RENAL EXCRETION OF UREA AND ELECTROLYTES IN A SMALL WILD RUMINANT: THE DIK DIK ANTELOPE (*RHYNCHOTRAGUS KIRKII*)

By

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D E C L A R A T I O N

I declare that the work presented in this thesis is my original work and has not been submitted in this or any other form for a degree in any other University.

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D E D I C A T I O N

This thesis is dedicated to MUHIZA and MUKASOMA with Great Love.

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GFR - Glomerular filtration rate

ETC - Endogenous True Creatinine

ADH - Antidiuretic hormone

U_k - Urinary potassium concentration

V_u - Rate of urine flow

C_k - Potassium clearance

P_k - Plasma potassium concentration

$U_{creat.}$ - Urinary creatinine concentration

$P_{creat.}$ - Plasma creatinine concentration

RPF - Renal plasma flow

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A B S T R A C T

A study to examine the glomerular filtration rate, renal mechanisms for potassium, sodium and urea excretion, urine osmolar concentration as well as saline drinking abilities of the dik dik antelope was carried out under controlled laboratory experiments.

Observations were made on the daily intake and excretion of electrolytes (K and Na) by dik diks fed only once daily and housed in metabolism cages. Food and faeces were analysed for dry matter, ash and electrolytes contents. Urine and plasma samples were analysed for osmolality, K, Na, Urea -N, NH_3-N and Endogenous true creatinine concentrations during control and various treatments.

In the control state, 73% of the total K recovered in both urine and faeces was excreted in urine while urine Na represented only 11% of the total Na recovered in urine and faeces. Renal tubular reabsorption for K, urea and Na was 39.9%, 55.3% and 99.9% of the filtered quantities, respectively. The glomerular filtration rate varied from 3.4 to 16.8 with a mean of 7.2 ml/min. Urine osmolality, K, Na, urea and creatinine concentrations varied inversely with the urine volume.

Dehydration was accompanied by significant decrease of glomerular filtration rate ($P< 0.05$) and urine flow rate and an increased tubular urea reabsorption. Solutes loading however tended to have opposite effects. Potassium loading

on the other hand increased the ratio of potassium clearance to creatinine clearance to over unity thereby reaching a maximum of 2.0. This provided evidence for potassium secretion by the antelope's renal tubules. Similarly, as solute excretion rate increased, urine osmolality decreased, resulting with the highest urine osmolality being observed at the lowest rates of solute excretion. Dik diks offered saline solutions as the only source of drinking water ranging from 0.1 to 0.5 mole/l NaCl could tolerate only a concentration of 0.3 mole/l NaCl.

The percentages and pattern of urinary potassium excretion as well as faecal sodium excretion were similar to the pattern found in both domestic and wild ruminants such as sheep, cattle and red deer thus far studied. Tubular potassium secretion was evidenced in the dik dik antelope and explains its tolerance for rich-potassium diets without any adverse effects. It was further observed that by increasing tubular water reabsorption and decreasing glomerular filtration rate, the dik dik antelope is able to excrete a very highly concentrated urine (4200 mOsm/kg H_2O) and conserve water.

In the dik dik antelope, as in the case of the mammalian kidney in general, 99.9% of filtered Na was reabsorbed along the renal tubules. The ability of their kidneys to increase urea reabsorption during dehydration was of interest and

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probably explains this species' ability to live in dry areas and withstand prolonged periods of drought mostly encountered in the East and Central African regions.

CHAPTER I

1.1 General introduction and literature review.

The dik dik antelopes are small ungulates (adult weights range between 2.0 - 5.0 kg) which inhabit extremely dry and semi-arid regions of East, Central and South-West Africa. They are so well adapted to their hot arid environment that they can survive for long periods without drinking water. They encounter high air temperatures and intensive solar radiation during the day, particularly during the hot seasons of the year (Dorst and Dandelot, 1970; Gotch, 1979).

Several aspects of the physiology of this small wild ruminant have been investigated in both controlled laboratory and field experiments (Schoen, 1972; Maloiy, 1973; Musewe, et al. 1976; Hoppe, 1976; 1977; Maskrey and Hoppe, 1979; Kamau, 1982). The studies on the water metabolism of the dik dik antelope (Schoen, 1972; Maloiy, 1973) have demonstrated that among the ungulates thus far studied the kidney of the dehydrated dik dik can excrete a highly osmoticaly concentrated urine (4,300 mOsm/kg H_2O) with a U_{osm}/P_{osm} ratio of 11. Further, the studies of Maloiy (1973) revealed high levels of urinary potassium concentration which were suggestive of the existence of an efficient renal potassium regulatory and excretory mechanism in the dik dik antelope.

Aspects of intestinal water and electrolytes conservation in relation to osmoregulation have been

investigated (Skadhauge and Maloiy, 1978). Further, the effects of dehydration and electrolyte concentrations and water content along the large intestines were investigated (Skadhauge, Clemens and Maloiy, 1980).

Studies on water turnover and water metabolism in hydrated and dehydrated dik diks under laboratory conditions have been carried out (Schoen, 1972; Maloiy, 1973; and Hoppe, 1976). These authors have shown that, the dik dik has a low water turnover and they attributed this low water expenditure to the dik dik's ability to concentrate urine as well as excretion of very dry faeces. Studies on the water metabolism of the dik dik antelope (Schoen, 1972; Maloiy, 1973; and Hoppe, 1976) and environmental physiology (Kamau, 1982), in particular, have further shown that its ability to survive on very little drinking water is partly due to the excretion of concentrated urine, as well as curtailing faecal and urinary water loss.

Hoppe (1977) reported that when dik diks were offered water ad libitum they drank very little (278 ml/day) equalling 83 $ml/kg^{0.82}$, yet the dry matter intake was very high ($3.8 \pm 0.5\%$ of body weight). Compared to the water content of faecal pellets of dehydrated camels (Schmidt-Nielsen, 1964), dik diks were found to excrete less water in their faeces (minimum of 64 g H_2O/100 g faecal dry matter during dehydration, Maloiy, 1973).

A comparison of maximal urinary osmolar concentrations of the East African ungulates thus far studied shows the

dik dik to emerge with the highest concentration of 4300-4700 mOsm/kg H_2O (Maloiy, 1972; Schoen, 1972). Further, Maloiy (1972) observed that dehydration in the dik dik was accompanied by several water conservation mechanisms. These included decreased evaporative water loss and urine volume. He calculated that with decreased evaporation the animal saves 70 - 100 g of water daily and a 50% reduction in urine volume saves 20 - 100 g of water daily. The other mechanisms that the dik dik was observed to employ are; excretion of drier faeces which saves up to 10-20 g of water daily, and a labile body temperature which saves 16 g of water daily through the process of heat storage. The urea concentrations in the urine often exceeded 1500 mmole/l and its excretion was considerably increased both by simulated desert conditions and by dehydration. Potassium was the principal ion excreted in the urine.

Dik diks, like other animals that live in hot, arid areas will be expected to experience potentially greater ionic and osmotic problems than the animals that live in wetter regions. This difference principally reflects additional evaporative water loss including that used for temperature regulation. In addition, however, supplies of drinking water are also usually more limited in such hot dry climates and the vegetation that is eaten by the dik dik may contain less water. The various aspects of the dik dik physiology reviewed above show that it is highly adapted to its environment; and this adaption is partly attributable to the dik dik's renal urine concentrating ability.

There has, however, been no detailed studies carried out to investigate the renal functions of the dik dik kidney.

Despite the poisity of literature on the renal studies in the wild ruminants, kidney function studies on the sheep, goat, cow, camel and other domestic species have been extensively studied. It is however, generally accepted that wild and domestic herbivores such as sheep, cattle, deer and antelopes feed on diets rich in potassium and poor or low in sodium, as opposed to the sodium-rich and potassium-poor diets of carnivorous animals like, man, dog, or cat. Variations in water or potassium intake have also been found to affect potassium excretion in sheep (Scott, 1969a). Further studies by Schmidt-Nielsen and her associates (Schmidt-Nielsen, Schmidt-Nielsen, Jarnum and Houpt, 1957; Schmidt-Nielsen and Osaki, 1958; Schmidt-Nielsen, Osaki, Murdough and O'Dell, 1958) and other workers (Livingston, Payne and Friend, 1962; Gans, 1966; Cocimano and Leng, 1967; Elliot and Topps, 1963) have demonstrated that ruminants fed a low-nitrogen diet are able to recycle urea in the rumen.

Renal regulation of urea excretion in domestic ruminants, has been the subject of several studies (Cocimano and Leng, 1967; Elliot and Topps, 1963; Schmidt-Nielsen, 1964; Maloiy and Scott, 1969). The amount of urinary urea excreted by these ruminants and other mammals is thought to be determined by both the amount of urea filtered and the extent of renal tubular reabsorption. It is not, however, clear whether urea reabsorption is brought about as a result of passive diffusion and active transport or regulated through changes in tubular permeability.

Renal studies on the salt and water excretion by the camel showed that dehydration was accompanied by a 57% decrease in urine flow and a 30% reduction in the glomerular filtration rate (Maloiy, 1972).

Salt loading increased glomerular filtration rate and urine flow by 52% and 103%,respectively. In the same study, dehydration led to an increase in urine and plasma osmolality as did the concentrations of both urinary and plasma electrolytes and urea. The most concentrated urine excreted by the camel being 3,200 mOsm/kg H_2O with urea contributing 900-1400 mmole/l.

Studies have been carried out on the salt tolerance of herbivores. The donkey (Maloiy, 1972) sheep and cattle (MacFarlane, 1971) tolerate concentrations of 180-220 mmole/l NaCl in their drinking water. Turkana goats are not affected by higher concentrations (250 mmole/l) and the concentration tolerated by Black Bedouin goats was 500 mmole/l. Drinking of sea water (1000 mmole/l) on the other hand, has been claimed by Dunson (1974) to improve the water economy of the goats that inhabit dry areas in the Galapogos Archiplago.

Maloiy (1972) found the camel to be unusual among herbivores in its salt tolerance. The highest concentration of salt in drinking water ingested by this animal with no ill-effects was about 1850 mmole/l. (5.5% NaCl). Even with this high salt intake, urine osmolality did not rise above 3,000 mOsm/kg H_2O. The ability of an animal to use salt solutions or sea water is an adaptive characteristic well

developed by some desert herbivores.

Among the terrestrial mammals, the dik dik kidney seems to rank second to desert rodents in urine concentrating ability. The highest osmolality achieved by the dik dik is 4762 mOsm/kg H_2O (Schoen, 1972) whereas a desert rodent (Notomys alexis) has a maximum urine osmolality of up to 9370 mOsm/kg H_2O (MacMillen and Lee, 1967, 1969). The highest urinary osmolality concentration achieved by human kidney is about 1200-1400 mOsm/kg H_2O. This is relatively modest especially when compared with some other mammals; e.g. dog 2300-2500 mOsm/kg H_2O; rat 3000-3200 mOsm/kg H_2O (Best, 1961).

The highest and lowest urine concentrations are produced only when solute excretion is at a relatively low level so that as solute excretion increases urine becomes less dilute and concentrated (Best, 1961). Similar findings were reported by Rabinowitz and Gunther (1972a) when they studied the renal concentrating ability in sheep during urea, mannitol and methylurea diuresis. They noted that during administration of each solute, the urine osmolality decreased as the solute excretion increased, the highest urine osmolality being observed at the lowest rates of solute excretion.

The proportion of the kidney occupied by the Medulla is highly correlated with the degree of aridity of the animal's habitat (Schmidt-Nielsen and O'Dell, 1961). This observation was confirmed by latter studies (Schoen, 1969)

on the water balance of three closely related mammals from different tropical habitats; the bushbuck, (Tragelaphus scriptus dama) from moist bushland; Uganda Kob (Adenota kob thomasi), from the dry savannah; and the dik dik (Rhynchotragus kirkii) from arid semi-desert habitats. Observations were taken both during conditions of normal hydration and dehydration. When dehydrated the urine excretion decreased as follows:- The bushbuck from 99.1 to 69.7 ± 2.0; the kob from 46.4 ± 3.7 to 27.2 ± 15.0, and the dik dik from 10.9 ± 0.77 to 1.3 ± 0.04 ml/kg$^{0.75}$/day ± S.E. respectively. Their urine osmolalities (mOsm/kg H_2O ± S.E.) increased as follows:- The bushbuck from 939 ± 52 to 1369 ± 52, the Uganda kob from 1109 ± 16 to 1594 ± 11 and the dik dik from 2235 ± 138 to 4762 ± 62.

A closer gross examination of the kidneys showed that the medulla occupied a mean of 31% in the bushbuck, 38% in the Uganda kob and 47% in the dik dik antelopes. Schoen (1969) concluded that if the relative medullary thickness is a measure of the total length of the loop of Henle, then it is logical to conclude that the maximum urine concentrating ability achieved must be related to the aridity of the bovids' habitats.

1.2 Osmoregulatory renal hormones

The kidney is implicated as a site of action of several hormones which affect water and electrolyte balance. These include the steroid mineralocorticoids produced by the adrenal cortex, the proteinaceous parathyroid hormone and

various peptide hormones of the neurohypophysis. The hormone whose action on the kidney is best understood is the Antidiuretic hormone (ADH).

The mechanism for water conservation by the kidney is dependent on the availability of ADH circulating in the blood. Following exposure of an animal to dehydrating conditions, ADH is secreted from its storage site in the neural lobe of the pituitary gland and thereby increasing circulating amounts in the blood (Fyhn, 1979). In the kidney, ADH exerts its effects by increasing the water permeability along the collecting duct system of the nephron (Grantham, 1974). This promotes water withdrawal from the collecting duct fluid thus concentrating and reducing the volume of the final urine.

It has been shown that desert rodents generally have a larger capacity for ADH synthesis and higher plasma levels of ADH than rodents from mesic and moist habitats (Bentley, 1971). Moreover, it had been previously noted by Itoh (1954) that ADH production by the pituitary in rats is high in summer. Robinson and Macfarlane (1956) found that the antidiuretic hormone activity of plasma was increased during heat-induced dehydration. Further, Macfarlane and Robinson (1957) provided evidence that this increase in plasma ADH levels in both man and in sheep showed seasonal fluctuations and concentrations. A seasonal variation in the plasma level of antidiuretic substances was also found by El-Husseini and Haggag (1974) in the desert rodents

(Jaculus jaculus) and the gerbill (Gerbillus gerbillus). Maximal antidiuretic activity of the plasma was found in animals during the summer when the advantage of an effective water economy would be greatest.

Aldosterone is the major mineralocorticoid that has an important role in sodium homeostasis and has been shown to have an effect on sodium transport in many tissues. There is evidence to suggest that aldosterone increases sodium absorption from the gastro intestinal tract (GIT). Adrenalectomy results in impaired sodium absorption from the intestine of rats (Clarke, 1939; Stein and Wertheimer, 1940) and dogs (Dennis and Wood, 1940) which can be restored by administration of deoxycorticosterone (Stein and Wertheimer, 1940).

Laragh (1960) reported that aldosterone decreased the faecal Na/K ratio and this was also found by Wong et al. (1961) using 9 -α- fluorocortisol. Poutsaika (1957) showed that in dogs the administration of 9 -α- fluorocortisol decreased sodium and increased potassium faecal excretion. Levitan and Ingelfinger (1965) have found that aldosterone increases sodium absorption from the human colon but had no effect on potassium excretion. Similarly, Edmunds and Marriott (1967) have also shown that aldosterone increases sodium absorption from the rat colon. Crocker and Munday (1970) using the rat's jejunum showed that both aldosterone and angiotensin increased sodium and water absorption from isolated

segments of the small intestine. They speculated that not only aldosterone but also angiotensin might directly affect active sodium transport in the kidney and thereby play an important role in the maintenance of sodium homeostasis.

It is interesting that aldosterone also stimulates sodium transport by other epithelial tissues in the body, namely, sweat and salivary glands. The net effect is the same as that exerted on the kidneys:- a reduction in the sodium content of the luminal fluid (Crocker and Munday, 1970). Thus, aldosterone is an all-purpose stimulator of sodium retention.

Hypotheses on factors controlling renin release include:-

- changes in the sodium load to the macula densa (Vander, 1967; Nash, et al. 1968; Vander and Carison, 1969);
- renal baroreceptor mechanisms (Skinner, McCubbin and Page, 1964; Blaine and Davis, 1971);
- sympathetic nervous activity (Vander, 1965; Gordon, et al. 1967; Mogil et al. 1969).

Studies by Blair-West et al. (1972) on the renin responses to water restriction and rehydration in sheep supported the theory that altered sodium load at the macula densa was the stimulus for renin release.

There is considerable evidence that another hormone (a natriuretic hormone) exists which increases sodium excretion by the kidney. Supposedly, this hormone is released when extracellular volume is expanded (e.g. following saline infusion (Vander, 1975)). However, the existence of this salt-losing hormone is still controversial.

1.3 Renal handling of potassium and sodium by the ruminants and monogastric animals

Because of differences in dietary K/Na ratio in monogastric and herbivorous animals; with the ratio being much lower in diets of the monogastrics than in ruminants, earlier studies paid increased attention in sodium metabolism and excretion than potassium. However, as more investigations were carried out on potassium metabolism it was found that there were differences in renal handling of potassium between ruminants and monogastric animals, the reason again being largely attributed to differences in dietary intakes of the two groups of animals.

There is little published information as to the actual ruminant electrolytes intake and requirements. However, potassium requirements for lambs of not less than 50 mEq or about 65 mg/kg b.wt. has been reported (Church et al. 1974). In cattle, heifers needed about 133 mEq/kg b.wt. daily for maintenance (St. Omer and Roberts, 1967), and steers required amounts ranging between 0.67 and 0.77% K of dry matter intake daily, values considerably higher than indicated for

sheep (Devlin et al. 1969). In the case of lactating dairy cows, it is reported (Church et al. 1974) that 0.15% is insufficient but 0.81% K dry matter intake appears to be adequate.

During administration of large doses of potassium salts in both normal dog and man, as well as in the animals with certain types of renal and hepatic disease, a renal tubular mechanism was demonstrated for the secretion of potassium (Berliner et al. 1950). Anderson and Pickering (1962) studied the renal response of the cow to intravenous infusion of a potassium salt. The results thus obtained resemble those that had been reported for man and the dog, despite the difference in the dietary electrolyte contents of ruminants and monogastric animals. They observed that the rate of the potassium excretion rose rapidly to equal the rate of administration, and clearance measurements showed an excess of potassium excreted over and above that filtered thereby implying that there was potassium secretion.

However, unlike the dog, where it had been shown that potassium loading led to a progressive rise in plasma potassium concentrations, unless the animal had been made 'tolerant' by addition of potassium salts to its diet for 2 weeks before infusion (Berliner et al. 1950), the bovine plasma potassium levels did not rise since the potassium excretion rose rapidly to equal the rate of administration.

In studies aimed at investigating the effects of urea and osmotic diuresis on the excretion of potassium in the dog, it was observed that both potassium and sodium excretion increased following the diuresis, but the increase in sodium excretion was much more pronounced than the increase in potassium excretion (Gonick et al. 1964) though this depended on the level of potassium intake.

Renal excretion of potassiun studies in sheep given a daily dietary intake of 400-600 mmole potassium and 50-60 mmole sodium respectively showed that about 87-94% of the total potassium recovered in urine and faeces was excreted in the urine and about 80-98% of the total sodium recovered was found in the faeces (Dewhurst and Harrison, 1966). In the same experiments, administration of potassium salts produced a marked kaliuresis and natriuresis as well in spite of the low sodium intake which did not usually coincide with maximal potassium excretion.

In such monogastric species as man, a mean ratio of K/Na of 0.43 was found in their urine samples (Keynes and Harrison, 1967). The picture is rather different in herbivorous animals because there is usually much more potassium than sodium in the diet. In the urine of dairy cows, a K/Na ratio of 5.4 was found (Anderson and Pickering, 1962). Studies on sheep found the urinary K/Na ratio to be very high, averaging not less than 175 (Dewhurst and Harrison, 1966; Dewhurst, Harrison and Keynes, 1968), but the authors

compromised this very high ratio to an overall of only 17 by pointing out that since under the conditions of their experiments only about a tenth of the excreted sodium was in urine, the other nine-tenths being recovered in the faeces.

Examination of renal function and potassium excretion in sheep receiving variations in potassium and water intake showed a fall both in osmotic pressure and potassium concentration in urine as the urine volume increased (Scott, 1969a). The amount of potassium excreted was, however, not affected by urine volume provided this was above 1.0 to 1.5l/day. Increasing the potassium intake within the range 236-1186 mEq/day led to a proportional increase in potassium excretion. Similarly, with intakes between 236-889 mEq/day, there was no change in the filtered amount of potassium at the glomerulus. However above this, the amount of filtered potassium across the glomerulus increased. This finding led Scott (1969a) to suggest that when potassium intake is very high, a proportion of the filtered potassium across the glomerulus may augment the secretory process in eliminating dietary potassium excesses (Scott, 1969a).

During intravenous potassium infusion, the rate of urinary potassium excretion exceeded the rate of potassium filtered across the glomerulus thus indicating net secretion of potassium by the renal tubules (Scott, 1969b). There was also an increase in the rate of excretion of Na in the urine. This sodium diuresis was most marked at the higher rates of infusion of potassium chloride.

Rabinowitz and Gunther (1972b) noted an antidiuretic fractional excretion of 0.01-0.02 for sodium and 0.8 for potassium. When an osmotic diuresis was induced, it reduced the urine-to-plasma inulin ratio from 200 to 2.5 and increased the fractional sodium excretion to 0.35 while increasing variably the fractional potassium excretion to values as high as 1.3, thus unequivocally indicating the role of tubular potassium secretion.

The same workers, while studying the renal potassium excretion in sheep during sodium-salt diuresis, observed an increase of sodium excretion rising at times to equal 25% of the filtered load. Urine flow increased and glomerular filtration rate increased only with infusion of isotonic saline (Rabinowitz and Gunther, 1978). No consistent change in potassium excretion occurred under any of these conditions. This finding contrasted with the increase in potassium excretion commonly seen in man, dog and rats intravenously loaded with sodium salts. However, more recent studies (Rabinowitz, personal communication) show that diuresis induced by sodium sulphate can increase urinary potassium excretion in fasted sheep; provided the sheep were initially excreting low urinary potassium concentrations.

When the pyrazine diuretic, amiloride was given to ewes intravenously, potassium excretion decreased to one-third of base-line value, and sodium excretion increased 6 to 180-fold (Rabinowitz and Gunther, 1979). This response was thus similar to what Baer et al. (1967) and Bull and Laragh (1968) had observed in non-ruminant animals where increase

in sodium and a decrease in potassium excretion resulted from amiloride administration. This diuretic was thus seen to be unlike many other diuretics which increases both potassium and sodium excretion.

The current and broadly accepted concept on renal potassium excretion is that whereas ruminants respond to increased potassium intake by promptly activating and relying on the tubular secretory mechanism; monogastric species need a prior exposure period to high levels of potassium before their secretory mechanisms are functional. However, recently, Rabinowitz et al. (1984) have shown that the rat will adapt at once to a high potassium diet.

The accepted hypothesis for the control system that maintains potassium balance considers, increase in plasma potassium concentrations as the signal subsequently leading to increased renal potassium excretion following high potassium intake (Rabinowitz et al. 1984; Laragh and Sealey, 1973). This may not be entirely true because studies by Berliner et al. (1950) and Rabinowitz et al. (1984) have shown that increased renal potassium excretion following increased potassium intakes is not always associated with a rise in plasma potassium concentration.

1.4 Renal handling of urea

Considerable literature on renal excretion of urea in domestic species is available (Schmidt-Nielsen, 1958). However, there has been no work done on renal urea handling in East African wild ruminants.

In a review of urinary urea concentration in rodents (Fyhn,1979), it is concluded that urea concentration is much higher in urine of desert rodents than in urine of rodents from moist habitats (maximum of 4320 mmole/l and 480 mmole/l) respectively. This minimises the urinary water loss necessary for urea excretion in desert rodents and may be regarded as an adaptation to water shortage.

Heteromyrids were shown to excrete a urine with urea concentrations up to 3.8 mole/l. These high concentrations of urinary urea were found in animals with plasma urea concentrations around 10 mmole/l and the urine was about 400 times as concentrated with respect to urea as the plasma (Schmidt-Nielsen et al. 1948). Such high urea U/P ratios have not been reported in other mammals. In man urea U/P ratio is almost 170, in dog about 220, in white rat and sheep 200 (Schmidt-Nielsen, 1958).

Among the few wild ruminants that have been studied (Maloiy and Scott, 1969) the concentration of urea in urine of the red deer was observed to decrease as the urine volume increased. Similarly an increase in urine volume was accompanied by a decrease in urine osmolality.

The renal mechanism for urea excretion in the camel was investigated (Schmidt-Nielsen et al. 1957) by measuring urea clearance and glomerular filtration rate (using the endogenous true creatinine clearance method). During normal nitrogen intake, about 40% of the urea filtered at the

glomeruli was excreted in the urine while during periods of low nitrogen intake only 1-2% was excreted. The variations in the urea clearance were independent of the plasma urea concentrations and of the glomerular filtration rate, but were related to the animals' nitrogen intake and rate of growth. No evidence of active tubular reabsorption of urea was found since the urine urea concentration at all times remained higher than the corresponding plasma urea concentration. Man excreted about twice as much nitrogen as camel, and this is due almost exclusively to a urea nitrogen excretion that is about 15 times higher in man than in the camel. Further, the camel, like other ruminants, possess an ability to recycle urea in the rumen (Schmidt-Nielsen et al. 1957).

