesthetizing the site of puncture. It is possible that the diuresis seen in our experiments was related to the laboratory and experimental conditions described. Stacy & Brook (1964*a*) reported an anti-diuretic response to feeding and subsequently (Stacy & Brook, 1965) published evidence of ADH activity in post-prandial urine but not in urine from unfed animals.

A delay of 2–3 hr occurred between feeding and the appearance of any large increase in renal K excretion. The delay was reduced but not abolished when additional loads of K were given by rumen fistula. Anderson & Pickering (1962) found that intravenous infusion of KCl in the cow produced a marked rise in K excretion within the first 30 min collection period. In later experiments on sheep in this laboratory we have found that KCl or potassium acetate infused by portal-vein catheter produced a rise in K excretion within 15–20 min. It is therefore likely that the delayed rise in K excretion seen in the present experiments is the result of delayed absorption of K and this phenomenon may be dependent upon movements of digesta from the rumen to another region of the digestive tract. In his studies on the flow of digesta from the omasum, Ash (see Phillipson & Ash, 1965) found that the introduction of varying quantities of rumen fluid into the rumen increased the flow from the omasum in proportion to the quantity introduced. In our experiments, therefore, the addition of 1 l. of solution to the rumen was likely to cause a period of increased flow of material from the rumen. When potassium solutions were given it may be presumed that digesta of higher K content flowed to the sites of absorption and, unless large amounts of K were absorbed directly from the rumen, this could account for the earlier rise of excretion in the urine.

Urine collected by bladder catheter differed little in volume or composition from that collected by voluntary micturition except for an increased loss of sodium after catheterization. At present we have no explanation for this finding but it is interesting to note that Stacy & Brook (1964*b*) observed an increased sodium loss following the unilateral preparation of a cutaneous ureterostomy in the sheep. Urine produced by the unoperated kidney and voided naturally via the bladder did not show this loss.

Less additional potassium was recovered in urine in the first 24 hr after giving the acetate (65 %) than after chloride (82 %, groups I and II combined). With NaCl treatment 12–40 % of the additional Na was excreted in urine in the first 24 hr, with higher values being observed in the group II experiments when urine was collected by bladder catheter. In spite of the doubling of the Na load when the acetate was given, only 43 % of the added

load was excreted in urine in the first 24 hr. However, with both NaCl and KCl over 80% of the additional Cl^- appeared to be excreted in the urine during the first 24 hr after treatment. It therefore appears unlikely that differences in Na and K excretion are simply due to anion effects.

In spite of the slight, but persistent, loss of sodium in the experiments where a bladder catheter was used, the natriuresis which followed an intraruminal load of K salts was similar to that observed in the earlier experiments without bladder catheterization. A similar effect has been reported by Berliner, Kennedy & Orloff (1951) in dogs; by Liddle, Bennett & Forsham (1953) in man, and by Anderson & Pickering (1962) in cattle.

Berliner *et al.* (1951) postulated a competition between hydrogen and potassium ions for some component of the ion exchange mechanism by which both are secreted in the distal tubule. In their experiments the observed potassium increment was less than the hydrogen ion decrement and, as sodium ions were considered to be the common component of the ion exchange system, the authors suggested that the inequality in turnover of hydrogen and potassium ions might account for the sodium loss observed. This explanation appears to require maximum sodium loss to be coincident with maximum potassium loss which was not observed in our experiments.

Liddle *et al.* (1953) added to the above explanation the possibility of displacement of body Na^+ by K^+ as a mechanism producing the natriuretic effect of potassium salts. It is possible that Na^+ could be displaced by K^+ from the rumen as has been suggested by Dobson, Scott & Bruce (1966) to explain a loss of sodium which they observed in sheep subjected to a change in diet. One might then expect the peak of sodium excretion to precede that of potassium, which is the opposite of the present observations on KCl administration. With potassium acetate, however, the peak of sodium excretion did precede that of potassium.

Anderson & Pickering (1962) suggested that part of the sodium loss seen in their experiments was a diuretic effect but again it has been noted in our experiments that maximum sodium loss did not always correspond with maximum diuresis (see pp. 613, 616). It would therefore seem that, at present, no adequately tested explanation exists for the natriuresis observed in response to treatment with potassium salts.

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