Renal function studies in calves showed that the ratio of maximal urea clearance and inulin clearance (C_u/C_1) is 0.5, indicating that about half the urea filtered at the glomerulus is reabsorbed in the tubules (Dalton, 1958). This is similar to the clearance ratios in adult humans which averages 0.6, with 40% of the urea reabsorbed by the tubules (Varley, 1967). In a study of the renal tubular excretion of urea in Kangaroo rats, Urea/Inulin clearance ratios greater than unity were observed and this was suggestive that a mechanism for urea secretion in the renal tubules of the Kangaroo rats was operative in spite of the fact that such a mechanism has not been demonstrated in other mammals (Schmidt-Nielsen, 1952).

In studies on the Marsupial (Trichosurs vulpecula), urea excretion initially decreased and then increased above control values during dehydration (Reid and McDonald, 1968). This was explained as a reflection of increased protein catabolism (since the plasma urea concentration also rose during this time). Similar studies on the Llama showed a significantly high plasma urea concentration during feed restriction than when the animals were fed the control diet (Hinderer and Engelhardt, 1975). Urea excretion averaged 0.09 ± 0.02 mmole/ $hr/kg^{0.75}$ b.wt. during the control period. During food restriction it increased to 0.11 ± 0.05 mmole/hr/kg.b.wt. The authors attributed this to increased protein catabolism. In comparison, farm animals excrete about 0.83 ± 0.64 mmole urea/hr/kg.b.wt. (Cocimano and Leng, 1967; Harmeyer and Varady, 1972).

During severe dietary protein restrictions the kidney conserves urea by markedly decreasing its excretion. The ratio of urea clearance to endogenous true creatinine clearance may fall to less than 5% under conditions of prolonged negative nitrogen balance (Dukes, 1970). This adaptation suggests the presence of an active urea transport system in the ruminant which is brought into play during conditions requiring maximum urea conservation. Active transport of urea however, has not been demonstrated in the mammalian kidney, and hence this hypothesis has not yet been confirmed.

In most species, urea clearance is affected by the rate of urine production and decreases with oliguria (Smith, 1936,

1951). This is in agreement with the general concept that, in addition to urea being filtered by the glomeruli, urea also undergoes tubular reabsorption to an extent depending on the urinary flow. Moreover, Schmidt-Nielsen et al. (1958) demonstrated that sheep regulate the urea excretion at the renal tubular level such that changes in dietary nitrogen intake effect regulatory changes, and these changes seem to be independent of the plasma urea levels. In addition to the process of "exaltation" where urea clearance is noted to be abnormally high during increased urine flows, Schmidt-Nielsen and associates described another process of 'abatement' where decrease in urine flow was accompanied by an abnormally low urea clearance rate.

Literature on the relation between fractional urea excretion and fractional water excretion in sheep fed high protein diets provide conflicting results, though they show an overall pattern which is common to all mammals. Schmidt-Nielsen et al. (1958) reported that fractional urea excretion remains constant when the U/P inulin ratio decreases below 10. Subsequently Gans (1966) found that fractional urea excretion increases over the entire U/P inulin ratio.

Rabinowitz and Gunther (1972c) report that tubular reabsorption of filtered urea depends primarily on the reabsorption of water and the consequent passive tubular transport of urea. There is a progressive increase of fractional urea excretion associated both with a progressive

increase in the fractional water excretion thereby indicating the importance of both water reabsorption and the resulting transtubular urea concentration gradient in driving urea reabsorption.

As shown by several studies (Schmidt-Nielsen and Kerr, 1970) urea has a pronounced effect on the concentrating capacity of rodents' as well as of the other mammalian kidneys. Following water restriction there is a parallel increase in urinary urea concentration and osmolality (Haines et al. 1973). When the protein content of the food is increased several rodent species exhibited an increase in urine osmolality (Grisard-Operschall, 1968; Haines and Schmidt-Nielsen, 1967; Schmidt-Nielsen and Haines, 1964). Increased urine osmolality has also been induced by intravenous urea administration in white rats, which have been deprived of dietary protein (Pennell et al. 1975; Heuer et al. 1974). Urea seems to enhance urinary concentration by accumulating in the interstitial fluid of the inner medulla causing an increment in osmotic water removal from the tubular fluid.

The ability of the mammalian kidney (especially of those mammals that inhabit hot arid lands) to conserve urea by decreasing its excretion and at the same time minimising water loss by excreting a highly concentrated urine is regarded as an adaptation to water scarcity. Urea is generally believed to highly enhance the urine concentrating ability in the mammalian kidney.

OBJECTIVES

Compared to domestic ruminants, relatively little is known about aspects of the renal physiology of most wild East African ruminants. This study, therefore, sought information on the following aspects of the renal physiology of a small wild East African ungulate: the dik dik antelope (*Rhynchotragus kirki*).

1. Renal urea and electrolytes (K and Na) excretion under different experimental conditions.

2. Glomerular filtration rate and tubular reabsorption of urea and electrolytes.

3. The effects of dehydration, water and salt loading and saline drinking as well as osmotic diuresis on glomerular filtration rate and urinary osmotic concentration.

4. The effects of intra-ruminal loading of KCl and NaCl on renal excretion of potassium and sodium.

5. The renal ability of the dik dik to tolerate salt solutions as its source of drinking water.

CHAPTER II

2.0 MATERIALS AND METHODS

2.1 Experimental animals

A total of eleven dik diks (7 males and 4 females) were used in this study. They were bought from local animal trappers and transfered to the animal house at Chiromo Campus, University of Nairobi, where the study was carried out. One male and two females were immature dik diks and the rest were adults. Their body weights ranged from 2.5-4.7 kgs. Four animals were used in each experiment except during the intra-ruminal loading experiments when only two animals were used. The young male dik dik was among the four that participated in the dehydration experiment together with the adults.

Since the animals were apprehensive and violent after captivity, an acclimatization period of about three weeks was allowed before any experimentation could be carried out on them. This enabled them to get used to the diet provided and to being handled. Those animals that sustained wounds during capture were given an intra muscular injection of 2 ml Terramycin (Pfizer, International Inc., New York) each on alternate days for a week when the wounds were observed to heal properly.

2.1.1 Diet

The basal diet of the animals comprised of Grewia similis leaves and early calf weaning pellets (Unga Ltd., Nairobi). The leaves were collected from the bush surrounding Chiromo University Campus and dried in the sun before feeding. Table 1 shows the nutrient composition of the experimental diet including its electrolytes (potassium and sodium) content.

Weighed amounts of both diets were mixed in a food container and put within easy access of each animal. Prior to experimentation a mineral lick (Unga Ltd., Nairobi) was added to the animal food but it was removed from the diet when the experiments commenced. Distilled water was used as drinking water except during the saline drinking experiments.

2.1.2 Animal housing

The animals were kept in the animal house for a week before being transfered to metabolism cages in the experimental room. The room in which all the experiments were carried out was a "climatic" room where ambient temperature and humidity were controlled at $22^{o}C$ and 30% respectively. While in the metabolism cages the animals were acclimatized to the experimental procedures and diet for two weeks before the start of each experiment.

Table 1: Nutrient values and composition of the experimental diets (Values are per cent of dry weight)

Nutrient	Early calf Weaning pellets	*Grewia similis* leaves
Dry matter (%)	91.3	92.3
Crude fibre (%)	6.2	11.8
Crude protein (%)	20.1	14.1
Potassium (%)	0.1	1.7
Sodium (%)	0.3	0.2
Total Ash (%)	8.1	10.4

Each animal was confined to its own cage which was constructed in such a way as to allow complete separation of faeces and urine without cross-contamination. The rectangular base of the cage was made of a small metallic square wire-mesh that permitted the faecal pellets of the dik dik to drop down into the funnel shaped receiver-component of the urine/faeces separator below the base of the cage. The hooves of the dik dik were however small enough to pass through the square wire-mesh. As this could cause injuries to the animals, protective socks made from soft cloth were fixed on the animals' hooves with elastoplast.

Food and water containers were placed in front of the cage on either corner. The animal could not turn round inside the cage but there was enough room for the animal to stand, lie and move short distances forwards and backwards. Throughout the experimental periods the animals remained inside these cages except when it was necessary to get them out so as to collect blood. This procedure took about 5 minutes for each animal.

2.1.3 Implantation of rumen infusion lines

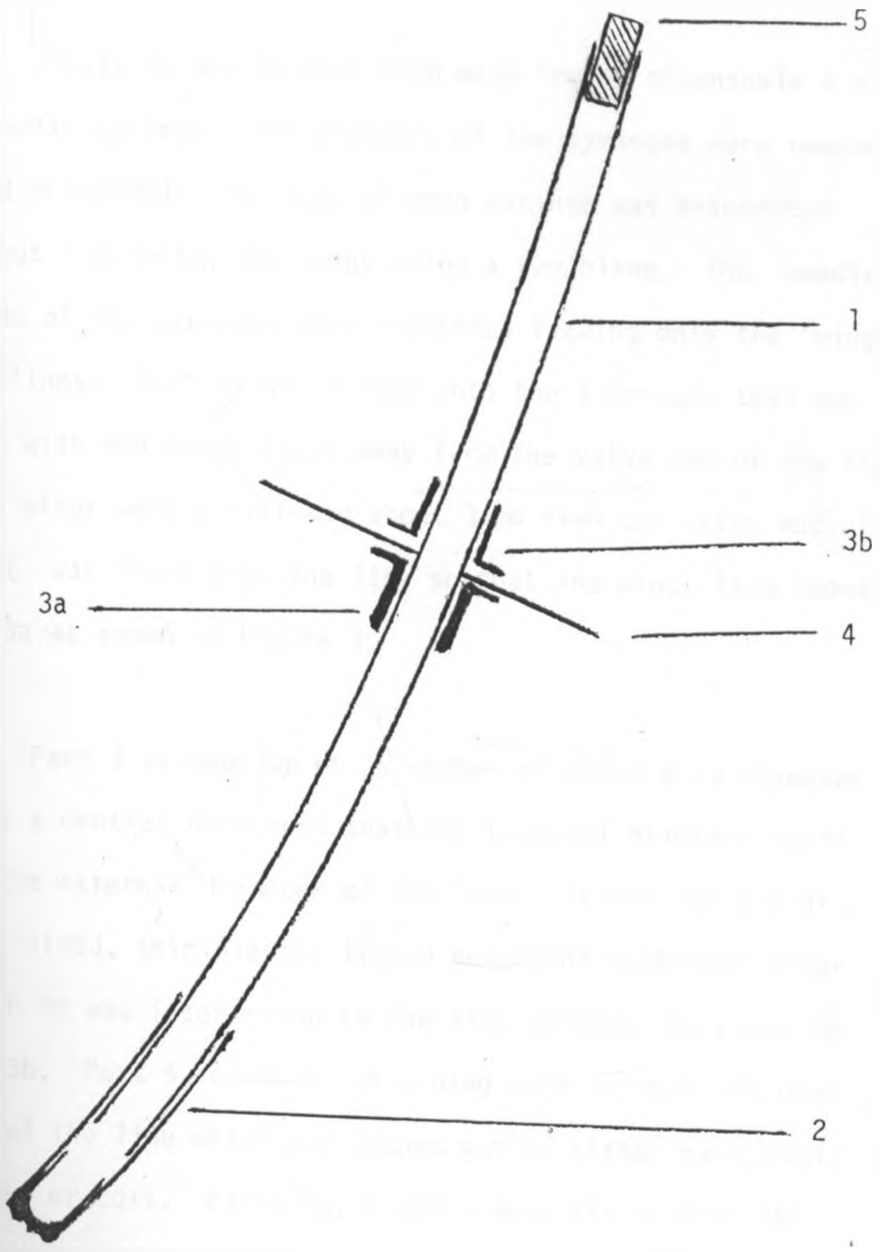
Intra-ruminal loading experiments entailed surgical implantation of permanent rumen infusion lines. This was done four weeks before the experiments began.

a) Preparation of the rumen infusion lines

The assembled infusion line with the component parts labelled is shown in Figure 1. Part 1 comprised of a 10 cm length of soft plastic tubing of 3 mm internal diameter and 5 mm external diameter. One end of the tube was sealed off by dipping it into prepared rapid setting glue ("Araldite", Ciba-Geigy) and then passing it over a flame after the glue had set. About 4-6 perforations were made through the tube 1 cm from the sealed end using a red-hot 19 gauge hypodermic needle.

Part 2 consisted of a 2.5 cm long piece, cut from a thin walled rubber tubing of 5 cm internal diameter. It was inserted over part 1 of the infusion line from the sealed end, so that it formed a sleeve over the last 3 cm. The rubber piece was immersed into soapy water before inserting it over the line to overcome static friction forces. It was then glued onto the line using the rapid setting glue - squeezed between it and the line for the proximal 0.5 cm. Since the internal diameter of the rubber tubing is equal to the external diameter of the infusion line, the sleeve formed by the rubber tubing on the line was closed but not tightly. Consequently, solutions can be easily squeezed out through the holes on the line using a syringe attached to the open end but the rubber sleeve acts as a valve, preventing suction of solutions into the line if and when suction pressure was applied from above.

Fig. 1: A permanent rumen infusion line with its component parts.


5
1
3b
3a
4
2

Parts 3a and 3b were each made from a disposable 1 ml plastic syringe. The plungers of the syringes were removed and discarded. The body of each syringe was transected about 1 cm below the wings using a saw blade. The needle ends of the syringes were discarded leaving only the 'winged' sections. Part 3a was fitted onto the line such that the end with the wings faces away from the valve end of the line. The wings were positioned about 3 cm from the valve end. The part was fixed onto the line so that the wings face those of 3a as shown in Figure 1.

Part 4 is made up of a washer of about 4 cm diameter with a central hole such that the internal diameter equal to the external diameter of the line. It was cut out of a flat-sided, thin plastic liquid detergent container after which it was inserted on to the line between the parts 3a and 3b. Part 5 consists of a plug made to seal the open end of the line which was shaped out of either hard wood, rubber or cork. Parts 3b, 4 and 5 were placed onto the infusion line after implantation of the line into the rumen and exteriorizing it through the abdominal wall.

b) Surgical technique for implantation

The animals were fasted for at least 18-24 hours before surgery. The infusion line was assembled leaving out parts 3b, 4 and 5 and was kept immersed in a 70% alcohol solution. The operation was performed under local infiltration anaesthesia using Xylotox (Willows Francis; Bolton, England). The animal was placed in right lateral recumbency position on a surgical table. The left sublumbar triangle was shaved and prepared aseptically for surgery. Surgical asepsis was maintained during the rest of the operation.

A surgical incision of about 4.5 cm long was made through the skin and subcutenous tissues midway between the last rib and the tuber coxae and about 3.4 cm below the line of the transverse processes of the lumber vertebrae. The abdominal muscles and peritoneum were perforated bluntly with surgical scissors and the muscle split along the lines of their fibres for the length of the skin incision. The rumen wall was identified and a relatively avascular portion was exteriorised through the incision and held in position at the corners of the incision with two pairs of peritoneal forceps. A purse string suture of about 2 cm diameter was made into the rumen wall using a non-absorbable suture material. An incision of about 1.5 cm was then made through the rumen wall between the purse string taking care not to spill out the contents. The valve of the infusion

line was inserted through this incision and the wings of part 3a manipulated into the rumen. The purse string was tightened and knotted around the line so that the wings of part 3a formed an intra-ruminal anchor. The line was exteriorised to the skin via a stab incision made through the abdominal wall about 3 cm in front or behind the main incision line,with the latter incision being sutured routinely.

The washer (part 4) and the external anchor (part 3b) were inserted onto the line and adjusted such that the pressure onto the rumen wall and abdominal wall caused by the external and internal anchors was minimal. The external anchor was then fixed onto the line by squeezing the rapid setting glue between them. The external part of the line was then shortened so that it protruded from the abdominal wall by about 3 cm with the external opening plugged with a stopper (part 5). Antibiotic cover was given for 3-4 days after surgery.

2.2 Experimental design and procedure

2.2.1 Design

A set of four experiments was carried out. A sequential design of experimentation was used and animals that came out of one experiment participated in the subsequent one after a rest-period of one to two weeks. If an animal developed unphysiological signs, it was immediately replaced by a healthy one.

2.2.2 General procedures

(a) Animal weighing

During the dehydration experiment, the animals were weighed on alternate days using a SALTER spring balance (Model 235). During the other experiments body weights were taken once weekly, at the beginning and the end of each experimental period.

b) Collection of urine

The volume of urine excreted daily was collected and measured using a clean calibrated measuring cylinder. A 20 ml aliquot sample was taken from the total daily urinary output of each animal, put in a labelled Universal bottle, and immediately frozen at -20^{o}C until required for analysis. Urine samples were collected in all the four experiments.

All chemical analyses were done within a period of one week after the collection, starting with creatinine. The urine/faeces separator of the metabolism cage was washed thoroughly and rinsed with distilled water after the day's samples had been taken. The inside circumference and bottom of the urine receiver was covered with an aluminium foil which was changed daily to prevent any external contamination. About 2-3 drops of paraffin oil or toluene was put inside the urine container to minimise urine evaporation.

c) Faeces collection

The daily faecal pellets were taken from the faeces-container of the metabolism cages and weighed at 9.00 a.m. The faeces were then dried overnight at 105^{o}C in an oven, weighed and a sample of about 10 g taken from the daily collection of each animal. Each sample was put in a labelled polythene bag and stored in a dry environment. At the end of the experiment all the daily sample collections for each individual animal were pooled together, mixed thoroughly and a sample of about 10 g taken for analysis.

d) Collection of plasma

In all the experiments 6-10 ml of blood was taken from the animals' jugular vein on alternate days. No blood collections were made in the rest-periods between two consecutive experiments. To prevent coagulation, heparinized syringes were used to withdraw the blood. The sampling was done between 9.30 and 10.30 a.m.

The blood was centrifuged immediately after collection for half an hour at 6000 r.p.m. using MSE centrifuge (Model GF-6). The plasma was then separated, put into labelled bottles and frozen at -20^{o}C until required for chemical analysis.

2.2.3 Experiment 1 Control measurements

Control measurements were made so as to establish the baseline levels of the different parameters. Four animals

(three males and one female) were used in the experiment. After the acclimatization period, the salt lick was withdrawn. A mixed diet of both early calf-weaning pellets and Grewia similis leaves weighing a total of 180 g (with known weights of the two separate dietary components), was put in food containers and each animal given its daily ration. Food and water containers were put within easy reach of the animal.

Each animal's daily food consumption was got by substracting the remainder from the previous day's ration. About 10 g of the food was sampled and kept for analysis. Similarly by subtracting the remaining water volume from the previous day's volume given, the amount drunk by each animal was obtained and recorded. Urine volume and amount of faeces excreted daily were recorded.

Samples of urine, faeces and plasma were taken as described in section 2.2.2. Urine and plasma samples were analysed for osmolality; potassium, sodium, urea-N, ammonia-N and creatinine concentrations. Faecal and food samples were analysed for proximate and electrolytes contents.

2.2.4 Experiment II Dehydration

In this study weight loss, as is common in similar studies, was used as an index of dehydration. In many studies on water-deprivation, the only measure of the degree of dehydration has been the weight loss of the experimental

animal (Siebert and Macfarlane, 1975). Adolph (1947) noted that young men remained active up to weight losses of 10% of the initial body weight and Schmidt-Nielsen (1964) considered that dogs that had lost 12% of their body weight,were in danger of death through explosive heat rise.

Loss in body weight following water-deprivation has been used to assess the degree of dehydration in dik dik antelopes (Maloiy, 1973; Kamau and Maloiy, 1983) until such a time body weight stabilized at 80-85% of the initial weight.

Dehydration was induced by gradually decreasing the amount of water available to the animals. For the first four days of the experiment, only 80 ml of water (this being about a half of the ad libitum intake) was given to the animals. This resulted in progressive loss in body weight. Further water restriction was adjusted per individual animal such that an overall average loss in body weight of 17% was achieved and maintained. Plasma samples collection commenced only when this level of dehydration was achieved. Urine and plasma samples were collected daily as described under the preceeding section on general procedures (section 2.2.2). Water restriction lasted for 21 days from beginning of experimental treatment.

2.2.5 Experiment III - Intra-ruminal electrolytes and water loading

In order to vary the dik dik antelope electrolytes intake indepedent of food consumption, it was necessary to

load the rumen with solutions of varying electrolyte concentration. Food and water were available ad libitum.

Two dik diks (a male and a female) were used in this experiment. A permanent rumen fistula was surgically implanted into the rumen of each animal four weeks before the experiment (Section 2.1.3).

The solutions given intra-ruminally to the animals were 0.3 and 0.5 mole/l KCl and 0.25 mole/l NaCl. Each concentration was prepared freshly with de-ionised water on the morning of the experiment. Each animal was intra-ruminally loaded with a single dose daily starting with 20 ml for each concentration. The volume was then increased progressively up to 120 ml. Each volume load was given for two days; so that loading lasted 12 days for every concentration. The animals were given a 6-7 day rest-period at the end of the experiment before the next concentrated solution was administered. Food and water intake were measured daily. Samples collected for analysis included urine and plasma. Faecal samples were not collected during this experiment.

2.2.6 Experiment IV Effect of saline drinking

In this set of experiments, the animals were given saline solutions as their only source of drinking water. The solutions ranged in concentration from 0.1-0.6 mole/l NaCl. Water was withdrawn from the animals and replaced with the saline solutions starting with the lowest concentration and

gradually increasing it to 0.6 mole/l. Each concentration was given for a period of 12 days except when the animals developed adverse signs, then that solution would be withdrawn and substituted with water.

By subtracting each day's remainder from that given the previous day, the amount drank per animal was obtained and recorded. The osmolality of each saline concentration was determined together with plasma and urine collected samples throughout the experiment.

2.3 Chemical methods of analysis

2.3.1 Urine and plasma creatinine concentration

Creatinine was determined using the Alkaline picrate method (Varley, 1967). The assay was carried out as follows:- Urine was diluted by a factor of a hundred. Three millilitres of the diluted urine was pipetted into a test tube and 1 ml of 0.04 M picric acid added followed by 1 ml of 0.75 N NaOH. Three millilitres of a standard creatinine solution of concentration 10 mg/100 ml and 3.00 ml of de-ionized water were treated in the same way. These acted as the standard and blank respectively. All test tubes were allowed to stand for fifteen minutes and then readings were taken using a Beckman spectrophotometer (Model DB-GT) at wavelength 500μ during the next half hour.

For plasma samples, 2 ml was diluted with 2 ml of distilled water and, proteins precipitated by adding 2 ml of 5% Sodium

tungstate and followed by 2 ml of 2/3 N Sulphuric acid drop by drop with constant shaking. The solution was then allowed to stand for 10 minutes and then centrifuged at a speed of 6000 r.p.m. using an MSE centrifuge (Model GF-6). Three millilitres of the supernatant (0.75 ml plasma) was treated in the same way as the above diluted urine samples.

Calculation of creatinine concentration

Since the standard contained 0.03 mg creatinine and 3 ml of diluted urine corresponded to 0.03 ml of the original urine, urine creatinine concentration (mg/100 ml) was estimated as follows:-

$$U_{creat.} = \frac{\text{Reading of unknown}}{\text{Reading of standard}} \times 0.03 \times \frac{1000}{0.03} \times \frac{1}{1000} \times 10$$

$$= \frac{\text{Reading of unknown}}{\text{Reading of standard}} \times 10$$

Plasma creatinine concentration (mg/100 ml) was similarly calculated as follows:

$$P_{creat.} = \frac{\text{Reading of unknown}}{\text{Reading of standard}} \times 0.015 \times \frac{100}{0.75}$$

$$= \frac{\text{Reading of unknown}}{\text{Reading of standard}} \times 2.0$$

2.3.2 Urine and plasma osmolality

Osmolality was determined by freezing point depression method using the KNAUER Micro-osmometer (Herbert Knauer & Co. Gmbh, Berlin 37 West Germany). Urine samples were diluted by

a factor of ten but plasma samples were analysed directly without any dilution. Samples were analysed in duplicate.

2.3.3 Urine and plasma electrolytes concentrations

Potassiun and sodium concentrations were analysed with an EEL Flame Photometer (Evans Electroselenium Ltd. Halstead, Essex, England). Urinary potassium concentration was estimated by diluting each sample by a factor of sixty to one hundred depending on the degree of concentration. After dilution 0.5 ml of the diluted urine was put into a 25 ml volumetric flask and the flask was then filled to the mark with de-ionized water. An appropriate potassium filter was employed before the reading was made.

For the urinary sodium analysis on urine, 0.1 ml of undiluted urine was put in a 50 ml volumetric flask which was filled to the mark with distilled water and the readings taken using a sodium filter. For plasma sodium estimations, 0.05 ml plasma was put into a 50 ml flask which was filled to the mark with dstilled water and readings taken.

2.3.4 Urinary and plasma urea -N and ammonia - N concentrations

Urea nitrogen was analysed using the Diacetyl Monoxide method (Natelson, 1957) on whole plasma and on urine diluted samples. Similarly ammonia nitrogen was determined by the Cornway microdiffusion method (Conway, 1957).

2.3.5 Food and faecal electrolytes concentrations

For analysis of potassium and sodium concentrations in food and faeces, the Wet-Ashing technique was used (Lindner and Harley, 1942, Miller and Miller, 1948).

The samples were dried in a forced-air oven at 70°C, then ground so as to pass through a 20 mesh screen and mixed thoroughly. An aliquot of each sample (about 0.4 g) was placed into a glass container and dried overnight in a forced-air oven at 105°C and after drying they were subsequently allowed to cool in a dessicator. This was followed by the dried samples being wet-ashed to remove organic matter and to convert the nutrients to a soluble or measurable form using Analar grade Conc. Sulphuric acid and 30% Hydrogen peroxide.

Potassium and sodium concentrations in the representative samples were estimated directly. Blank solutions containing the same amounts of the reagents (H_2SO_4 and H_2O_2) were used. The potassium and sodium contents were then given as a per centage dry matter of the dried samples.

2.4 Calculations and statistical methods

2.4.1 Glomerular filtration rate (GFR)

Glomerular filtration rate is defined as the volume of fluid that is filtered per minute across the glomerular capillary bed of both kidneys. The endogenous true creatinine (E.T.C.) clearance defined as the volume of plasma that is

completely cleared of creatinine per minute was used as a measure of glomerular filtration rate.

This method has been used to estimate GFR in the camel, sheep, dog, cat and rabbit (Schmidt-Nielsen et al. 1957; 1958). One advantage of using this method is that the only manipulation of the animal required is that related to blood and urine collection. This method is less cumbersome and entails less manipulations on the animal than other methods.

Furthermore, the creatinine clearance and the inulin clearance, which is more often used to estimate GFR, have been shown to be identical in the dog (Richard et al. 1936; Shannon, 1936), rabbit (Kaplan and Smith, 1935; Pitts, 1968), sheep (Shannon, 1937; Pitts, 1968), and cat (Gammeltoft and Kjeruef-Jensen, 1943) though this is not the case in man (Yagil and Berlyne, 1977).

On the strength of these studies on various animals, the clearance of creatinine was thus assumed to be equivalent to the rate of glomerular filtration even for the dik dik antelope. It was calculated using the corresponding values of plasma creatinine concentrations, urine creatinine concentrations and urine flow rates obtained in the different experiments.

The following equation was used:

$$GFR = \frac{U_c \times V_u}{P_c}$$

Where GFR = Glomerular filtration rate (ml/min.)

U_c = Urinary creatinine concentration (mg %)

V_u = Urine flow rate (ml/min.)

P_c = Plasma and hence ultra-filtrate creatinine concentration (mg %)

2.4.2 Fractions of filtered urea reabsorbed or excreted

The renal clearance of creatinine is taken to be equal to the GFR. For all substances which are freely filtered through the glomerular membrane - like urea, the difference between their clearances and that of creatinine gives an indication of the extent of tubular secretion or reabsorption.

In this study, this formed the basis for assessment of the tubular secretion or reabsorption of urea, potassium and sodium. The fraction of filtered urea that is reabsorbed along the renal tubules ($F_{\text{urea reabsorbed}}$) and the fraction of urea filtered that is excreted ($F_{\text{urea excreted}}$) were calculated as follows:-

$$F_{(\text{urea reabsorbed})} = \frac{\text{Amount filtered - Amount excreted}}{\text{Amount filtered}}$$

$$= \frac{\text{Creatinine clearance} \times (\text{Urea})_p - \frac{\text{Urea}}{\text{clearance}} \times (\text{Urea})_p}{\text{Creatinine clearance}}$$

$$= 1 - \frac{\text{Urea clearance}}{\text{Creatinine clearance}}$$

$$F_{(\text{urea excreted})} = \frac{\text{Amount excreted}}{\text{Amount filtered}}$$

$$= \frac{\text{Urea clearance} \times (\text{Urea})_p}{\text{Creatinine clearance} \times (\text{Urea})_p}$$

$$= \frac{\text{Urea clearance}}{\text{Creatinine clearance}}$$

2.4.3 Statistical analysis of the results

The mean values for individual dik diks and means of means as well as the standard error of the mean (SEM) were calculated for each experimental data. The student t-test was used to analyse the significance of the difference between the mean of the data in the control period and the mean of the data of each of the various treatments.

Where the t-test was done between two means, the differences are refered to as "significant" when ($P < 0.05$). The exact P values are given in Appendix VII. Where ($P > 0.05$), this is refered to as "not significantly different" in the text.

Linear regression analysis was done to examine the relationship between the data on urine flow rate and the fraction of filtered urea that is excreted. The relationship between the data was given by the coefficient of correlation (r). The methods that were employed for statistical tests are described by Kempthorne (1969).

CHAPTER III

3.0 RESULTS

3.1 Control observations

3.1.1 Intake and daily excretion of potassium, Sodium, Urea and Nitrogen

During the control experiment, each dik dik on average consumed 115.0 ± 2.6 g (± SEM) of early calf-weaning pellets and 33.9 ± 0.6 g (± SEM) of *Grewia similis* leaves. This diet provided 50.7 ± 0.9 mmole of potassium and 17.0 ± 0.9 mmole of sodium daily. The mean daily water intake was 251 ± 8.2 ml/day.

There were animal to animal variations in the volume of urine excreted daily. Urine output was found to be generally constant for each individual animal. The overall average daily urine volume excreted was 121.4 ± 9.1 ml/day. Dik dik B voided the highest recorded urine volume averaging 186.8 ± 20.1 ml/day while dik dik C voided the lowest urine volume averaging 38.3 ± 2.0 ml/day. Animals A and D excreted 140.9±10.6 and 120.9 ± 9.5 ml/day of urine respectively.

Urinary potassium excretion on average accounted for approximately 73.0 ± 1.0% of the combined total potassium recovered in the urine and faeces while faecal sodium represented 89.2 ± 1.2% of the total sodium recovered in urine

and faeces. Data on the mean daily output of electrolytes in urine and feaces of the individual animals are given in Table 2 and Appendix I.

Individual animal differences were observed in the measured urine osmolality. Dik dik C had the highest urine osmolality averaging 3461.5 ± 86.0 mOsm/kg H_2O, while dik dik B had the lowest osmolality of 1469.0 ± 85.0 mOsm/kg H_2O. Animal A and D excreted urine with an osmolality of 1808.0 ± 0 106.0 and 1632.1 ± 75.8 mOsm/kg H_2O, respectively. The mean overall urine osmolality for the four animals was 1989.3 ± 103.0 mOsm/kg H_2O (Table 3 shows urine osmolality together with electrolytes and urea-N concentrations for the individual animals).

There was little individual animal variations in plasma osmolalities as shown in Table 4. The overall plasma osmolality was 2322.0 ± 0.9 mOsm/kg H_2O. Urinary urea-N concentration was highly variable from animal to animal and among samples collected from the same animal. The highest concentrations were observed in dik dik C which had an average urea-N concentration of 916.2 ± 17.0 mmole/l while the lowest values were found in dik dik A (Table 3). The overall urinary urea-N concentration was 813.1 ± 37.0 mmole/l. Urinary urea accounted for 40% of the total urine osmolality while potassium accounted for 16%.

Table 2: *Daily excretion of sodium and potassium in urine and faeces of dik diks receiving the maintenance ration* (Means ± SEM).

Dik dik	No. of days	Potassium excretion			Sodium excretion		
		Urine (mmole/day)	Faeces (mmole/day)	% in urine	Urine (mmole/day	Faeces (mmole/day	% in urine
A	21	34.6±1.0	12.6±0.4	73.3±0.9	2.9±02	8.7±0.3	25.0±1.5
B	14	35.7±1.4	13.1±0.6	73.2±1.2	3.7±0.2	9.4±0.7	28.2±1.7
C	15	24.4±1.2	12.3±0.3	66.5±2.0	0.5±0.3	11.7±0.6	4.1±0.3
D	16	32.4±0.9	9.3±0.2	77.7±1.0	2.8±0.15	5.0±0.2	35.8±2.1
Mean of means		31.9±1.0	11.8±0.3	72.7±1.1	2.4±0.16	8.7±0.3	23.5±1.6

Table 3: Urine osmolality, urea-N and electrolytes concentrations for the individual animals during control experiments (Means ± SEM)

Dik dik	No. of days	U R I N E				Daily nitrogen intake (g/day)	Daily urinary urea-N excreted (g/day)
		Osmolality (mOsm/kg H_2O)	Urea conc. (mmole/l)	K conc. (mmole/l)	Na conc. (mmole/l)		
A	19	1808.0±106.0	689.1±20.0	297.9±59.0	21.7±3.5	25.6±1.1	0.6±0.01
B	14	1469.0±85.0	752.6±32.0	196.5±23.9	18.9±1.9	21.4±1.4	1.3±0.04
C	10	3461.5±86.0	916.2±17.0	586.8±27.1	13.2±1.2	23.5±0.9	1.4±0.02
D	15	1632.1±75.8	886.7±21.0	198.9±19.0	21.9±2.5	17.9±1.0	1.0±0.02
Mean of means		1989.3±87.2	813.1±21.3	319.0±32.4	19.7±1.9	22.2±1.0	1.1±0.006

Table 4: Plasma osmolality, urea-N and electrolytes concentrations during control experiment (Means ±SEM)

Dik dik	No. of days	P L A S M A			
		Osmolality (mOsm/kg H_2O)	Urea conc. (mmole/l)	K conc. (mmole/l)	Na conc. (mmole/l)
A	10	322.0±1.4	15.0±0.2	3.2±0.2	112.0±4.6
B	12	324.0±2.3	16.9±0.6	3.1±0.2	121.6±2.9
C	11	323.4±1.3	13.6±0.5	3.7±0.2	118.6±5.3
D	10	323.0±1.9	15.4±0.4	3.6±0.2	117.0±2.2
Mean of means		322.0±1.4	15.4±0.4	3.4±0.1	117.4±3.5

Individual animal variations were observed in urinary potassium excretion. The overall average urinary potassium concentration was 319.0 ± 11.8 mmole/l. The highest concentrations were observed in dik dik C with an average of 586.8 ± 27.1 and the lowest values recorded in dik dik B with a mean of 196.5 ± 23.9 mmole/l. Despite the variation in urinary potassium concentration between the animals, the proportion of the urine osmolality represented by potassium concentration was hardly variable and averaged 16% for all the animals. Potassium was the principal cation excreted in urine.

Urinary sodium concentration did not vary significantly from animal to animal. It ranged from 6.0 to 36 mmole/l with a mean of 19.7 ± 1.9 mmole/l. The fraction of total urinary osmolality represented by sodium was very minimal;(less than 1%).

The mean overall plasma urea concentration for the four animals was found to be 15.4 ± 0.3 mmole/l. There was little variation amongst the animals and within samples from the same animal. All values were however above 10 mmole/l. Except in three samples from dik dik A where plasma urea values exceeded urinary urea concentration values, all the other plasma urea values were lower than their corresponding urinary values.

The plasma potassium and sodium concentrations were 3.3 ± 0.1 and 117.4 ± 1.5 mmole/l respectively. The

concentrations of the two ions did not vary significantly from either animal to animal or within samples from one animal.

Urinary ammonia-N concentration averaged 55.2 ± 3.6 (range betweed 29.0 - 87.5 mmole/l). Similarly creatinine concentration in urine averaged 164.7 ± 15.7 (range between 47.1 - 386.8 mg/100 ml). On average, the daily urinary nitrogen excretion in terms of creatine, urea and ammonia was 0.15±0.007, 1.12± 0.01 and 0.04 ± 0.002 g,respectively.

3.1.2 Glomerular filtration rate and tubular reabsorption

In the control experiment the GFR of the did dik antelope ranged between 83.6 - 336.0 ml/min /100 kg b.wt. while the urine flow rate ranged between 0.03-0.22 ml/min. The glomerular filtration and urine flow rates for the individual animals areshown in Appendix II.

There were individual animals variations in the amount of urea being filtered at the glomerulus. It ranged between 72.4-230.8 µ-mole/min. with an average of 109.3 µ-mole/min. Out of this approximately 48.8 µ-mole/min. of the filtered urea was excreted in urine. However, urea excretion also varied with values ranging between 25.5 - 77.0 µ-mole/min. Tubular reabsorption of urea along the tubules on the average accounted for 55.3 ± 6.2% of the total amount filtered at the glomerulus.

The average amount of potassium filtered at the glomerulus was 27.4 µ-mole/min. with 15.5 ± 0.6 µ-mole/min being excreted in urine and 40.0 ± 3.5% was reabsorbed. All potassium clearances during the control experiment were observed to be lower than the corresponding creatinine clearances. There was therefore no evidence (as far as clearance observations could reveal) of tubular potassium secretion. The amount of potassium and urea filtered, reabsorbed and excreted by the individual dik diks are shown in Appendix II.

The average amount of sodium filtered at the glomerulus was 833.5 ± 36.4 µ-mole/min. Despite these large quantities of sodium filtered, almost all of it was reabsorbed (about 832.2 µ-mole/min.). Thus, reabsorption accounted for 99.9% of the filtered sodium.

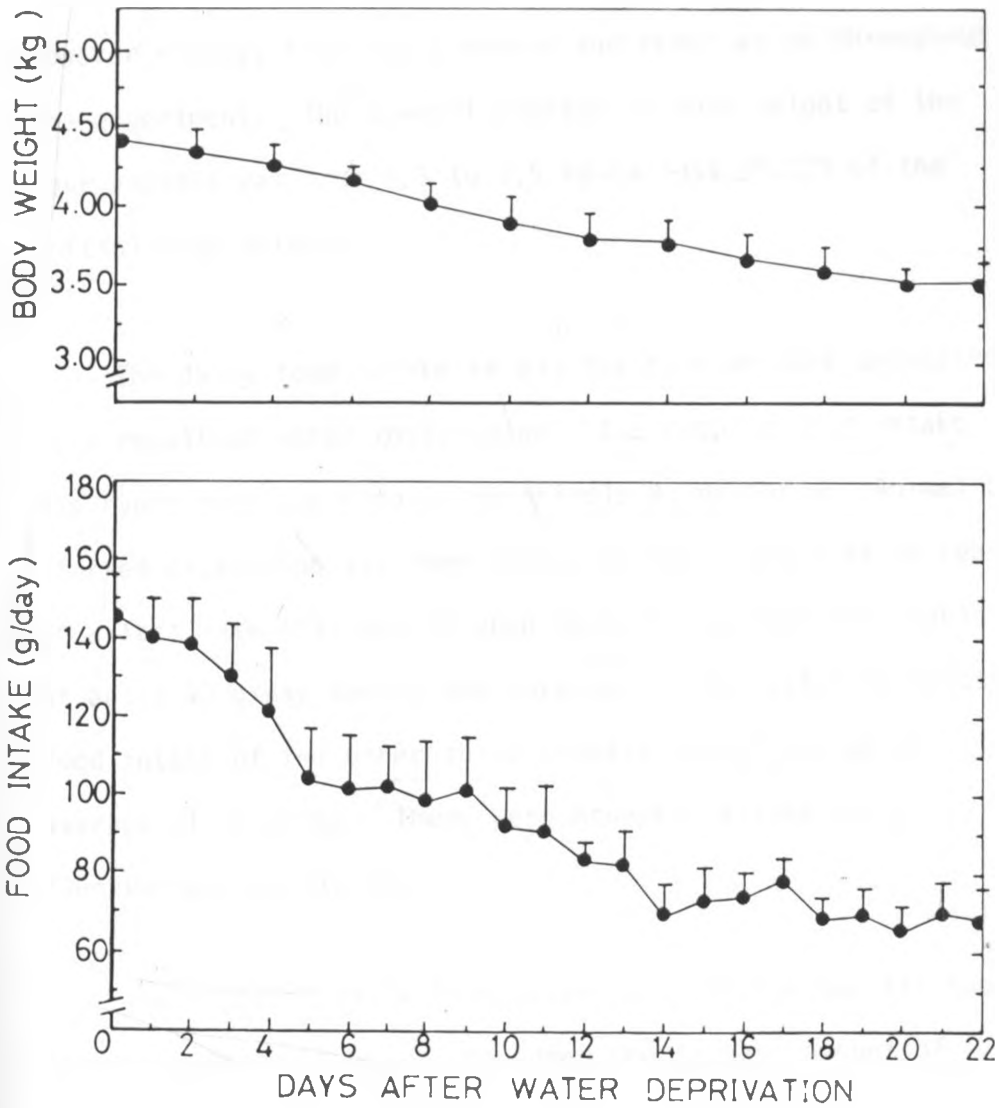
3.2 Effects of dehydration

3.2.1 General effects

The day-to-day changes in body weights and food intake for the dik diks during water restriction for a period of 22 days are shown in Figure 2. There was a steady decrease in body weight throughout the water restriction period.

The rate of loss in weight was rapid between day 2 and day 8 for dik diks A, B and D, then becoming slow but steady for the rest of the period for dik diks A and B. Animal B tended to increase weight slightly from day 16 to day 22

Fig. 2: The day-to-day changes in body weights and food intake of the animals during water restriction.


BODY WEIGHT (kg)
5.00
4.50
4.00
3.50
3.00
FOOD INTAKE (g/day)
180
160
140
120
100
80
60
0
2
4
6
8
10
12
14
16
18
20
22
DAYS AFTER WATER DEPRIVATION

(increases ranging from 3.4 to 3.6 kg).

The absolute rate of loss in weight by animal C was lowest of the four animals. While animals A and B lost about 1.2 kg each, animal C lost only 0.7 kg. Its weight loss was however steady, from day 2 onward and remained so throughout the experiment. The overall average in body weight of the four animals was from 4.5 to 3.5 kg (a loss of 22% of the initial body weight).

The daily food intake in all the four animals decreased as a result of water restriction. The drop in food intake was rapid from day 1 to 6 in animals A, B, and D. Animal C started decreasing its food intake on day 3 and kept decreasing at a fast rate till day 12 when food intake remained stable at about 90 g/day during the duration of the water restriction. Food intake of the other three animals stabilized at an average of 70 g/day. There were however, slight daily fluctuations on day 12.

The trend of daily food intake was similar for all the animals. Animal C which consumed the largest amount of food during control experiment, was still consuming more food than any of the other animals at the end of the period of dehydration. The overall drop in daily food intake was from a mean of 146 - 69 g/day thus giving rise to a 53% decrease. Animal A tended to increase its food intake from a minimum of 50 - 75 g on days 14 and 16, respectively. The intake fluctuated thereafter till the end of the

experiment. The individual dik dik daily food intake and body weights during water restriction period are shown in Figure 2 and Appendix III.

During dehydration plasma samples were taken on day 8 after the onset of water restriction,when the desired level of dehydration was thought to have been achieved,and continued till day 22. Plasma osmolality increased from the control value of 322.0 ± 1.4 to 332.4 ± 2.2 mOsm/kg H_2O following dehydration.

Dehydration also led to an increase in plasma urea concentration from the control value of 15.4 ± 0.1 to 22.4 ± 0.9 mmole/l. Similarly following dehydration, there was an increase in plasma potassium concentration from 3.4 ± 0.1 to 4.4 ± 0.08 mmole/l. Plasma sodium concentration increased from 117.4 ± 2.0 to 158.1 ± 1.8 mmole/l. Table 5 shows plasma osmolality, urea-N, K and Na concentrations during dehydration of individual animals.

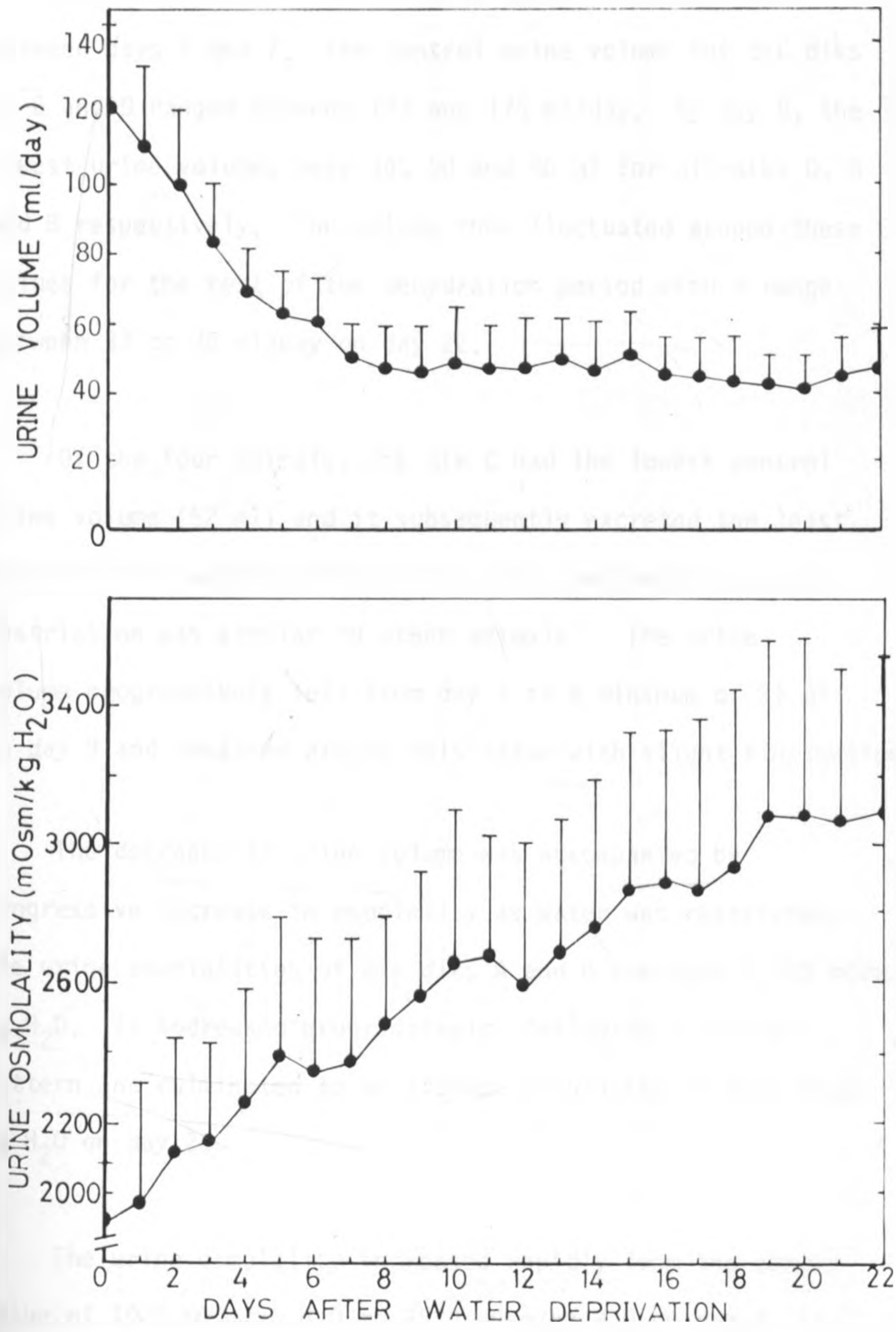
3.2.2 Renal effects

During water restriction and the subsequent resulting dehydration, there was a rapid fall in daily urine volume in all the four dik diks. This fall in urine volume was accompanied by an increase in urine osmolality. Figure 3 depicts the day-to-day changes in urine volume and osmolality during dehydration. The values used to draw this figure are given in Appendix III.

Table 5: Individual animal plasma osmolality and concentrations of urea-N, potassium and sodium during dehydration. Values are Means ± SEM.

Dik dik	No. of days	P L A S M A			
		Osmolality (mOsk/kg H_2O)	Urea conc. (mmole/l)	K conc. (mmole/l)	Na conc. (mmole/l)
A	10	334.2±3.4	24.4±0.8	4.7±0.1	163.0±3.4
B	10	339.4±5.5	25.8±1.6	4.7±0.1	164.4±3.6
C	10	323.6±4.8	19.2±1.4	4.1±0.1	153.0±3.4
D	10	332.4±2.3	20.1±0.6	4.1±0.1	152.0±1.7
Mean of means		332.4±3.7	22.4±0.9	4.4±0.1	158.1±2.9

Fig. 3: The day-to-day changes in urine volume and urine osmolality during water restriction.


URINE VOLUME (ml/day)
140
120
100
80
60
40
20
0
URINE OSMOLALITY (mOsm/kg H_2O)
3400
3000
2600
2200
2000
0
2
4
6
8
10
12
14
16
18
20
22
DAYS AFTER WATER DEPRIVATION

The rate of fall in the daily urine output was high between days 1 and 7. The control urine volume for dik diks A, B and D ranged between 117 and 175 ml/day. By day 8, the lowest urine volumes were 34, 50 and 80 ml for dik-diks D, A and B respectively. The volume then fluctuated around these values for the rest of the dehydration period with a range between 33 to 75 ml/day on day 22.

Of the four animals, dik dik C had the lowest control urine volume (52 ml) and it subsequently excreted the least volume during dehydration (23 ml). Its response to water restriction was similar to other animals'. The urine volume progressively fell from day 1 to a minimum of 21 ml on day 9 and remained around this value with slight fluctuations.

The decrease in urine volume was accompanied by progressive increase in osmolality as water was restricted. The urine osmolalities of dik diks A and B averaged 1,550 mOsm/kg H_2O. It increased progressively, following a similar pattern and culminated to an average osmolality of 3100 mOsm/kg H_2O on day 22.

The urine osmolality increased rapidly from the control value of 1520 mOsm/kg H_2O to 2520 mOsm/kg H_2O on day 4. It further increased at a slower but steady rate to a maximum of 3,760 mOsm/kg H_2O on day 19. There was then a slight fall to 3,560 mOsm/kg H_2O on the last day of the experiment. The low daily urine volume of dik dik C was, as expected, accompanied

by an increase in urine osmolality. The control value averaged about 3020 mOsm/kg H_2O and as water restriction commenced, the urine osmolality progressively increased reaching a high value of 4,200 mOsm/kg H_2O on day 20. This was the highest urine osmolality recorded throughout the study.

Dehydration decreased glomerular filtration rate in all the four dik diks. The largest decrease in GFR was observed in dik dik D where it fell from a control value of 206.8 to 120.0 ml/min /100 kg b.wt. Individual dik dik GFR values during both control and dehydration periods are shown in Table 6. There was a slight decrease in GFR in dik dik C. The overall average decrease in GFR was from a control value of 182.6 $\pm$ 11.7 to 141.7 $\pm$ 11.4 ml/min /100 kg b.wt. resulting in a 22% decrease .

Table 7 shows the amount of urea filtered at the glomerulus, excreted in urine and the percentage reabsorbed along the tubules in individual dik diks during control and dehydration experiments. There was no significant difference in the amounts of urea filtered at the glomerulus in the two experiments (average values of 109.3 $\pm$ 8.9 and 100.8 $\pm$ 6.9 µ-mole/min. during control and dehydration respectively). Unlike the other three animals where less urea was filtered during dehydration, a slight increase in the amount of filtered urea was observed in dik dik A.

Table 6: Glomerular filtration rate values during control and dehydration experiments (Means ± SEM).

Dik dik	No. of days	Glomerular filtration rate (ml/min /100 kg b.wt.)	
		Control	Dehydration
A	10	164.0±14.3	127.2±14.5
B	10	187.9±14.9	124.2±15.8
C	10	189.4±19.4	172.6±15.7
D	10	206.8±22.7	120.0±13.7
Mean of means		187.0 ± 14.7	136.0 ± 14.4

Table 7: The amount of urea filtered, excreted and reabsorbed during control and dehydration experiments (Means ± SEM).

Dik dik	No. of days	Urea filtered (μ-mole/min.)		Urea excreted (μ-mole/min.)		Percent urea filtered reabsorbed (%)	
		Control	Dehydrated	Control	Dehydrated	Control	Dehydrated
A	10	76.5±12.1	97.7±8.8	53.7±7.2	24.2±2.5	34.7±3.7	75.4±1.2
B	10	105.6±11.8	84.4±6.7	37.5±4.5	26.8±3.6	63.5±4.9	69.1±2.3
C	10	121.7±14.3	121.6±12.4	51.1±5.2	27.6±3.9	58.3±5.6	76.1±1.9
D	10	129.4±12.6	105.0±8.4	55.7±6.1	22.3±2.7	56.9±4.1	79.4±2.7
Mean of means		109.3±12.2	102.2 ± 6.9	48.8±5.5	24.9±2.9	55.3±4.4	77.2±1.3

As is shown in Table 7, dehydration led to a drop in urinary urea excretion in all the did diks. The highest rate of urea excretion during control was 55.7 ± 6.1 µ-mole/min. in dik dik D. This dropped to 22.3 ± 2.7 µ-mole/min. during dehydration. The lowest rate of excretion by dik dik B was 37.5 ± 4.5 and 26.8 ± 3.6 µ-mole/min. during control and dehydration periods respectively. The overall means for urea excretion rates during control and dehydration periods were 48.8 ± 2.9 and 24.9 ± 1.6 µ-mole/min. respectively; a 48% decrease.

The percent urea filtered which was reabsorbed along the tubules during dehydration in individual animals averaged 77.2 ± 1.3% and ranged between 69.1 and 79.4%. In the control experiment, the mean value was 55.3 ± 2.6% and the range between 34.7 and 63.5%. Thus dehydration resulted in an increase in the percentage of urea filtered that was subsequently reabsorbed.

Table 8 shows the amounts of electrolytes filtered and excreted by different animals during control and dehydration experiments. Following dehydration, the amount of potassium filtered at the glomerulus decreased from a mean of 27.4 ± 1.5 to 20.8 ± 1.7 µ-mole/min. There was also a decrease in the amount of sodium filtered from a mean value of 835.5 ± 23.4 to 711.4 ± 19.4 µ-mole/min. During the dehydration, urinary potassium and sodium excretions averaged 12.3 ± 0.7 and 0.84 ± 0.05 µ-mole/min, respectively.

Table 8: The amounts of electrolytes filtered and excreted during control and dehydration experiments (Means ± SEM).

Animal	GFR (ml/min.)	Plasma K conc. (mmole/l)	K filtered (µ-mole/min.)	Plasma Na conc. (mmole/l)	Na filtered (µ-mole/min.)	K excreted (µ-mole/min.)	Na excreted (µ-mole/min.)
CONTROL							
A	6.2±0.5	3.2±0.2	19.8±2.1	112.0±4.6	694.4±33.2	15.8±1.0	0.94±0.15
B	7.2±1.0	3.1±0.2	22.3±2.7	121.6±2.9	875.5±32.5	16.7±0.7	1.73±0.23
C	8.1±1.2	3.7±0.2	29.9±1.9	118.6±6.3	960.6±29.1	14.6±1.3	1.80±0.13
D	7.6±0.9	3.6±2.6	27.4±2.6	117.0±2.2	889.2±36.4	15.8±0.7	1.37±0.33
Mean of means	7.3±0.7	3.4±0.6	27.4±2.2	117.4±3.5	833.5±23.4	16.1±0.8	1.6±0.09
DEHYDRATED							
A	4.4±0.6	4.7±0.5	21.2±3.1	163.0±3.5	717.2±29.5	11.6±0.9	0.67±0.11
B	4.5±0.7	4.3±0.6	19.8±2.5	164.4±3.6	739.8±36.2	13.2±1.2	0.82±0.09
C	4.7±0.4	3.8±0.4	19.6±2.1	153.0±3.4	719.1±21.4	9.9±0.8	0.91±0.10
D	4.6±0.5	4.9±0.3	24.6±2.1	152.0±1.7	699.2±27.1	13.5±1.5	0.71±0.08
Mean of means	4.5±0.5	4.4±0.4	20.8±2.4	158.1±1.8	711.4±25.6	12.7±0.6	0.84±0.05

3.3 Effects of water loading

Intra-ruminal infusion of water did not cause any measurable changes in either the body weights or the amount of daily food intake of all experimental animals. There was, however, a decline in water intake. The reduction in the amount of water drunk was approximately equal to the quantity introduced into the rumen.

The results of the water loading experiment are given in Table 9. The concentrations pattern observed for both urine and plasma parameters were similar to those recorded during the control experiment. Urine and plasma osmolalities were 2126.5 $\pm$ 88.0 and 325.2 $\pm$ 1.4 mOsm/kg H_2O, respectively. Urine and plasma urea concentrations were 816.5 $\pm$ 15.1 and 9.5 $\pm$ 0.7 mmole/l, respectively. The plasma urea concentration was however less than that observed during the control experiment. The mean urine and plasma potassium concentrations were 328 $\pm$ 11.8 and 3.3 $\pm$ 0.1 mmole/l while urine and plasma sodium concentrations were 12.3 $\pm$ 0.7 and 125.0 $\pm$ 1.9 mmole/l, respectively.

3.4 Effects of acute salts loading

3.4.1 Potassium loading

Intra-ruminal potassium loading did not affect the amount of daily food intake and body weights of the dik diks. Table 10

Table 9: The urine volume, glomerular filtration rate, concentrations of urinary and plasma parameters of the two dik diks used in water loading experiment (Means ± SEM).

		Dik dik M	Dik dik R	Mean of means
Number of days		12	11	
Urine volume (ml/day)		106.5±8.2	135.6±10.1	120.4 ± 8.6
GFR (ml/min./100 kg b.wt.)		175.2±17.9	206.6±14.5	192.5± 16.2
URINE	Osmolality (mOsm/kg H_2O)	2315.7±98	1865.2±109.0	2126.5± 101
	Urea (mmole/l)	804.9±19.4	829.2±24.3	816.5± 22.1
	Potassium (mmole/l)	338.5±15.2	311.5±12.8	324.6±11.8
	Sodium (mmole/l)	19.8±0.9	14.2±1.2	17.1±1.0
PLASMA	Osmolality (mOsm/kg H_2O)	324.0±1.9	326.6±1.5	325.2±1.4
	Urea (mmole/l)	8.9±0.8	12.3±0.9	10.5 ± 0.8
	Potassium (mmole/l)	3.3±0.1	3.6±0.2	3.4 ± 0.1
	Sodium (mmole/l)	122.0± 2.4	126.8±2.9	125.0± 2.5

Table 10: *The urine volume, glomerular filtration rate, concentrations of different urinary and plasma parameters of the two dik diks used in solute loading experiments (Means ± SEM).*

		Potassium loading		Sodium loading	
		Dik dik M	Dik dik R	Dik dik M	Dik dik R
Urine volume (ml/day)		163.2 ± 14.7	204.6 ± 15.8	156.9 ± 16.2	182.0 ± 18.2
GFR (ml/min /100 kg b.wt.)		198.7 ± 19.4	253.7 ± 24.0	187.3 ± 11.0	224.7 ± 15.2
URINE	Osmolality (mOsm/kg H_2O)	1594.0 ± 61.0	1063.8 ± 54.0	1819.0 ± 105.0	1571 ± 121.0
	Urea (mmole/l)	612.9 ± 27.0	520.6 ± 31.0	791.3 ± 22.0	611.8 ± 17.3
	Potassium (mmole/l)	342.1 ± 20.6	186.9 ± 17.4	241.3 ± 39.1	174.0 ± 25.1
	Sodium (mmole/l)	49.8 ± 6.1	34.2 ± 5.5	141.0 ± 16.3	111.6 ± 18.2
PLASMA	Osmolality (mOsm/kg H_2O)	325.5 ± 1.6	329.0 ± 1.1	328.4 ± 2.1	331.6 ± 2.4
	Urea (mmole/l)	9.7 + 0.8	12.3 ± 0.5	12.4 ± 0.8	16.2 ± 1.3
	Potassium (mmole/l)	3.3 ± 0.2	3.4 ± 0.2	3.2 ± 0.1	3.4 ± 0.2
	Sodium (mmole/l)	116.6 ± 2.8	119. 8 ± 2.4	134.0 ± 3.1	142.3 ± 2.9

shows the glomerular filtration rate, urine and plasma values of the various parameters during both potassium and sodium intra-ruminal loadings. Plasma and urine osmolalities were 327.0 ± 1.1 and 1323.6 ± 129.7 mOsm/kg H_2O respectively during potassium loading. The glomerular filtration rate values averaged 225.9 ± 19.1 ml/min /100 kg b.wt. Urinary potassium and sodium concentrations were 309.6 ± 20.6 and 42.0 ± 5.5 mmole/l.

The effects of intra-ruminal infusion of KCl on the urinary excretion of potassium are shown in Figure 4 and Table 11. Intra-ruminal infusion of KCl resulted in an increase of the rate of urinary potassium excretion. The increase was from a control value of 16.1 to a maximum of about 50.3 μ-mole/min. during infusion of 0.5 mole/l KCl solution. The increased amount of potassium excretion was approximately equal to the amount infused. For example an infusion of 15 mmoles of potassium resulted in 32 μ-mole/min. being excreted in the urine. This was twice as much as the control excretion rate of about 16 μ-mole/min. Infusion of 30 and 45 mmole per day led to an excretion rate of 45 and 54 μ-mole/min, respectively.

The effects of intra-ruminal KCl infusion on the ratio of potassium to creatinine clearances are shown in Figure 5. During KCl infusion, the ratio steadily increased from a control value of 0.42.

Fig. 4: The effect of intra-ruminal infusion of KCl on the rate of excretion of potassium. Note that infusion of 50 mmoles led to excretion of potassium over 5 times the control rate. Symbols ○ and + represent Dik diks M and R respectively.

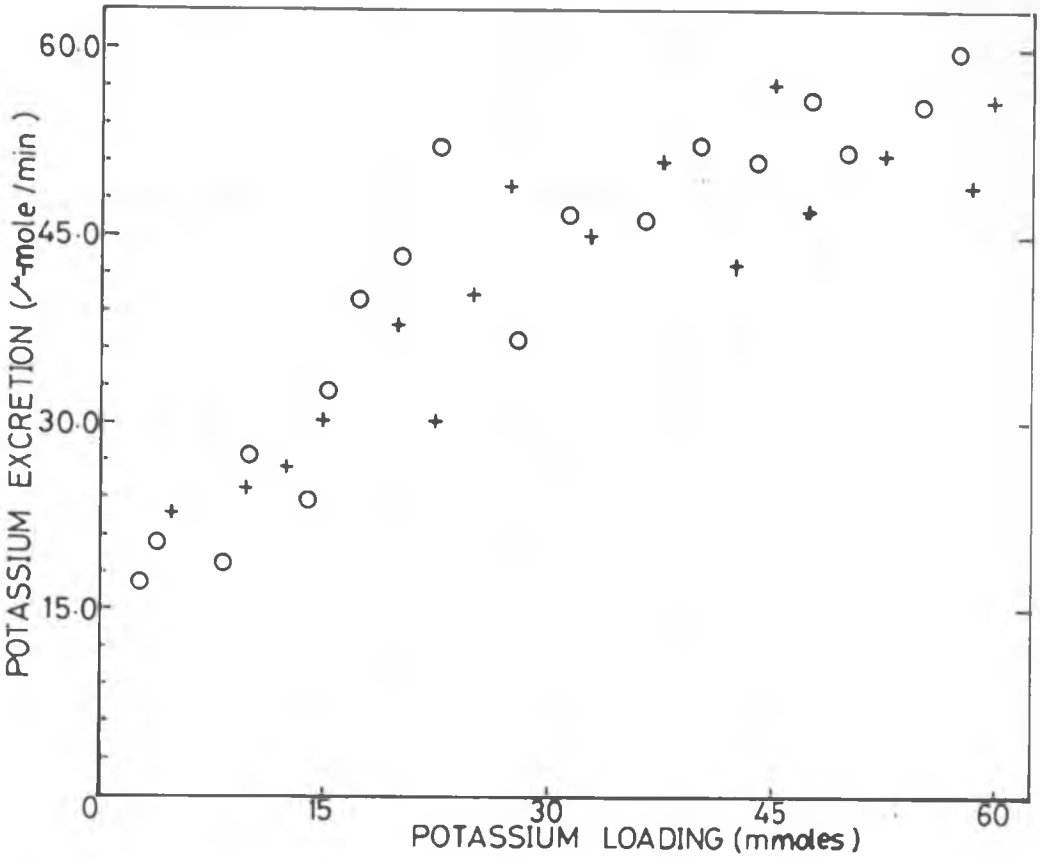
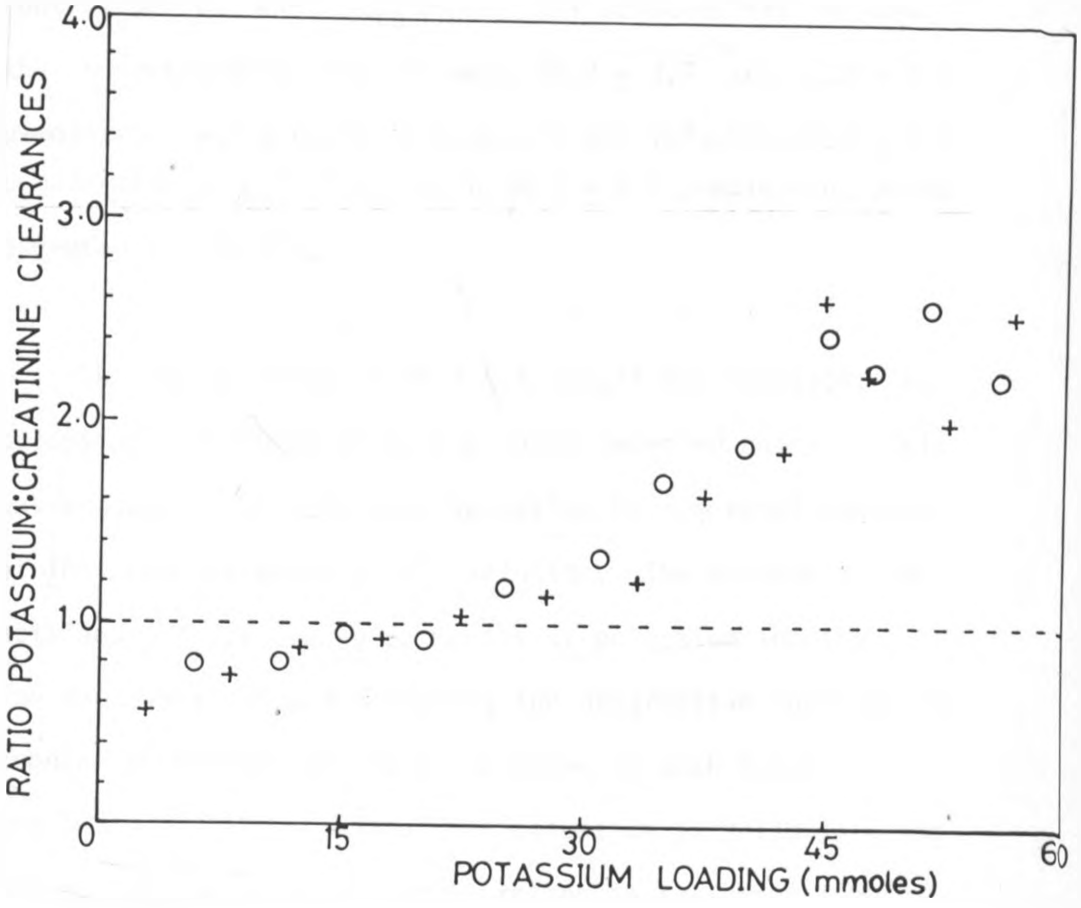

60·0
45·0
30·0
15·0
0
15
30
45
60
POTASSIUM EXCRETION (µ-mole/min)
POTASSIUM LOADING (mmoles)

Table 11: *The relation between the amount of dietary potassium intake, potassium filtered at the glomerulus and the amount excreted in the urine* (Mean ± SEM)

Condition	Dietary potassium intake (mmole/day)	CLEARANCE		Potassium filtered at the glomerulus (µ-mole/min.)	Potassium excreted in the urine (µ-mole/min.)	% K filtered that is reabsorbed (+) or excreted that is secreted (-)	$\frac{U_k V_u}{C_k}$
		Creatinine (ml/min.)	Potassium (ml/min.)				
Control	50.7±0.5	7.1±0.1	4.1±0.1	26.8±1.9	16.1±0.4	39.9^{+}	3.9
Potassium loading (0.3 mole/l)	73.2±1.2	8.9±0.7	7.5±0.7	38.7±3.8	32.0±3.1*	17.3^{+}	4.2
Potassium loading (0.5 mole/l)	100.7±1.3	9.0±0.6	17.1±1.8	22.3±1.5	50.3±2.2*	55.6^{-}	2.9

*Indicates means that are significantly different from the control mean.

Fig. 5: The effect of intra-ruminal infusion of KCl on the ratio of potassium to creatinine clearances. Note the evidence of potassium secretion from the loading of about 20 mmoles when the ratio starts exceeding 1.0. It remained above 1.0 throughout the rest of the potassium loading.


RATIO POTASSIUM:CREATININE CLEARANCES
4·0
3·0
2·0
1·0
0
15
30
45
60
POTASSIUM LOADING (mmoles)

During infusion of 0.3 mole/l KCl solution the ratio increased to 0.6-0.8. On increasing the volume of the solution infused, the ratio increased further to 1.0-1.1; thus suggesting that some potassium was being secreted by the renal tubules. Out of 26.8 ± 1.9 μ-mole/min. of potassium filtered only 16.1 ± 0.4 μ-mole/min. was excreted during the control period. When a 0.3 mole/l KCl solution was infused, the corresponding figures were 38.7 ± 3.7 and 32.0 ± 3.1 μ-mole/min. while during 0.5 mole/l KCl infusion, 22.3 ± 1.5 μ-mole/min. were filtered with 50.3 ± 2.1 μ-mole/min. being excreted (Table 11).

Throughout infusion of a 0.5 mole/l KCl solution, the potassium:creatinine clearance ratio exceeded unity. This was suggestive of potassium secretion by the renal tubules at this concentration of KCl infusion. The maximum ratio attained was 2.4 during 55 mmoles of potassium infusion. The data obtained and depicting the progressive increase in tubular potassium secretion is shown in both Appendix II and Table 11. About 55% of the potassium excreted in urine was attributed to potassium secretion in the renal tubules during infusion of the 0.5 mmole/l KCl solution.

Figure 6 shows measured data for GFR during intra-ruminal infusion of KCl solutions. There was a slight increase in the GFR during infusion of both 0.3 and 0.5 mole/l KCl solutions. Infusion of KCl resulted in diuresis. This is shown in Figure 7 which shows the effects of intra-ruminal

Fig. 6: The effect of intra-ruminal infusion of KCl solutions on the rate of glomerular filtration.

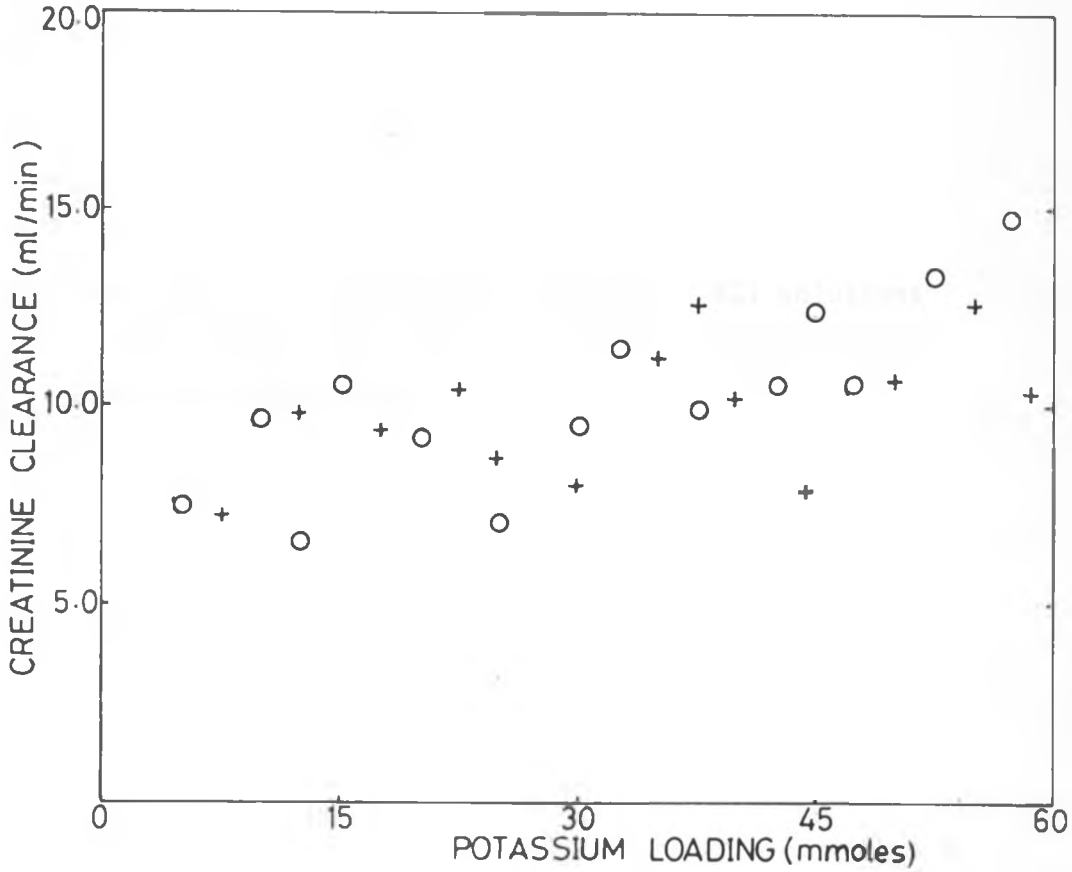
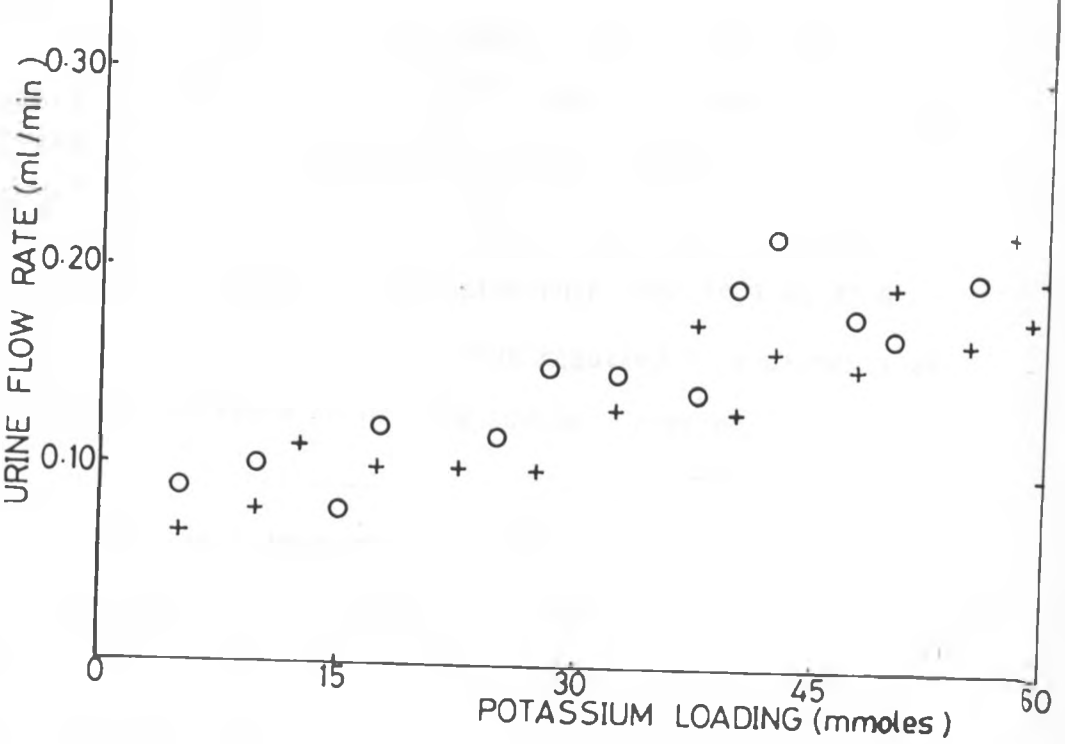

20·0
15·0
10·0
5·0
0
15
30
45
60
CREATININE CLEARANCE (ml/min)
POTASSIUM LOADING (mmoles)

Fig. 7: The effect of intra-ruminal infusion of KCl solutions on the rate of urine flow. The steady increase in the flow rate was observed.


0·30
0·20
0·10
URINE FLOW RATE (ml/min)
0
15
30
45
60
POTASSIUM LOADING (mmoles)

infusion of KCl on the rate of urine flow. The observed rate of urine flow rose to 0.10 ml/min. following infusion of 0.3 mole/l KCl solution and increased further to a maximum value of 0.22 ml/min. during infusion of over 40 mmoles per day of potassium.

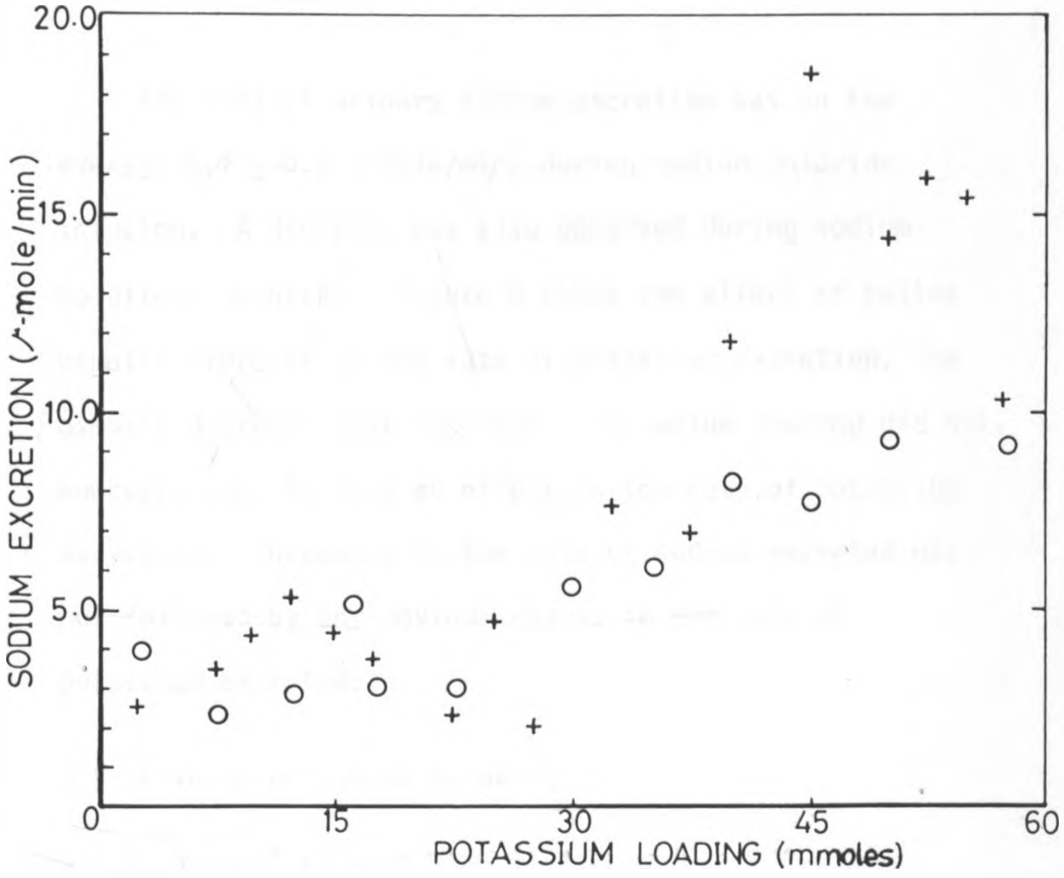
Infusion of KCl also led to a natriuresis. The effect of KCl infusion on the rate of sodium excretion is depicted on Figure 8. Sodium excretion rate during the control period was very low (about 1 μ-mole/min.). It increased to 2.5 ± 0.3 μ-mole/min. during infusion of 10 mmoles; and then to 10 μ-mole/min. when 40 mmoles were infused (a rate 10 times the control excretion rate). The urinary sodium concentration during KCl infusion rose from 19.7 to 42.0 mmole/l. Potassium infusion thus resulted in a diuresis as well as an increase in urinary sodium excretion.

There was a decrease in the amount of sodium filtered and subsequently reabsorbed in the renal tubules from a control value of 99.9% to 98.8% during intra-ruminal infusion of 0.5 mole/l KCl (Appendix IV). This decrease of about 1% may seem small but it is undoubtedly a considerable amount considering the high plasma Na concentration and thus large quantities filtered.

3.4.2 Sodium loading

During intra-ruminal sodium infusion no change was noted in the body weights of the animals. A slight increase in food intake was however observed. Plasma and urine

Fig. 8: The effect of intra-ruminal infusion of KCl on the rate of sodium excretion. Note the steady increase in sodium excretion rate with increase in KCl infusions.


20·0
15·0
10·0
5·0
0
15
30
45
60
SODIUM EXCRETION (μ-mole/min)
POTASSIUM LOADING (mmoles)

osmolalities were 330.6 ± 2.1 and 1695.3 + 129.7 mOsm/kg H_2O respectively (Table 10). The recorded glomerular filtration rate was 206.9 ± 9.3 ml/min/100 kg b.wt.

The potassium concentration in urine was 201.3 ± 4.8 mmole/l, while that of sodium was 126.5 ± 17.3 mmole/l during sodium loading. Plasma sodium concentration was 138.0 ± 2.9 mmole/l.

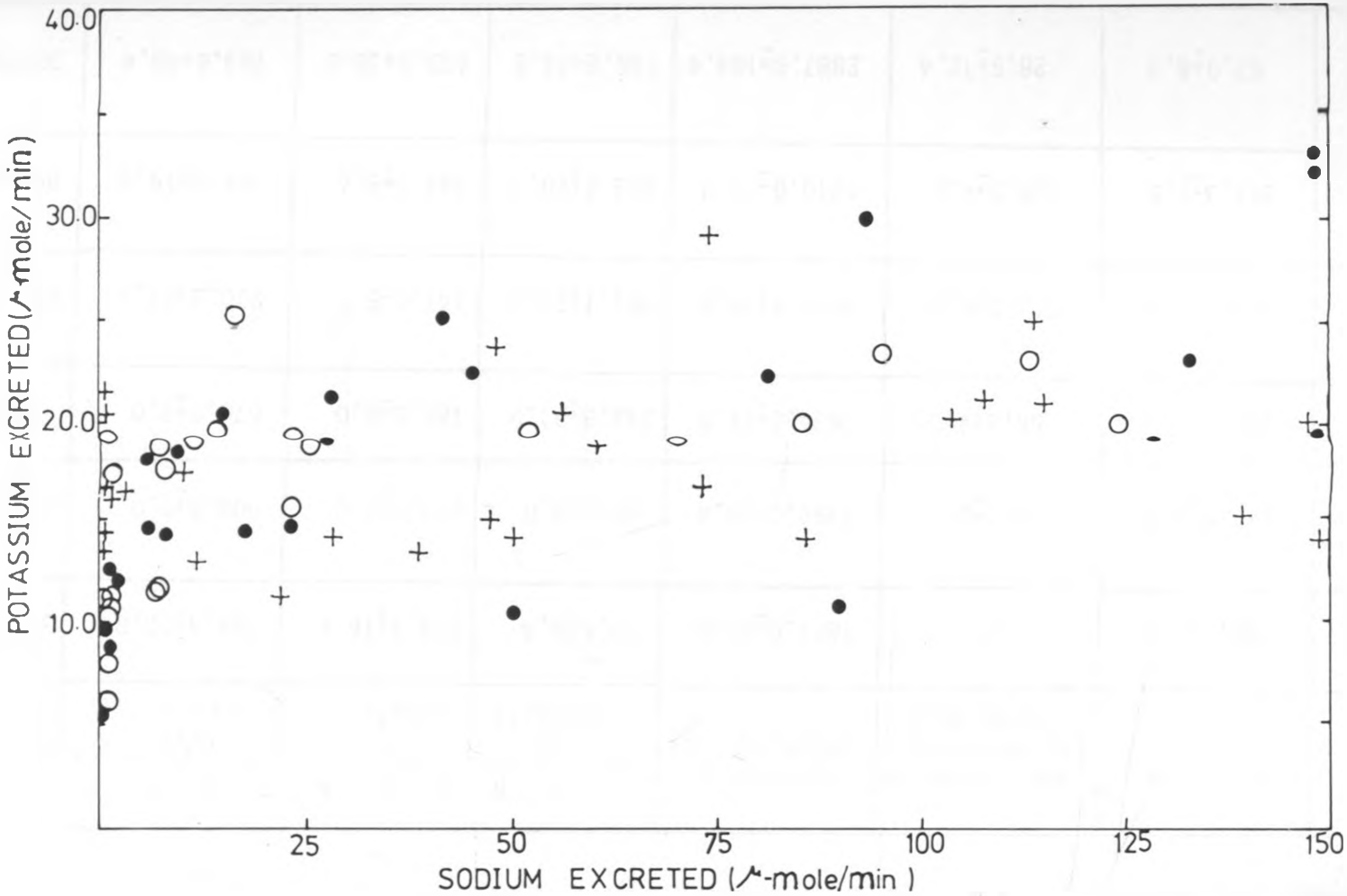
The rate of urinary sodium excretion was on the average 8.7 ± 0.7 u-mole/min. during sodium chloride infusion. A diuresis was also observed during sodium solutions infusion. Figure 9 shows the effect of saline osmotic diuresis on the rate of potassium excretion. The osmotic diuresis that resulted from sodium loading did not, however, seem to have an effect on the rate of potassium excretion. Increases in the rate of sodium excreted was not followed by any obvious change in the rate of potassium excreted.

3.5 Effects of saline drinking

3.5.1 General effects

The voluntary intake of freshwater and saline solutions of concentrations from 0.1 to 0.5 mole/l NaCl was measured (Table 12). The average water intake was 230.5 ml/day. When saline solutions were offered as the only source of drinking water, the fluid intake rose and reached a maximum of 373.9 ml/day at 0.3 mole/l NaCl concentration, while NaCl intake from the

Fig. 9: Effect of saline osmotic diuresis on the rate of urinary potassium excretion.


40·0
30·0
20·0
10·0
POTASSIUM EXCRETED (μ-mole/min)
25
50
75
100
125
150
SODIUM EXCRETED (μ-mole/min)

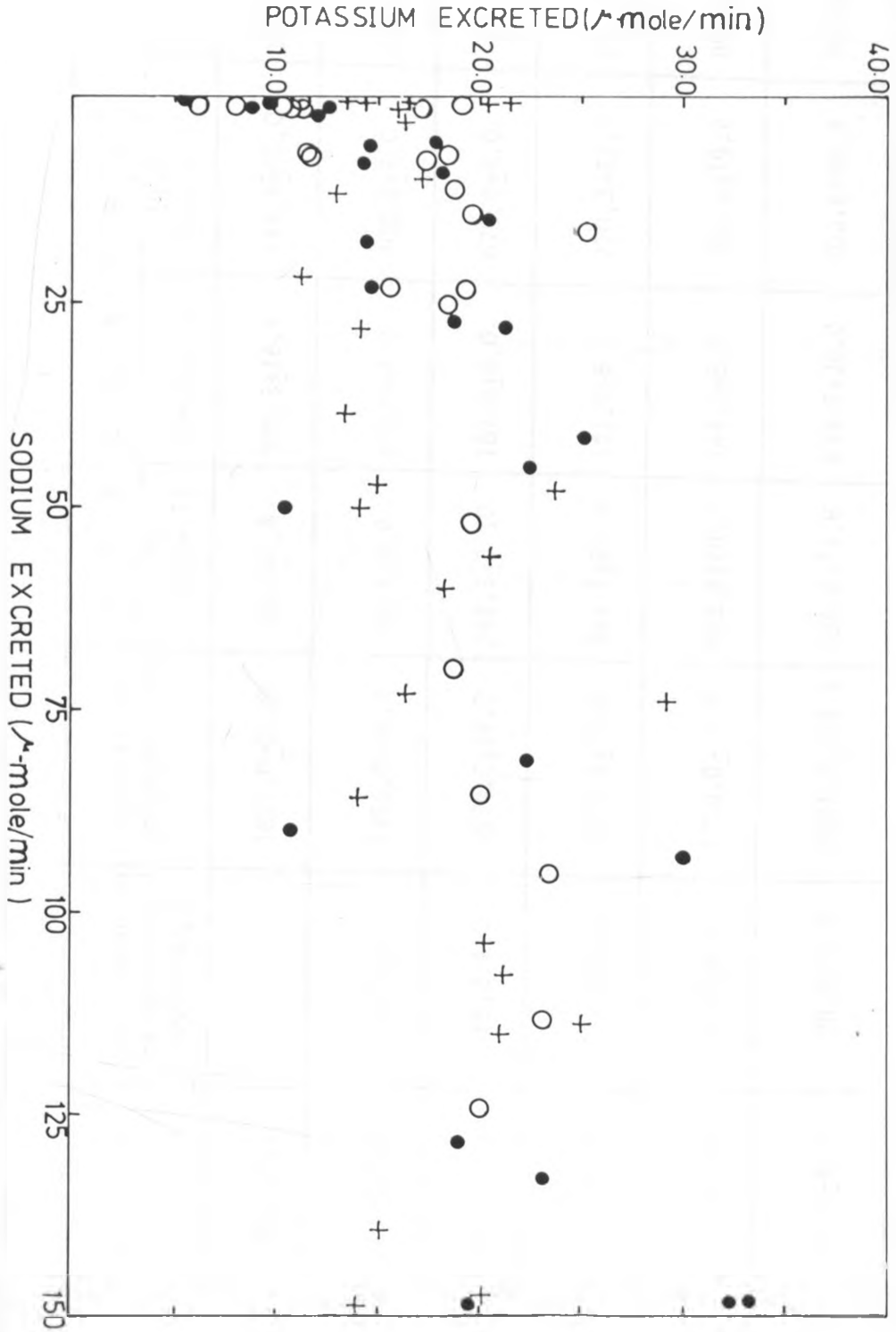

POTASSIUM EXCRETED(μ-mole/min)
10.0
20.0
30.0
40.0
SODIUM EXCRETED (μ-mole/min)
25
50
75
100
125
150

Table 12: *The effects of saline intake on fluid intake, urine osmolality, sodium, potassium creatinine and urea concentrations* (Mean ± SEM).

Treatment	Fluid intake	NaCl taken in by drinking (mmole/day)	Osmolality (mOsm/kg H_2O)	C O N C E N T R A T I O N			
				Na (mmole/l)	K (mmole/l)	Urea (mmole/l)	Creatinine (mg/100 ml
H_2O ad lib.	230.5±5.2	-	1821.0±23.0	19.5±2.4	329.3±16.6	794.4±10.0	318.8±10.8
0.1 mole/l NaCl	240.9±9.2	24.1±3.1	1756.0±29.4	92.6±8.0	213.8±7.0	908.8±9.0	236.4±10.2
0.2 mole/l NaCl	281.5±6.3	56.3±4.0	1634.0±19.0	242.8±21.0	187.0±6.0	670.0±8.0	82.0±9.6
0.3 mole/l NaCl	373.9±7.4	112.2±4.8	1510.4±19.0	384.7±23.5	141.0±5	270.3±22.4	67.9±8.3
0.4 mole/l NaCl	321.3±5.6	128.5±4.6	1710.0±21.4	403.2±20.7	144.3±5.4	356.6±19.2	85.2±9.1
0.5 mole/l NaCl	57.0±8.3	28.5±12.4	2887.9±104.4	186.2+24.8	439.5+39.0	703.6+40.4	308.8+34.8

water also reached a maximum of 0.4 mole/l NaCl where the intake was 128.5 mmole/day (Figure 10). This is an 8-fold increase above the intake of sodium during the control where the only source of sodium was dietary.

At higher salinities, the fluid intake fell and at 0.5 mole/l, some animals did not drink at all. As the salinity of the drinking fluid was increased, the animals responded by decreasing fluid intake at the concentrations between 0.3 and 0.5 mole/l NaCl.

Figure 11 and Appendix V show the day-to-day changes in the rate of both fluid and NaCl intake by drinking when 0.4 mole/l NaCl was offered to the animals. All the experimental animals displayed a similar pattern in the intakes of both fluid and NaCl solutions. From the first to the fifth day when 0.4 mole/l NaCl was offered, the animals drank more saline. The NaCl intake was also found to increase. From the sixth day, there was a steady decline in the amount of saline drunk. A minimum of fluid intake was observed on the fifteenth day when only 48 ml was drunk while some animals did not drink at all. This corresponded to a minimum NaCl intake of about 23 mmole/day. Thus less and less fluid was drank as the fluid salinity increased beyond 0.3 mole/l NaCl (osmolality 545 mOsm/kg H_2O).

Fig. 10: Drinking rate, intake of NaCl as functions of salinity of the drinking fluid.

DRINKING RATE.
DRINKING RATE (ml/day)
400
300
200
100
H2O ad lib
0·1
0·2
0·3
0·4
0·5
mole/l NaCl

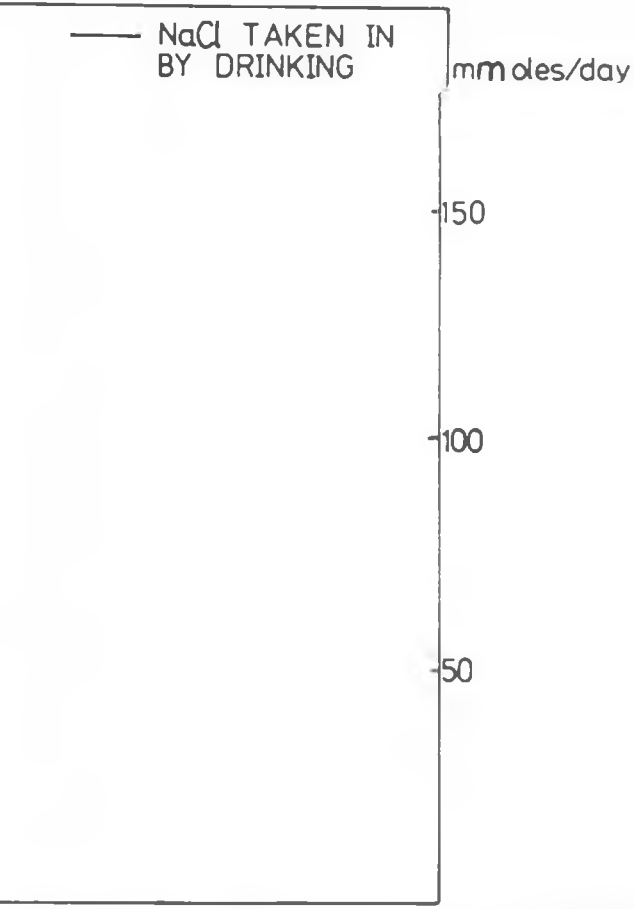
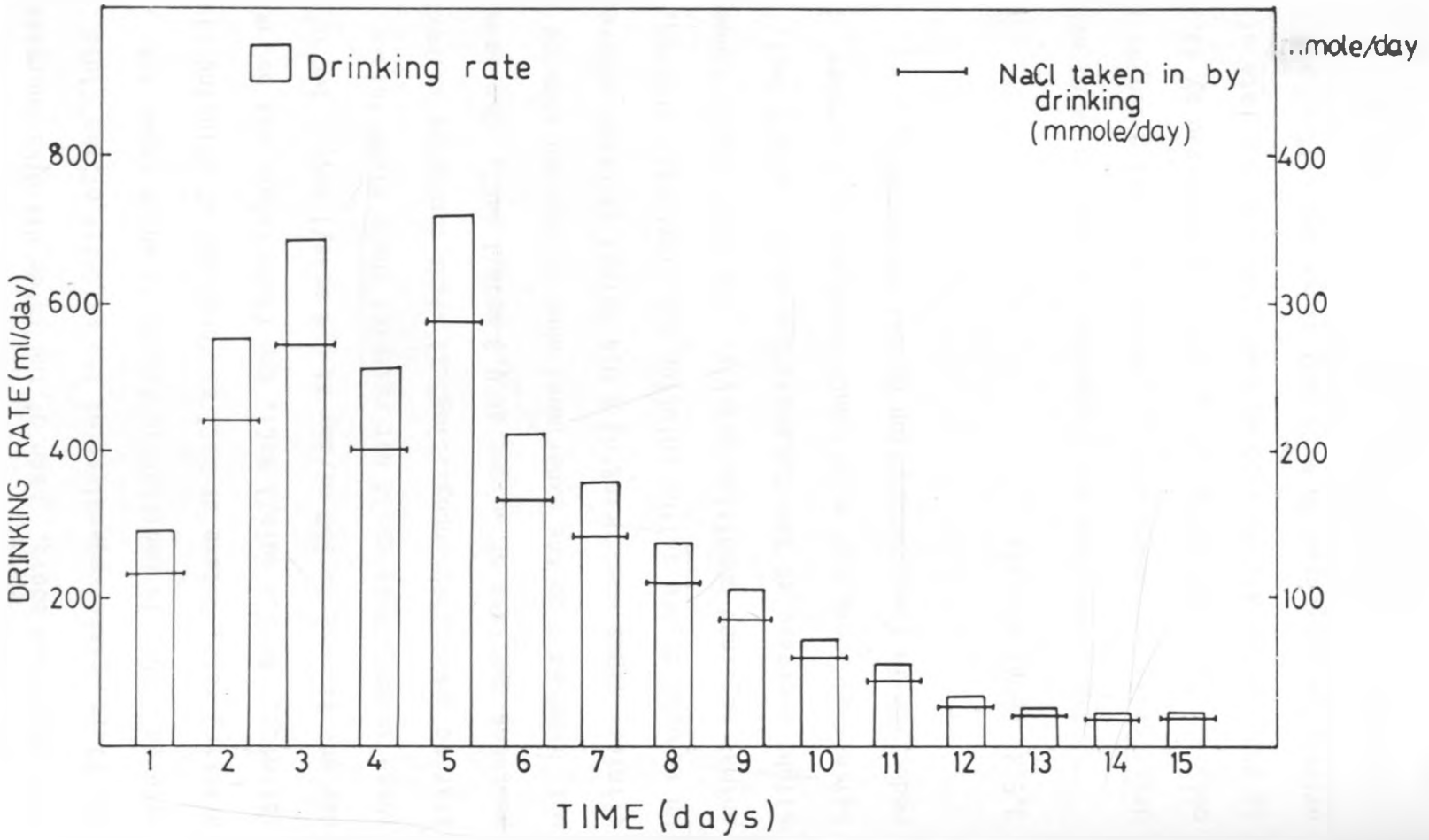

NaCl TAKEN IN
BY DRINKING
mmoles/day
150
100
50

Fig. 11: The effect of 0.4 mole/l NaCl drinking on the day-to-day changes in fluid and NaCl intake.

Fig. 11: The effect of 0.4 mole/l NaCl drinking on the day-to-day changes in fluid and NaCl intake.


Drinking rate
NaCl taken in by drinking (mmole/day)
..mole/day
DRINKING RATE (ml/day)
800
600
400
200
400
300
200
100
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
TIME (days)

Three animals however showed a different response from that described above. Each of the three dik diks increased its fluid intake regardless of the salinity of the fluid offered. This is depicted in Figure 12 which shows the drinking rate, intake of NaCl as functions of drinking fluid salinity. At 0.3 mole/l NaCl, the fluid intake was 650 ml/day and it rose to 950 ml/day at 0.4 mole/l NaCl. Two of these animals that could not restrict their fluid intake started developing unphysiological signs including anorexia, weakness and loss of weight at 0.3 mole/l NaCl. One animal was removed from the experiment when it started showing the clinical signs when drinking a 0.4 mole/l solution offered. On removal of the saline solution and freshwater offered, the animal regained condition quickly. The food intake showed a slight increase at the concentration of 0.1 mole/l NaCl. Salinities above 0.3 mole/l NaCl resulted in a further reduction in food consumption by all the animals.

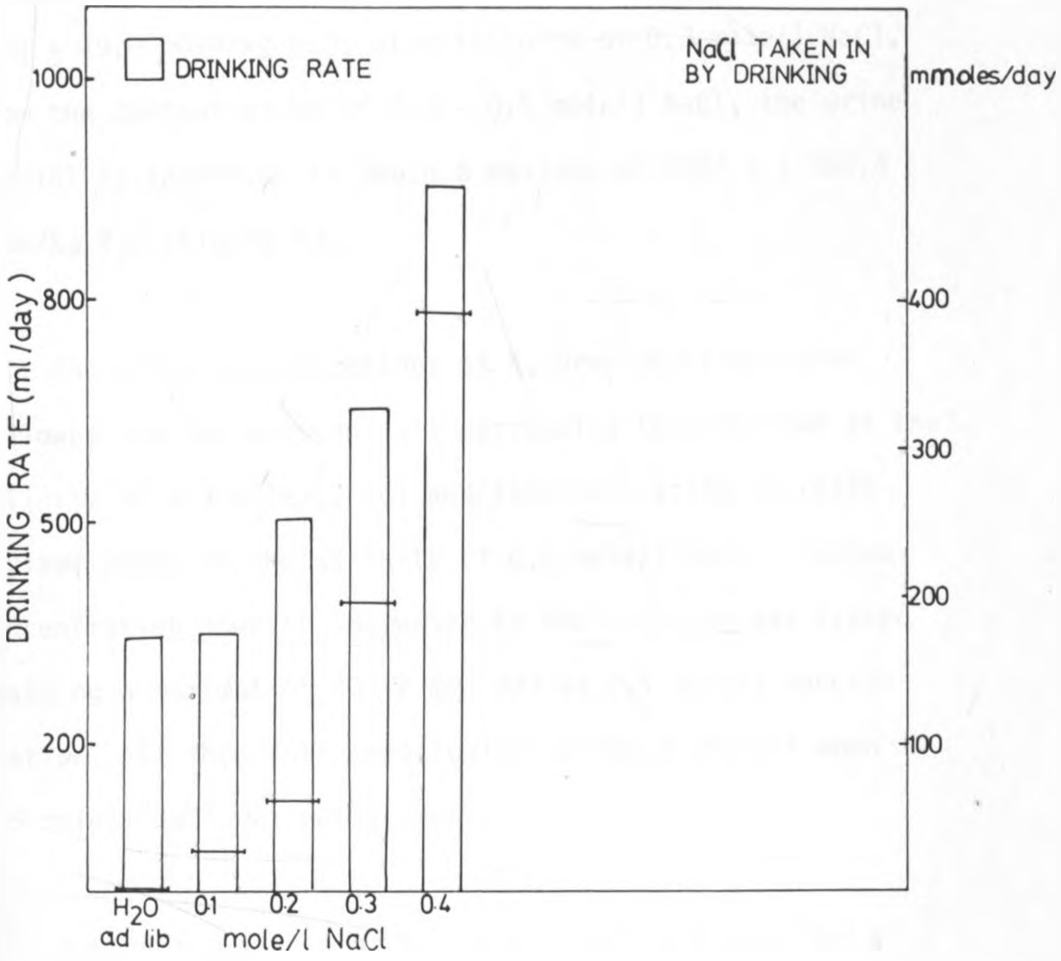
3.5.2 Renal effects

The urine flow and glomerular filtration rates were drastically increased when 0.3 mole/l NaCl was given as the only source of drinking water. The GFR increased by 43.7% to 262.5 $\pm$ 9.4 ml/min /100 kg b.wt., whereas the rate of urine flow increased to more than twice the control value. The percent sodium filtered that was reabsorbed decreased from a control value of 99.9% to 93.2% following ingestion of 0.3 mole/l NaCl solution. The rate of sodium excretion increased by over 60-fold from 1.6 $\pm$ 0.2 to 75.1 $\pm$ 5.0 µ-mole/l

Fig. 12: Intake of NaCl and fluid as functions of the drinking fluid salinity.

Fig. 12: Intake of NaCl and fluid as functions of the drinking fluid salinity.

Fig. 12: Intake of NaCl and fluid as functions of the drinking fluid salinity.


DRINKING RATE
NaCl TAKEN IN BY DRINKING
mmoles/day
DRINKING RATE (ml/day)
1000
800
500
200
400
300
200
100
H2O ad lib
0·1
0·2
0·3
0·4
mole/l NaCl

following 0.3 mole/l NaCl drinking. Urinary sodium concentration increased from 19.7 ± 1.4 to 403.2 ± 20.7 mmole/l.

The urine osmolality and the Na, K, urea and creatinine concentrations of dik diks receiving freshwater as well as drinking NaCl solutions of 0.1 - 0.5 mole/l are given in Table 12. The urine osmolality decreased to a minimum of 1510 ± 19.0 mOsm/kg H_2O; at a salinity of 0.3 mole/l NaCl. From the concentration of 0.3 - 0.5 mole/l NaCl, the urine osmolality increased to reach a maximum of 2887.9 ± 104.4 mOsm/kg H_2O (Figure 13).

The urine concentrations of K, urea and creatinine followed similar pattern; all decreasing to a minimum at the salinity of 0.3 mole/l NaCl and then increasing to reach maximal level at the salinity of 0.5 mole/l NaCl. Sodium concentration however increased as the salinity was raised reaching a maximum of 403.2 mmole/l at 0.4 mole/l concentration. It then fell drastically to 186.2 mmole/l when 0.5 mole/l NaCl was being drunk.

During the course of 0.4 mole/l NaCl drinking for a period lasting 15 days, the day-to-day changes in urine osmolality and electrolyte concentrations (Na and K) are shown in Figure 14. The osmolality together with potassium concetration decreased from the first day to a minimum on the third and fifth days respectively. During this period, the sodium concentration increased, reaching a maximum on the sixth day. From the fourth and sixth day, urine

Fig. 13: The relationship between urine osmolality and salinity of the drinking fluid. Note the slight decrease followed by an abrupt increase in urine osmolality.

Fig. 13: The relationship between urine osmolality and salinity of the drinking fluid. Note the slight decrease followed by an abrupt increase in urine osmolality.

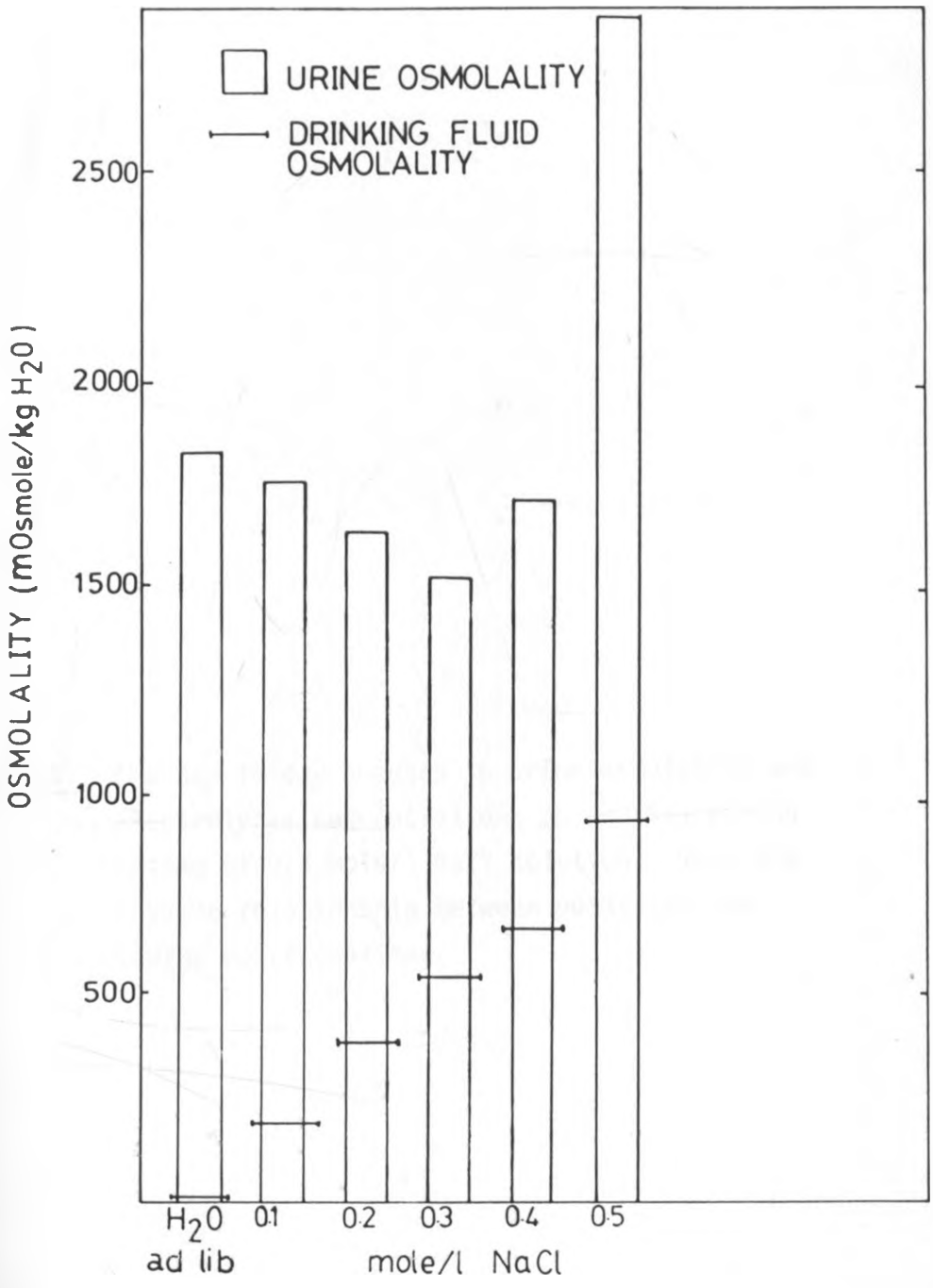
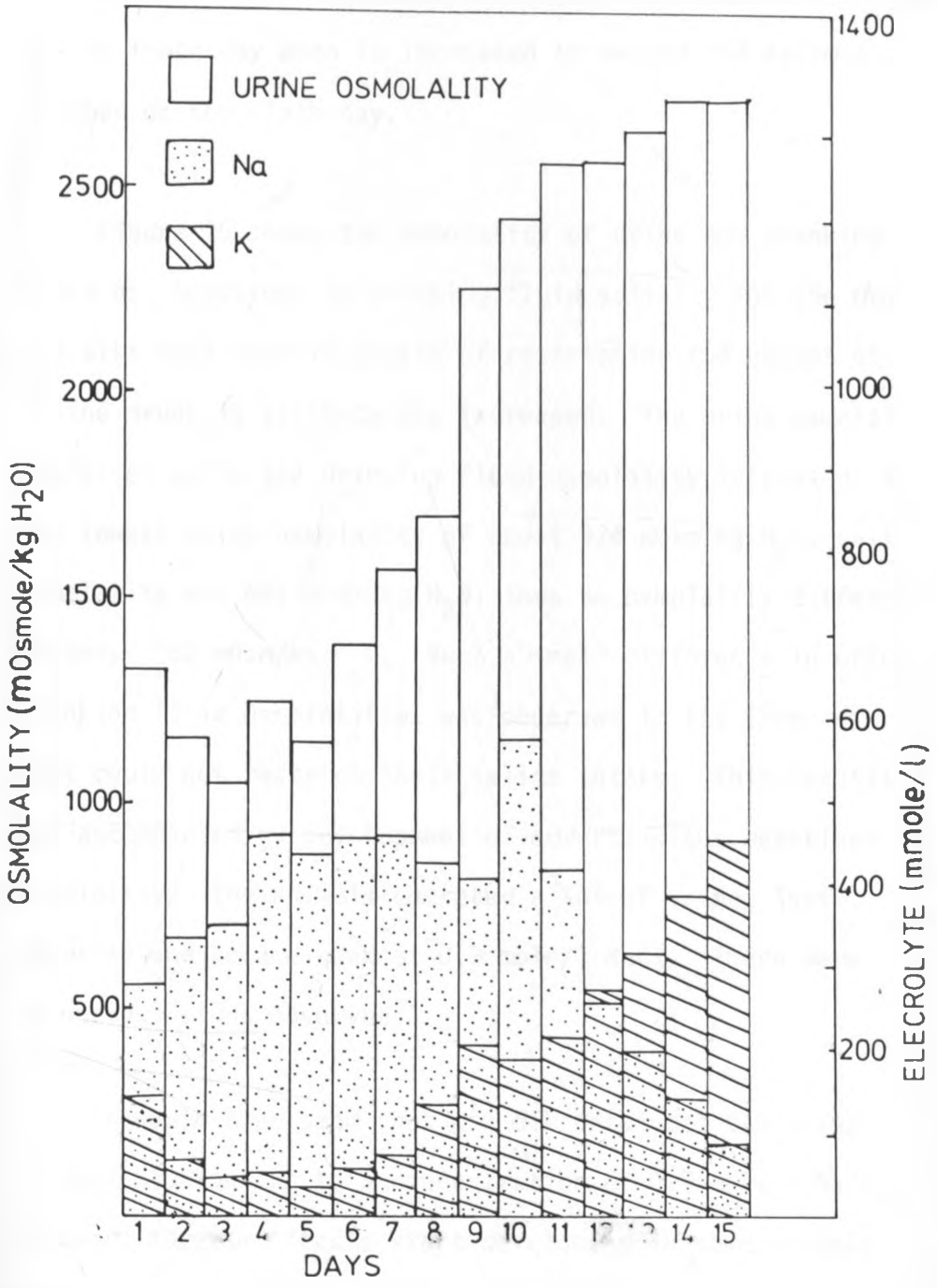

URINE OSMOLALITY
DRINKING FLUID OSMOLALITY
OSMOLALITY (mOsmole/kg H2O)
2500
2000
1500
1000
500
H2O ad lib
0·1
0·2
0·3
0·4
0·5
mole/l NaCl

Fig. 14: The day-to-day changes in urine osmolality and electrolytes concentrations (K and Na) during intake of 0.4 mole/l NaCl solution. Note the inverse relationship between potassium and sodium concentrations.

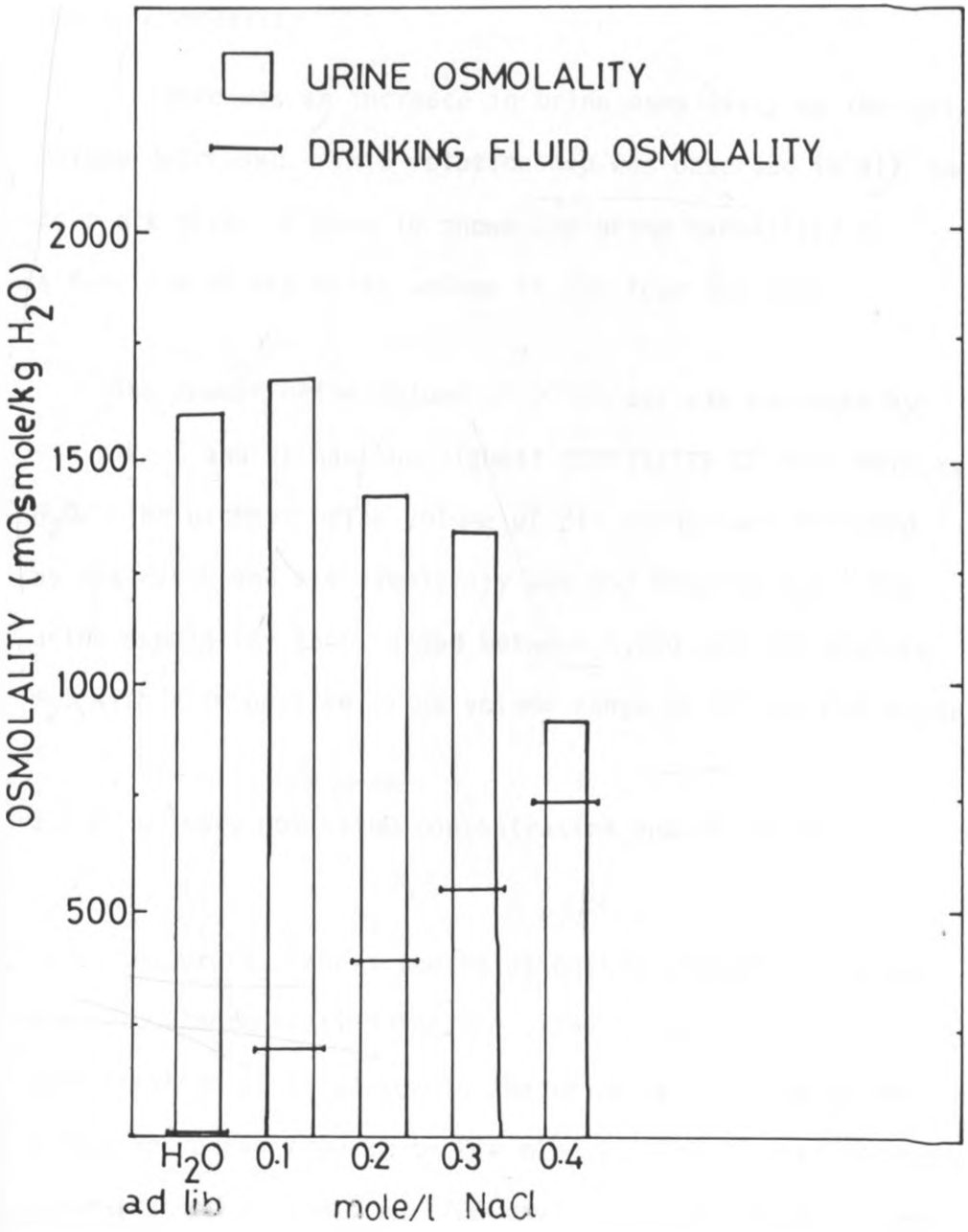

URINE OSMOLALITY
Na
K
OSMOLALITY (mOsmole/kg H_2O)
ELECROLYTE (mmole/l)
DAYS
500
1000
1500
2000
2500
200
400
600
800
1000
1400
1 2 3 4 5 6 7 8 9 10 11 12 14 15

osmolality and potassium concentration respectively increased till the last day of the experiment. Sodium concentration decreased from the eighth day throughout the experiment except on the tenth day when it increased to exceed the maximum reached on the sixth day.

Figure 15 shows the osmolality of urine and drinking fluid as functions of drinking fluid salinity for the three dik diks that were incapable of restricting the amount of saline drunk as salinity was increased. The urine osmolality decreased while the drinking fluid osmolality increased. At the lowest urine osmolality of about 924 mOsm/kg H_2O, saline osmolality was 662 mOsm/kg H_2O; thus an osmolality difference of only 262 mOsm/kg H_2O. Such a small difference in urine and drinking fluid osmolalities was observed in the three dik diks that could not restrict their saline intake. This inability was accompanied by development of adverse signs described previously. The animals excreted a lot of urine, lost appetite and became weak at 0.3 mole/l NaCl. There were no nervous signs observed.

It would thus seem that dik dik antelopes can drink saline solutions up to a concentration of 0.5 mole/l NaCl. However, adverse effects start developing in some animals at the concentration of 0.3 mole/l NaCl solution.

Fig. 15: The osmolality of urine and drinking fluid as functions of drinking fluid salinity for dik dik A which had to be removed from the experiment when 0.4 mole/l NaCl was offered.


URINE OSMOLALITY
DRINKING FLUID OSMOLALITY
OSMOLALITY (mOsmole/kg H_2O)
2000
1500
1000
500
H_2O ad lib
0.1
0.2
0.3
0.4
mole/l NaCl

3.6 Relationship of variations in urine volume to urine osmolality, urea and potassium concentrations

3.6.1 Osmolality

There was an increase in urine osmolality as the urine volume decreased. This relationship was observed in all the four dik diks. Figure 16 shows the urine osmolality as a function of the urine volume in the four dik diks.

The lowest urine volume of 23 ml/day was excreted by dik dik C and it had the highest osmolality of 4200 mOsm/kg H_2O. The highest urine volume of 214 ml/day was excreted by dik dik B and its osmolality was 850 mOsm/kg H_2O. The urine osmolality thus ranged between 4,200 and 850 mOsm/kg H_2O with a respective urine volume range of 23 and 214 ml/day.

3.6.2 Urinary potassium concentration and excretion

Figure 17 shows the relationship between the urine potassium concentration and the urine volume. The concentration of potassium in the urine fell as the urine volume increased from 21 to 214 ml/day. The highest potassium concentration attained was 768 mmole/l and the lowest concentration was 108 mmole/l. The relationship between the urine osmolality and potassium concentration was such that potassium in the urine on the average accounted for 18% of the total urine osmolality.

Fig. 16: The relationship between urine volume and osmolality. The urine volume was varied by gradually restricting the amount of water intake. Each symbol represents a different animal and the same symbols are used in the subsequent figures.

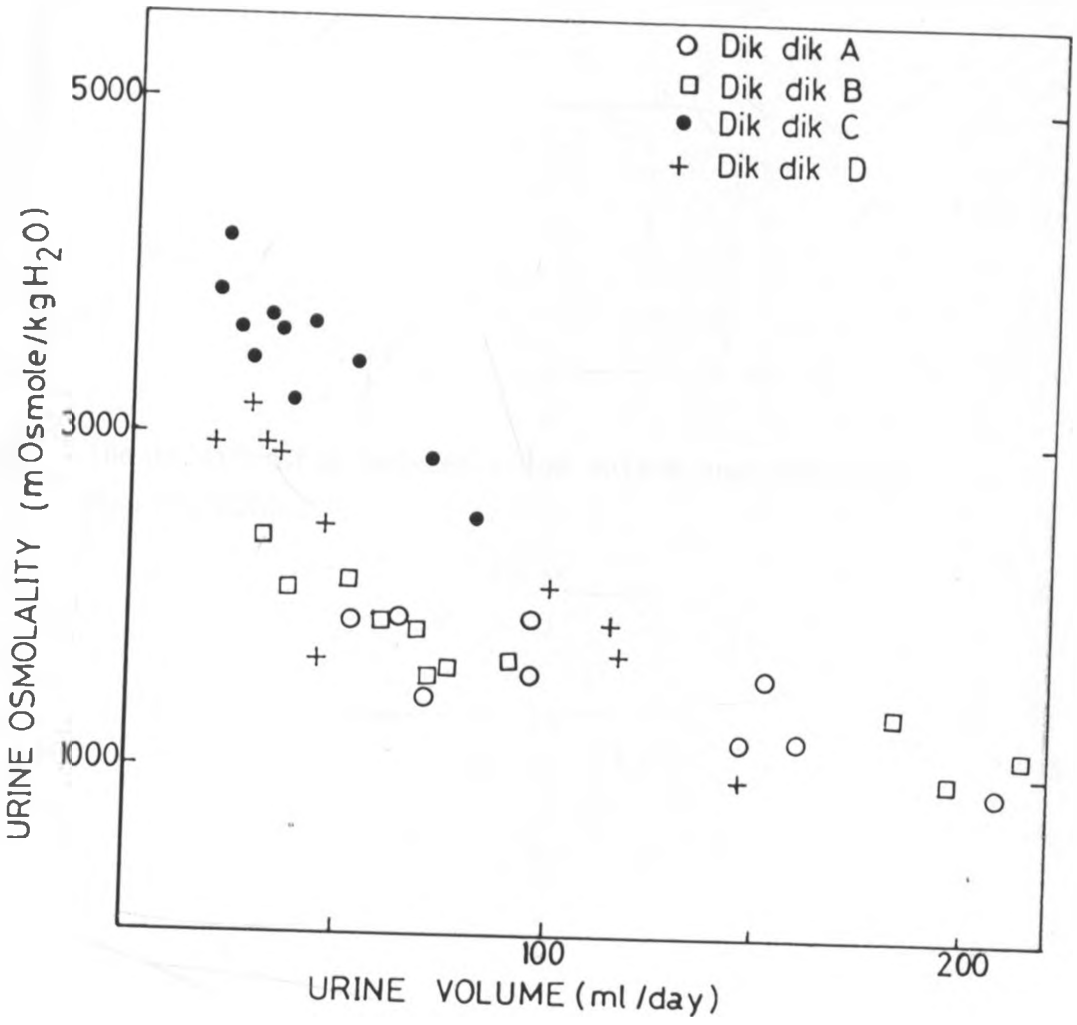
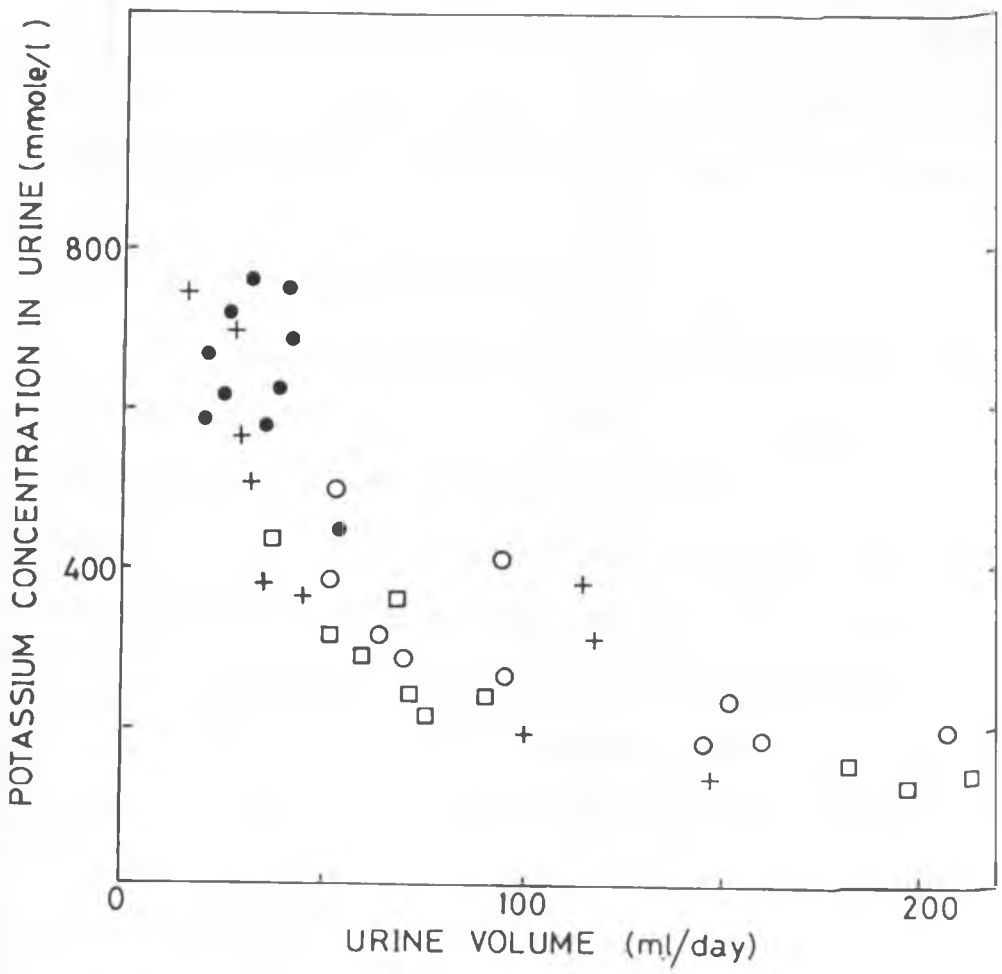

Dik dik A
Dik dik B
Dik dik C
Dik dik D
5000
3000
1000
URINE OSMOLALITY (mOsmole/kgH2O)
100
200
URINE VOLUME (ml/day)

Fig. 17: The relationship between urine volume and potassium concentration.


POTASSIUM CONCENTRATION IN URINE (mmole/l)
800
400
0
100
200
URINE VOLUME (ml/day)

Except in dik dik C, there was apparently no relationship between the total amount of daily potassium excreted and urine volume (Figure 18). Dik dik C excreted very little urine even when water was given ad libitum and tended to increase the daily potassium excretion from 12.0 to 33.1 mmole/day as the urine volume increased from 20-45 ml/day. Potassium excretion by the other animals averaged 23.3 ± 1.2 mmole/day or 60.1% of the daily potassium intake. This amount did not vary much despite the increase in urine volume from 30 to 214 ml/day.

3.6.3 Urinary urea concentration

The concentration of urea in the urine decreased as the urine volume increased (Figure 19). The highest urea concentrations of over 800 mmole/l were observed at urine outputs below 50 ml/day; and the lowest concentrations of about 2.0 mmole/l were attained when the urine volume exceeded 200 ml/day. In dik dik A, the urinary urea concentration was lower in two samples than the corresponding plasma urea concentration (2.0 and 15.3 mmole/l respectively). This was an immature male that was observed to be gaining weight and its horns were still growing.

3.7 Food intake and renal responses to the various treatments.

The voluntary daily food intake averaged 150 g/day. Daily food intake decreased in all the dik diks following dehydration to about 80 g/day (Figure 3). Water and potassium loading did not affect daily food intake. Sodium

Fig. 18: The relationship between the daily renal excretion of potassium and the urine volume. The broken line indicates the daily potassium intake.

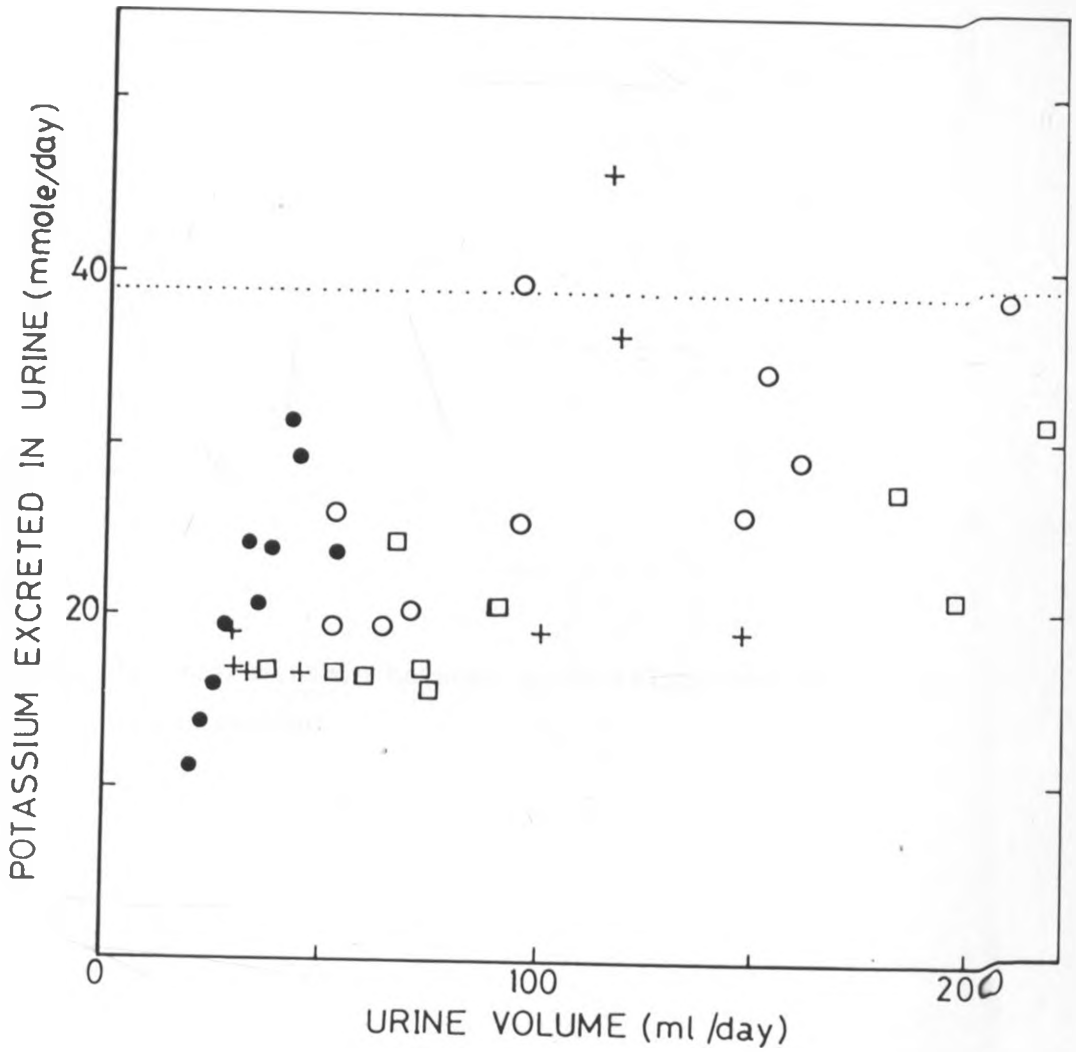
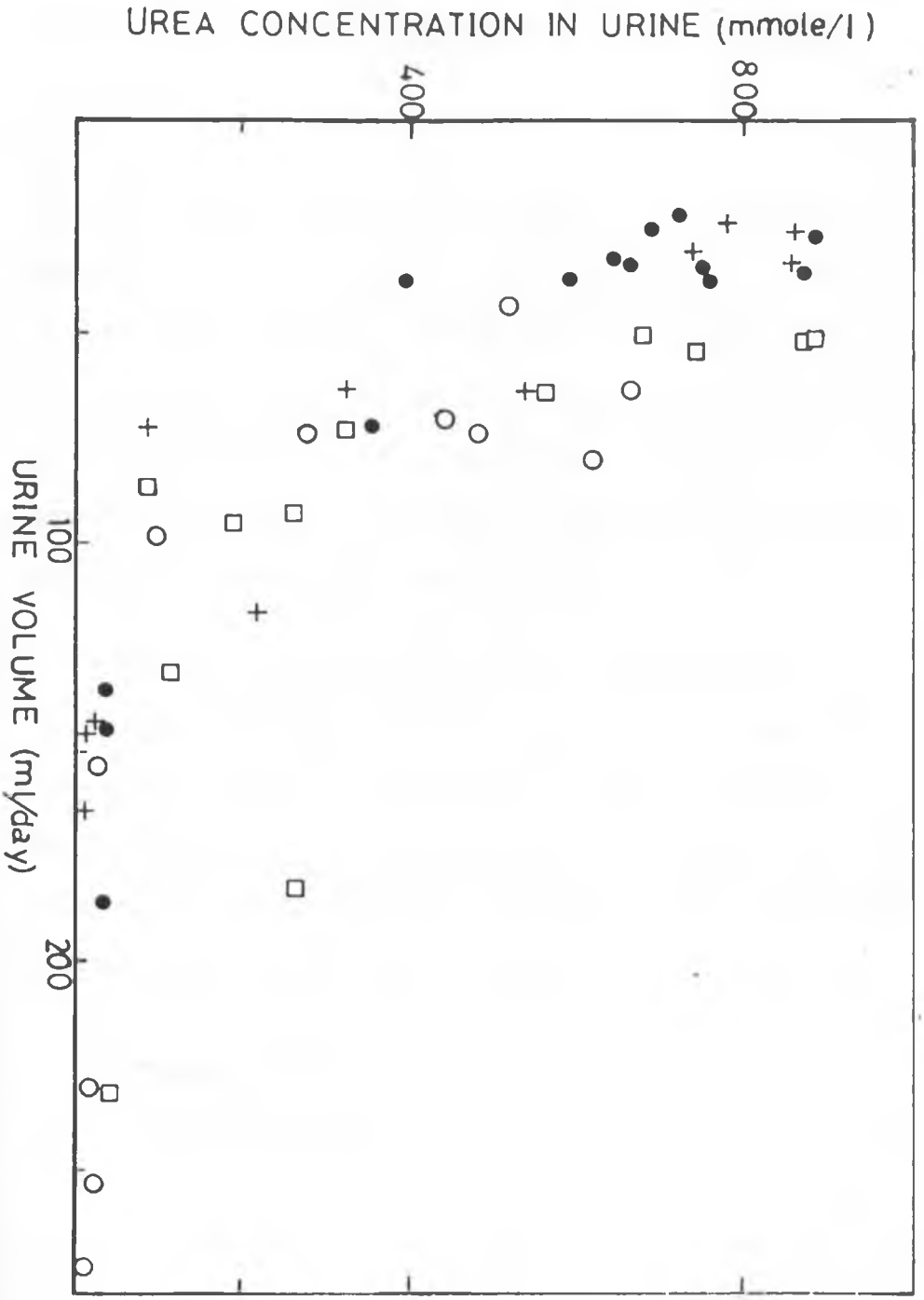

POTASSIUM EXCRETED IN URINE (mmole/day)
40
20
0
100
200
URINE VOLUME (ml /day)

Fig. 19: The relationship between urine volume and urea concentration.


UREA CONCENTRATION IN URINE (mmole/l)
400
800
URINE VOLUME (ml/day)
100
200

loading and saline drinking resulted in a slight increase in food intake. However, saline solutions of concentrations above 0.3 mole/l were observed to decrease food intake drastically.

As a result of reduction in food intake following dehydration, daily nitrogen intake also decreased from a control intake of 21.3 ± 0.5 to 13.7 ± 0.4 g/day. Table 13 and Figure 20 show the daily nitrogen intake and daily nitrogen excretion in the form of urea, creatinine and ammonia. Dehydration resulted in a reduction of the daily amount of creatinine excreted in urine.

Urinary urea excretion decreased significantly ($P < 0.05$) following dehydration from a control mean of 1.12 ± 0.02 to 0.90 ± 0.01 g/day. Potassium and sodium loading as well as saline drinking all resulted in increased urinary urea excretion. Water loading did not affect either urinary urea or creatinine excretion.

Dehydration significantly ($P< 0.05$) decreased the daily volume of urine excreted while the solutes loading as well as saline drinking increased the daily urine volume. Table 14 shows the effects of dehydration, solutes and water loading as well as saline drinking on urine volume, urine osmolality and its constituent concentrations. During dehydration the volume of urine voided was 48.4 ml/day. Saline drinking led to an excretion of urine volume averaging 311.8 ± 43.3 ml/day.

Table 13: Daily urinary nitrogen excretion in the form of creatinine, urea and ammonia during various experimental conditions (Mean ± SEM).

Experimental condition	Daily nitrogen intake (g/day)	Creatinine (g/day)	Urea (g/day)	NH_3 (g/day)
Control	21.3±0.5	0.15±0.007	1.12±0.02	0.04±0.002
Dehydration	13.7±0.4	0.07±0.008	0.90±0.01	0.08±0.003
Potassium loading	20.6±0.6	0.20±0.003	2.10±0.033	0.03±0.01
Sodium loading	23.1±0.7	0.17±0.006	1.98±0.03	0.04±0.01
Saline drinking	18.9±0.5	0.17±0.2	1.70±0.3	0.04±0.02
Water loading	19.8±0.4	0.15±0.006	1.08±0.03	0.05±0.004

Fig. 20: Nitrogen intake and urinary nitrogen excretion in form of creatinine, urea-N and ammonia-N presented in grammes-N per day. Other nitrogen compounds were not accounted for. Data was from 21 samples from each of the four dik diks.

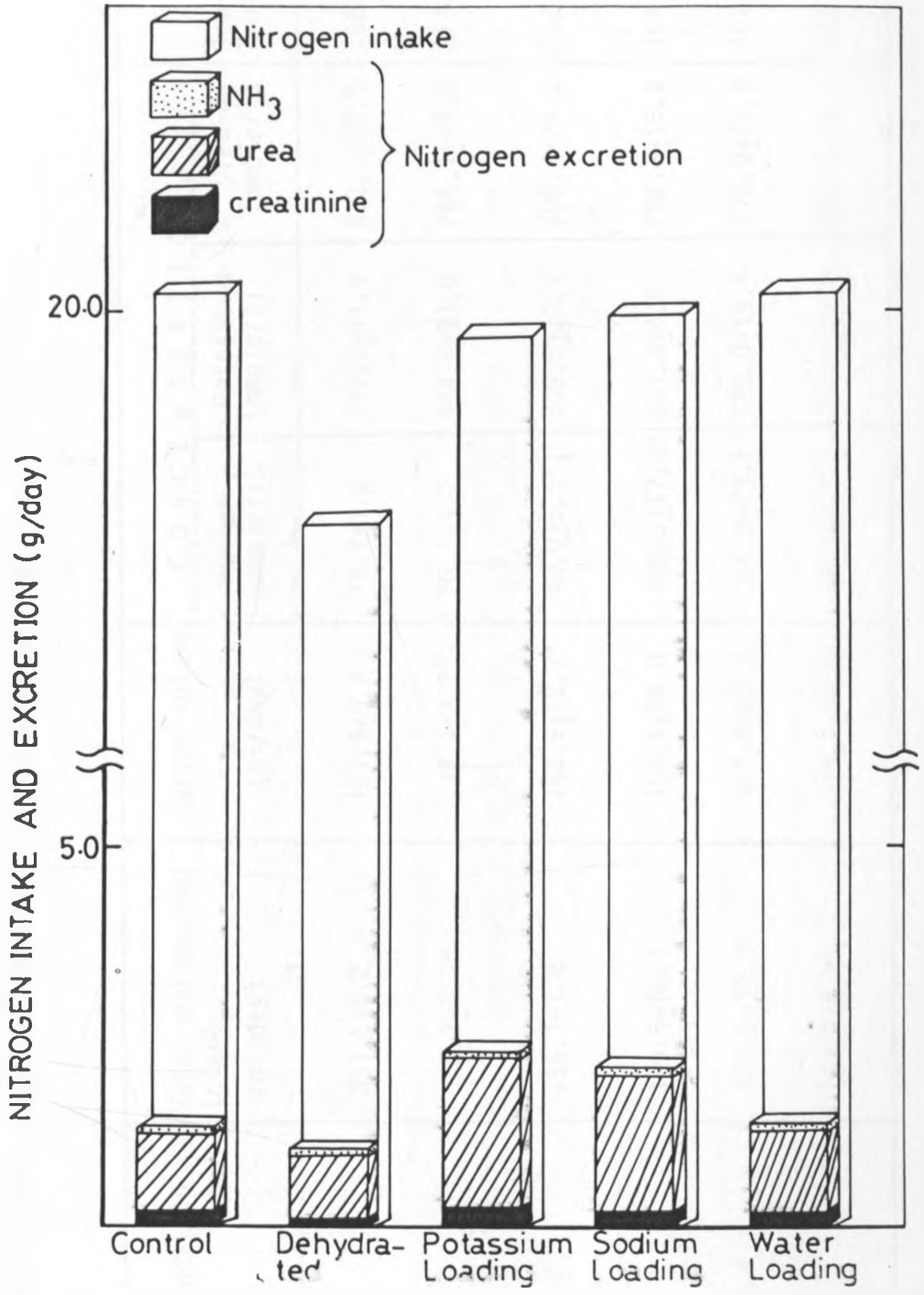

Nitrogen intake
NH3
urea
creatinine
Nitrogen excretion
NITROGEN INTAKE AND EXCRETION (g/day)
20·0
5·0
Control
Dehydra-
ted
Potassium
Loading
Sodium
Loading
Water
Loading

Table 14: *The effects of dehydration, potassium loading and saline drinking on urine volume, urine osmolality and urinary concentrations of potassium, sodium and urea-N (Mean ± SEM). Values shown for saline drinking are only those observed during the drinking of 0.3 mole/l NaCl.*

Experimental condition	Water and saline intake (ml/day)	Urine volume (ml/day)	CONCENTRATION			
			Sodium (mmole/l)	Potassium (mmole/l)	Urea-N (mmole/l)	Osmolality (mOsm/kg H_2O
Control	251.5±8.2	121.4±9.4	19.7±1.9	319.0±11.8	813.1±37.0	1989.3±103.0
Dehydrated	86.7±0.4*	48.4±3.2*	20.3±1.2	444.4±21.0	764.1±17.0	2738.1±136.6*
Potassium loading	156.1±7.8	183.9±12.7*	42.0±5.5*	309.6±20.6	606.4±24.6	1328.6±60.0*
Sodium loading	189.5±10.1	165.4±15.8	126.5±17.3*	201.3±4.8	782.8±15.2	1695.3±129.7
Saline drinking	471.1±37.3*	311.8±43.3	384.8±23.6	125.3±11.4	270.0±22.9	1510±19.0*
Water loading	164.7±9.4	128.1±10.2	18.1±0.7	324.6±11.8	816.2±15.1	2126.5±88.0

*Indicates means that are significantly different from the control mean.

Both sodium and potassium loading and saline drinking led to a significant ($P< 0.05$) increase in urinary sodium concentration. During saline drinking, the sodium concentration was as high as 384 ± 23.6 mmole/l. Potassium concentration in urine was increased during dehydration but it decreased following solutes loading and saline drinking. This decrease was found to be in inverse proportion to the diuresis that resulted from these treatments.

Urine osmolality was significantly ($P< 0.05$) increased as a result of dehydration. It rose from normal hydration value of 1,989.2±103.0 to 2,738.1±136.6 mOsm/kg H_2O during dehydration. Solute loading and saline drinking led to a decrease in urinary osmolality. The most dilute urine was excreted during potassium loading followed by saline drinking (osmolalities of 1,328.6 ± 60.0 and 1,510.4 ± 19.0 mOsm/kg H_2O respectively).

During dehydration, plasma urea, potassium and sodium concentrations were increased significantly ($P< 0.05$) from values of 15.4 ± 0.1, 3.4 ± 0.1 and 117.4 ± 2.0 to values of 22.4 ± 0.9, 4.4 ± 0.08 and 158.1 ± 1.8 mmole/l respectively. Plasma osmolality also increased from 322.0 ± 0.9 to 332.4±2.2 mOsm/kg H_2O. Sodium loading led to slight increases in both plasma osmolality and sodium concentration (330 mOsk/kg H_2O and 138 mmole/l respectively).

The glomerular filtration rate during control experiments was found to be 182.6 ± 11.7 ml/min /100 kg b.wt. It decreased significantly ($P< 0.05$) during dehydration to 141 ± 11.4 ml/min / 100 kg b.wt. Potassium loading led to a significant increase ($P< 0.05$) in GFR to 225.9 ± 19.1 ml/min /100 kg b.wt. There was a slight but statistically insignificant ($P > 0.05$) increase in GFR following sodium loading.

As can be seen in Table 15 which shows a comparison of GFR, rates of urine flow, sodium and potassium excretion during various treatments, the GFR significantly ($P< 0.05$) increased to 262.5 ± 9.4 ml/min /100 kg b.wt. The difference in GFR values during sodium loading and saline drinking is most likely due to the difference in the quantity of sodium intake in the two treatments. More sodium was taken in during drinking of saline solutions of different concentrations than during sodium loading (where only a concentration of 0.25 mole/l NaCl was loaded). Glomerular filtration rate did not change as a result of water loading.

During control experiment only 1.6 ± 0.2 µ-mole/min. of sodium was being excreted in the urine. Dehydration decreased this value to 0.7 ± 0.1 µ-mole/min. Potassium loading significantly ($P <0.05$) increased sodium excretion rate so that during the 0.5 mole/l KCl loading as much as 10.0 ± 1.2 µ-mole/min. of sodium was being excreted. This was even higher than the 8.7 ± 0.7 µ-mole/min. of sodium that was excreted during sodium loading. The highest rate of sodium excretion was noted to be 75.1 ± 5.0 µ-mole/min. during saline

Table 15: A comparison of GFR, urine flow rates, sodium and potassium excretion rates during various experimental treatments in the dik dik (Mean ± SEM).

Experimental condition	Urine flow rate (ml/min.)	Glomerular filtration rate (ml/min /100 kg b.wt.)	Sodium excretion (µ-mole/min.)	Potassium excretion (µ-mole/min.)
Control	0.06±0.005	182.6±11.7	1.6±0.2	16.1±0.4
Dehydration	0.03±0.002*	141.7±11.4*	0.7±0.1*	12.7±0.6
0.3 mole/l KCl loading	0.09±0.006	223.1±17.9*	2.5±0.3*	32.0±3.1*
0.5 mole/l KCl loading	0.22±0.01*	225.9±19.1*	10.0±1.2*	50.3±2.2*
0.25 mole/l NaCl loading	0.07±0.006	206.9±12.6	8.7±0.7*	13.9±1.8
0.3 mole/l NaCl drinking	0.28±0.4*	262.5±9.4*	75.1±5.0*	35.0±3.5*
Water loading	0.08±0.01	203±3.6	1.4±0.5	20.6±1.1

*Indicates means that are significantly different ($P < 0.05$) from the control mean.

drinking experiment. Water loading did not change the rate of urinary sodium excretion.

The rate of urinary potassium excretion was significantly increased from 16.1 ± 0.4 to 50.3 ± 2.2 μ-mole/min. during potassium loading. Sodium loading had no effect on the rate of urinary potassium excretion, but 0.3 mole/l NaCl drinking increased the rate to 35.0 ± 3.5 μ-mole/min.

Table 16 shows the amount of urea filtered, the percent reabsorbed and excreted during the various treatments. Except during saline drinking, there was no significant ($P > 0.05$) difference in the amount of urea filtered between control period and the other treatments. There was however a significant ($P < 0.05$) decrease in the amount of urea excreted per minute during dehydration. Significantly more urea was excreted during saline drinking than during control experiment. Though more urea seemed to be excreted during solutes loading, the values were not statistically significant.

Tubular urea reabsorption was significantly increased following dehydration from a control value of 55.3 ± 2.6 to 77.2 ± 1.6% during dehydration. Potassium loading decreased urea reabsorption slightly to a value of 49.0 ± 3.6%.

While dehydration had an overall effect of enhancing renal tubular urea reabsorption and thus decreasing the amount excreted, diuresis resulting from both solutes loading and saline drinking tended to increase the fraction of urea

Table 16: *The amount of urea filtered at the glomerulus, the percentage reabsorbed in the renal tubules and the amount excreted in the urine during control and various experimental conditions (Mean ± SEM).*

Experimental condition	Urine flow rate (ml/min.)	UREA CONCENTRATION		CLEARANCE		UREA		% Filtered urea reabsorbed
		Plasma (mmole/l)	Urine (mmole/l)	Creatinine (ml/min.)	Urea (ml/min.)	Filtered (µ-mole/min.)	Excreted (µ-mole/min.)	
Control	0.06±0.005	15.4±0.1	813.1±37	7.1±0.5	3.1±0.2	109.3±8.9	48.8±2.9	55.3±2.6
Dehydrated	0.03±0.01	22.4±0.9	764.1±17	4.5±0.8	0.9±0.1	100.8±6.9	22.9±0.9*	77.2±1.6*
Potassium loading	0.11±0.005	11.1±0.4	606.4±24.6	8.9±0.6	4.5±0.3	98.7±9.6	50.3±3.8	49.0±3.6
Water loading	0.06±0.02	14.9±0.9	826.8±19	7.3±0.3	3.4±0.2	108.7±5.0	49.6±2.7	54.4±5.1
NaCl loading	0.07±0.006	14.3±1.0	701.3±18	8.3±0.3	3.4±0.2	118.6±4.6	49.1±2.9	58.6±3.8
Saline drinking	0.22±0.04	14.3±0.4	321.0±41	10.4±1.4	4.9±0.3	148.7±5.2*	70.6±3.0*	52.5±2.9

*Indicates means that are significantly different ($P < 0.05$) from the control mean.

filtered that was ultimately excreted. This can be seen in Figure 21 which depicts the Urea E.T.C. clearance ratio as a function of E.T.C. Urine/Plasma ratio. The Urea /E.T.C. clearance ratio fell from 0.75 during diuresis to a minimum of 0.14 during antidiuresis. There was no change in plasma urea concentration though a slight increase in GFR was observed. This can not however account for the change in fractional urea excretion. It seems that the change in the ratio was due to alterations in the tubular urea reabsorption.

The relationship between urine osmolality and solute excretion rate is shown in Figure 22. During infusion or ingestion of the solute, the urine osmolality decreased as the solute excretion rate increased. The highest urine osmolality was observed at the lowest rates of solute excretion. Control, antidiuretic values of urine osmolality were within the range 2,000 - 2,500 mOsm/kg H_2O. All urine osmolality values were greater than the corresponding plasma osmolality values (U_{osm}/P_{osm} ratio of 8). At a solute excretion rate of about 160 mmole/min , the urine osmolality was as low as 800 mOsm/kg H_2O.

Comparing clearance of the urine (C_{osm}) to the Negative Free Water Clearance ($T^c_{H_2O}$); it is seen that the former constitutes a greater fraction of the total volume flow (Figure 23). In the same figure, which gives the relation of the Negative free water clearance, ($T^c_{H_2O}$), to the Osmolar

Fig. 21: Effect of urine flow (measured as the E.T.C. urine: plasma ratio) upon the fraction of filtered urea that is excreted (measured as the Urea/E.T.C. clearance ratio).
The solid line represents the regression analysis of these parameters and the colleration coefficient (r) - 0.63.

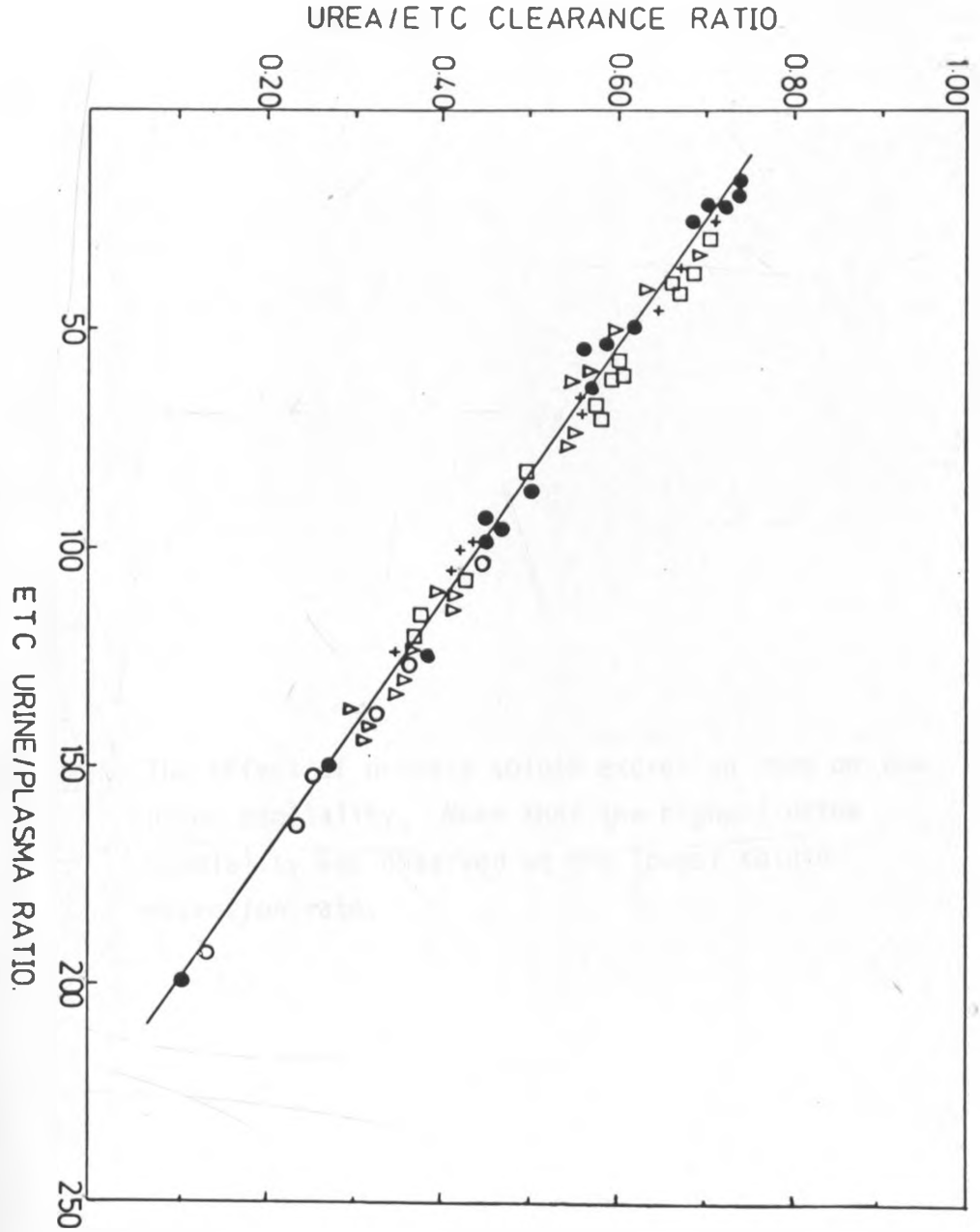

UREA/ETC CLEARANCE RATIO
0.20
0.40
0.60
0.80
1.00
50
100
150
200
250
ETC URINE/PLASMA RATIO.

Fig. 22: The effect of urinary solute excretion rate on the urine osmolality. Note that the highest urine osmolality was observed at the lowest solute excretion rate.

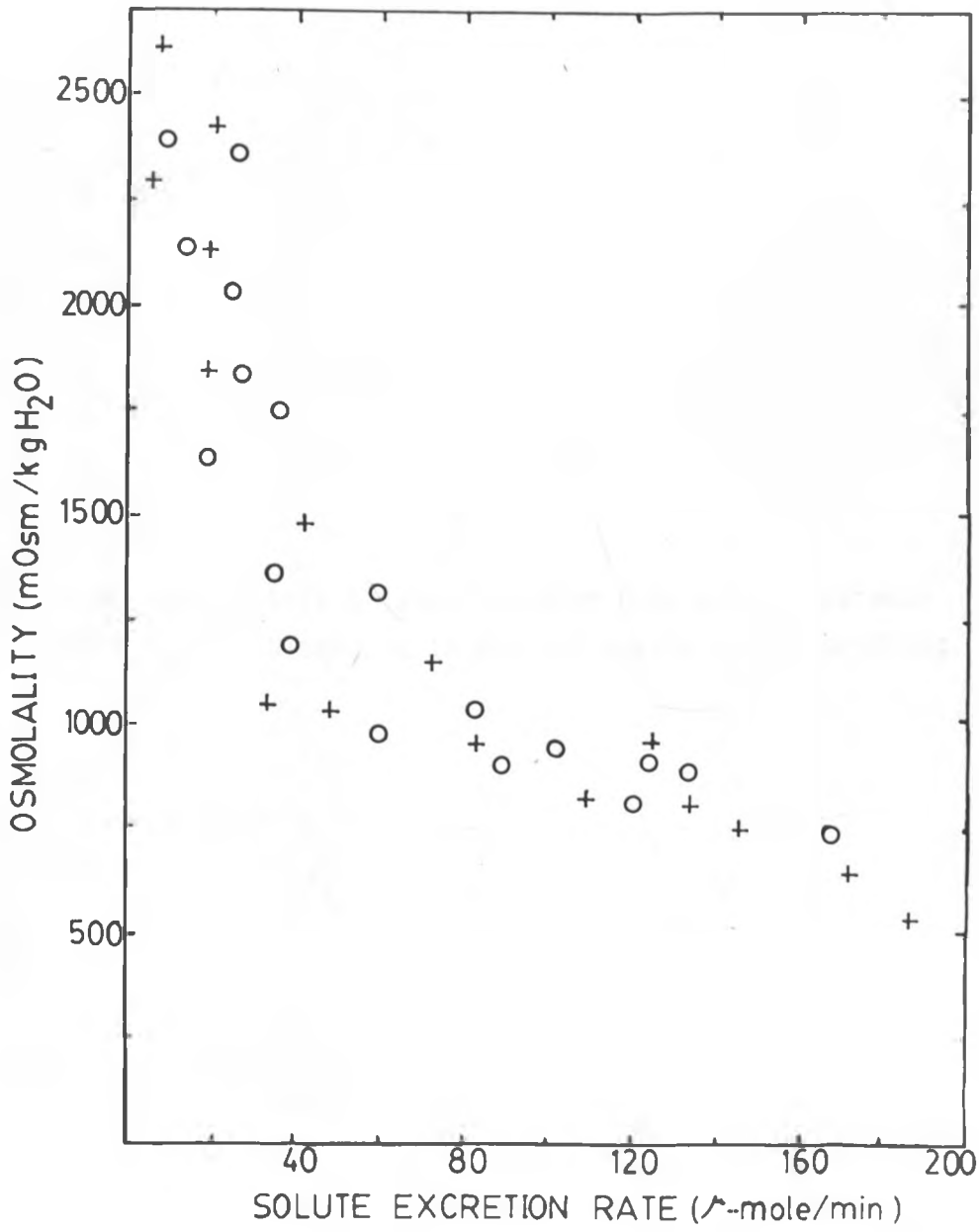
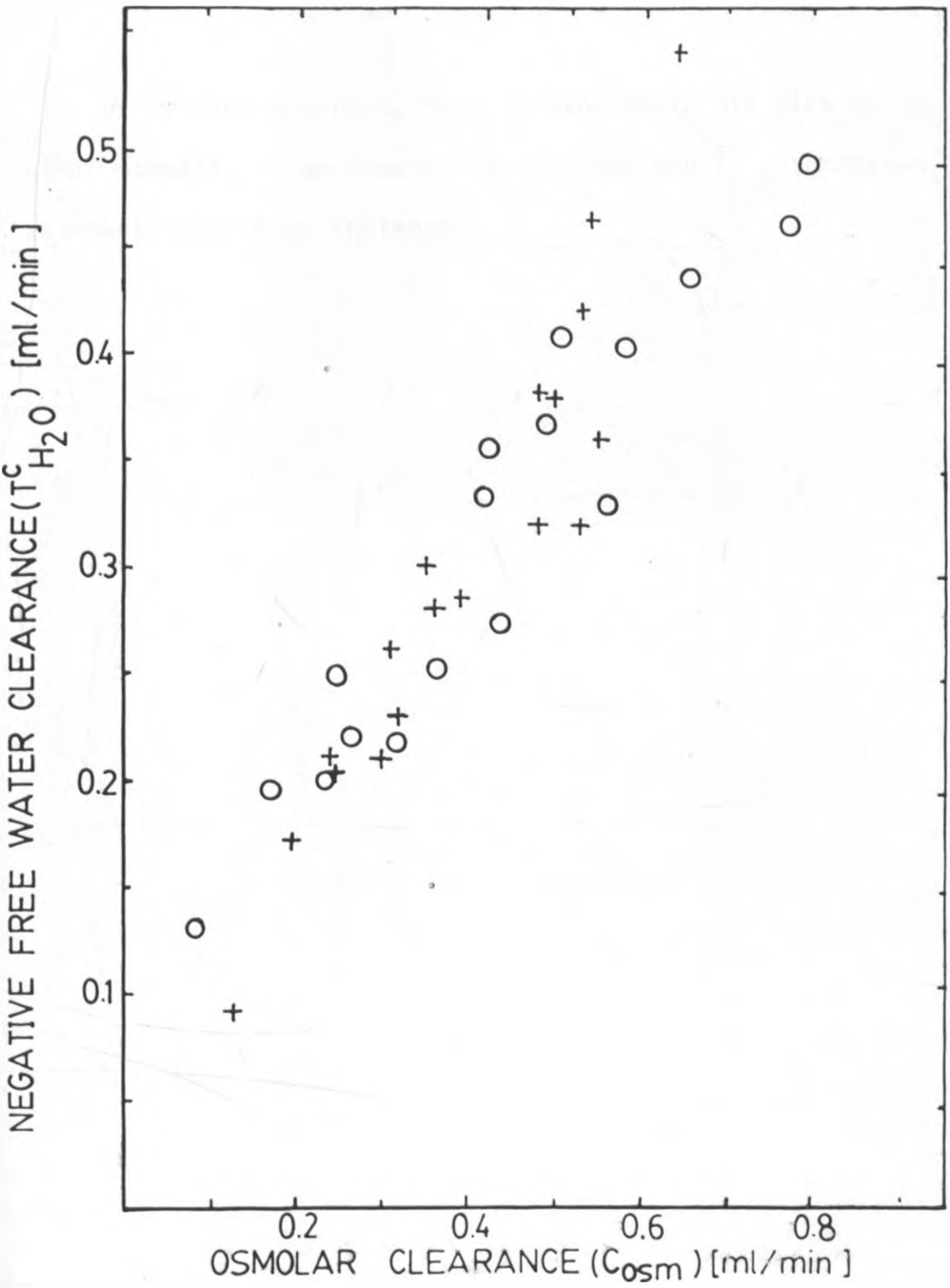

2500
2000
1500
1000
500
OSMOLALITY (mOsm/kgH2O)
40
80
120
160
200
SOLUTE EXCRETION RATE (μ-mole/min)

Fig. 23: The relationship between Negative Free Water clearance and Osmolar clearance in dik dik during saline drinking.


NEGATIVE FREE WATER CLEARANCE ($T^c_{H_2O}$) [ml/min]
0.5
0.4
0.3
0.2
0.1
0.2
0.4
0.6
0.8
OSMOLAR CLEARANCE (C_{osm}) [ml/min]

clearance (C_{osm}); it is seen that an increase in osmolar clearance leads to an increase in the negative free water clearance.

It is thus apparent, that in hydropenic dik diks as in other mammals, urine osmolality declines and $T^c_{H_2O}$ increases as solute excretion increases.

C H A P T E R IV

4.0 DISCUSSION

Objectives of this study included estimating the glomerular filtration rate of the dik dik antelope; examining the mechanisms for renal excretion of potassium, sodium and urea as well as renal responses to various experimental treatments. The dik dik's ability to drink and survive on saline solutions was also examined.

4.1 Glomerular filtration rate

Renal clearance methods were employed to evaluate the overall function. This approach deals with, essentially, comparison of filtered moities of electrolytes and water with those appearing in the final urine. These methods depend on an adequate reference substance for the measurement of GFR and transtubular water movement.

In this study endogenous creatinine (thus endogenous true creatinine method) was used as the reference substance. This method has the advantage of not causing any unphysiological interference with the animal other than blood and urine collection. It has been used in such animals as the camel and sheep (Schmidt-Nielsen et al. 1957; 1958); dog (Richards et al. 1936; Shannon, 1936); rabbit (Kaplan and Smith, 1935; Pitts, 1968); sheep (Shannon, 1937; Pitts, 1968);

and cat (Gammeltoft and Kjeruef-Jansen, 1943). The endogenous true creatinine method for GFR determination,was particularly suitable for the small wild dik dik antelopes that would have been rather difficult to restrain and manipulate,if bladder and jugular vein catheterization was carried out as well as if substances like inulin were to be constantly infused. This would undoubtedly have given rise to such changes in GFR and other parameters in view of the fact that pain, fear, and a variety of other factors are known to alter renal function especially via the ADH secretion mechanism (Vander, 1975).

The glomerular filtration rate of the dik dik antelope was found to vary from 3.4 to 16.8 ml/min. with a mean of 7.2 ml/min. Siebert and Macfarlane (1975) reported the glomerular filtration rate of cattle to vary from 115 to 260 ml/min /100 kg b.wt. and that of camel to vary from 50-85 ml/min / 100 kg b.wt. when the animals were normally hydrated. The GFR values observed in this study for the dik dik antelope ranged between 83.8 and 336 ml/min /100 kg b.wt. These values are higher when compared to those of both cattle and camel.

Table 17, shows a comparison of the glomerular filtration rates of various mammals (Orloff et al. 1973). The mean GFR values for the dik dik (186.8 ml/min /100 kg b.wt.) obtained in this study are higher than those reported for the horse, cattle and camel. They are slightly higher than those reported for goat (146.2 ml/min /100 kg b.wt.), sheep (158.2 ml/min /

Table 17: The Glomerular filtration rates of various animals

Animal species	Body weight (g)	GFR (ml/min.)
Rat	200 - 400	1.2 - 2.3
Rabbit	$1.8 - 2.5 \times 10^3$	4.0 - 12.0
Guinea pig	565	21
Horse	503×10^3	390.0
Goat	54×10^3	79.0
Sheep	55×10^3	87.0
Ox	470×10^3	385.0
Pig	131×10^3	184.0
Cat	3×10^3	5.9 - 10.5
Dog	$10 - 20 \times 10^3$	43.0 - 97.3
Man	70×10^3	130.0
Dik Dik	3.8×10^3	7.1 (This study)

The data is adapted from Renal Physiology Editted by Orloff, J., Berliner, R.W. and Geiger, S.R. Handbook of Physiology Section 8. American Physiological Society Washington D.C., (1973).

100 kg b.wt.) and pig (140.5 ml/min /100 kg b.wt.); but are close to those reported for man (185.7 ml/min /100 kg b.wt.).

Dehydration is known to decrease GFR in most animals. In the dik dik for example, dehydration led to both a 22% decrease in GFR and a 55% in urine flow. Glomerular filtration rate decreased in camels that had been dehydrated for 3 days from a range of 50-85 to 42-65 ml/min /100 kg b.wt. (Siebert and Macfarlane, 1975). When the same animals were dehydrated for 10 days, the GFR decreased further to a range between 8-42 ml/min /100 kg b.wt. Similarly, in studies by the same authors GFR decreased in dehydrated cattle from a range between 115-260 ml/min /100 kg b.wt. to 43-50 ml/min /100 kg b.wt. Maloiy (1972) observed that following dehydration, camels decreased their GFR by 30% and the rate of urine flow by 57%.

The results of this study indicate that,the kidney plays an important role in the regulation of water balance in the dik dik antelope. It was found out that following dehydration, a reduction in renal water loss was achieved by an increase in tubular water reabsorption and at the same time a decrease in glomerular filtration rate. Dehydration was accompanied by tubular water reabsorption increasing from 99.1% to 99.3% of the filtered amount. Though other hormones may have played part in effecting the water retention by the kidney, it is most likely that Antidiuretic hormone (ADH) probably may have had the greatest influence, leading to increased excretion

of a highly concentrated urine by acting on the distal tubule and the collecting ducts thereby making them more permeable to water.

Antidiuretic hormone plasma activity varies seasonally in rats, man and sheep (Itoh, 1954; Macfarlane and Robinson, 1957), increasing in concentration during summer and decreasing during winter. Heat-induced dehydration also increases plasma ADH concentration in rats (Macfarlane and Robinson, 1957). One could therefore expect the dik dik when compared with other mammals that inhabit arid and hot environments, to have high circulating plasma ADH concentrations. These high levels of plasma ADH, presumably enable its kidney to excrete an osmotically highly concentrated urine.

Angiotensin, besides the enhancement of salts and water absorption in the alimentary canal (Crocker and Munday, 1970, Edmunds and Marriot, 1970); is also possibly involved in mediating a decrease in GFR as well as the renal plasma flow (RPF) (Maloiy, 1972). Moreover, angiotensin is also believed to stimulate thirst in many mammals (Fitzsimons and Simons, 1969). It is thus justifiable to tentatively suggest that the observed water retention ability of the dik dik kidney was under the influence of both ADH and angiotensin.

4.2 Potassium excretion

The dik dik antelopes are browsers, selecting fruits and protein-rich dicotyledenous foliage (Hofmann, 1973). Like other ruminants,

they consume far larger amounts of potassium than that which could be accounted for on the basis of their body weight. Both urinary and faecal electrolytes excretion were investigated in this study. It was noted that urinary potassium excretion accounted for 73% of the total potassium excreted while faecal sodium excretion represented 89% of the total sodium recovered in urine and faeces. The urinary K/Na ratio was 16.8. These results closely resemble those observed in sheep (Dewhurst, Harrison and Keynes, 1968). Unlike the monogastric species, which have a mean ratio of K/Na of 0.43, the dik dik's ratio of 16.8 is within range that has been found in both wild and domestic ruminants thus far studied.

Potassium and sodium concentrations in the urine decreased as the urine volume increased, but, there was however no relation between the total daily potassium excreted and the urine volume (Fig. 18). For any given urine volume, urinary potassium excretion accounted for approximately 60.1% of the daily intake.

Intra-ruminal potassium loading increased potassium excretion rate. The potassium:creatinine ratio rose from a control value of 0.42 to 1.1 during 0.3 mole/l KCl loading and then to a ratio of 1.8 during 0.5 mole/l KCl loading. This is suggestive of renal tubular potassium secretion by the dik dik. Renal tubular potassium secretion accounted for about 55% of the total amount excreted in the urine (Table 11).

Evidence for tubular potassium secretion has been demonstrated in studies on such animals as man and dog (Berliner et al. 1950); cow (Anderson and Pickering, 1962) and sheep (Scott, 1969b). In monogastric species (man and dog) potassium loading led to a progressive rise in plasma potassium levels but the subjects later became "tolerant" to the electrolyte loading, at which time the plasma potassium level dropped to the initial value; by which time the excreted potassium exceeded the filtered amount.

These findings led to the current and broadly accepted concept that monogastric species need a prior priming period to high levels of potassium concentrations before their secretory mechanism is brought into play. This hypothesis may not necessarily be true to all monogastrics because in recent studies by Rabinowitz et al. (1984), it has been shown that the rat will adapt at once to a high potassium diet.

Like other ruminants so far studied, the dik dik was able to rely upon its tubular secretory mechanism when potassium loading was instituted. Of more interest was the observation of a decrease in plasma potassium concentration during potassium loading (Table 11). The importance of alterations in plasma potassium concentration in bringing about adaptation to increased potassium intake is not resolved. Recently, however, Rabinowitz et al. (1984) noted that the large rise in potassium excretion following increased potassium intake in sheep was not always associated with a rise in plasma potassium concentration.

In earlier studies, Berliner et al. (1950) had noted the independence between potassium excretion and plasma potassium in the adapted animal. These authors further stated that: "It is also striking that the plasma potassium concentration and the rate at which potassium is filtered at the glomerulus are relatively unimportant factors; wide variations in potassium may be found at any level of plasma potassium or filtered load".

These observations together with the results obtained in this study, where plasma potassium is noted to decrease, probably imply that a rise in plasma potassium concentration cannot be the signal for increased potassium excretion during higher potassium intakes. This statement is not, however, in agreement with the widely accepted hypothesis for the control system that maintains potassium balance. This hypothesis states that alterations in potassium intake produce parallel alterations in plasma potassium. This in turn directly influences potassium excretion by the action of plasma potassium at the distal nephron secretory sites and indirectly by modulating secretion of aldosterone, a well known stimulant of potassium excretion. The increased renal potassium excretion serves both to maintain external balance and to maintain constancy of plasma potassium (Rabinowitz et al. 1984; Laragh and Sealey, 1973).

If plasma potassium concentration is not the signal for increased potassium excretion; then it is probable that there

are other sensors elsewhere in the body that detect increased potassium load and effect,through yet ununderstood kaliuretic regulatory factors,increased potassium excretion as observed in the present study on the dik dik antelope.

The presence of enteric potassium-sensitive receptors in the rumen, hepatic portal vein, or liver, serving as components of an afferent limb of the excretory control system has been suggested by Rabinowitz et al. (1984). This hypothesis is in agreement with results here obtained and would probably give a clear explanation as to how the kidney detects an increased potassium intake before it can respond by increasing excretion.

There was a diuresis and a natriuresis following potassium loading (Fig. 7, 8 and Table 14). The natriuresis was even higher than that resulting from 0.25 mole/l NaCl intraruminal loading. Similarly natriuresis has been observed in the sheep and cattle (Anderson and Pickering, 1962; Dewhurst, Harrison and Keynes, 1968; Scott, 1969b). These authors suggested that this may relate in part to the increased solute load in the glomerular filtrate. This could result in an osmotic diuresis which would wash sodium out of the proximal convoluted tubules more rapidly than could be absorbed distally. Faecal samples were not analysed for sodium content and hence it is not possible to indicate whether this natriuresis was associated with a negative sodium balance or with a decreased faecal sodium excretion.

4.3 Sodium excretion

Nearly all of the filtered sodium at the glomerulus was reabsorbed (99.96%) by the renal tubules of the dik dik. This efficient tubular sodium reabsorption ability is characteristic of the mammalian kidney. Osmotic diuresis induced by potassium loading and saline drinking increased sodium excretion by 1.2% and 6.7% of the filtered load respectively (Table 18). This was a moderate increase in sodium excretion during osmotic diuresis compared to higher ratios (25% excretion of the filtered load) reported in sheep (Robinowitz and Gunther, 1978). Plasma sodium concentration increased to 158 mmoles/l (a rise of 35%).

Sodium diuresis did not seem to cause any consistent change in potassium excretion (Fig. 9). This finding is in agreement with the observation of Rabinowitz and Gunther (1978) in sheep during salt loading. The results thus obtained in the sheep and dik dik contrast with the observed increase in potassium excretion reported in man, dog and rats following intravenous infusion of sodium salts. However, recent studies by Rabinowitz and associates (personal communication), have shown that diuresis induced by sodium sulphate can increase urinary potassium excretion in fasted sheep provided the sheep were initially excreting low urinary potassium concentrations.

4.4 Urea excretion

Urinary urea excretion accounted for a major portion of all the nitrogen excreted in our experimental conditions and

Table 18: Plasma and urinary sodium concentrations and percentage tubular sodium reabsorption during intra-ruminal KCl loading and 0.3 mole/l NaCl drinking (Means ± SEM)

Experimental condition	Sodium concentration		Percent sodium filtered Reabsorbed (%)
	Plasma (mmole/l)	Urine (mmole/l)	
Control	117.0 ± 3.6	19.7 ± 1.4	99.96
0.3 mole/l KCl loading	147.3 ± 3.2	29.8 ± 4.3	99.76
0.5 mole/l KCl loading	122.6 ± 3.5	71.6 ± 5.6	98.80
0.3 mole/l NaCl drinking	158.0 ± 3.7	307.8 ± 16.6	93.20

analytical limitations. Of the filtered urea 55.3% was reabsorbed in the renal tubules leaving 44.7% to be excreted in the urine. Table 19 shows a comparison of the percentages of filtered urea that is reabsorbed and excreted in some species of mammals during normal food and water intake. The dik dik antelope ranks second to the camel in its ability to reabsorb urea whereas in man most of the urea is excreted.

There is conflicting information in the literature concerning the amount of urea reabsorbed by the renal tubules of man. Schmidt-Nielsen (1958) noted that about 20% of the filtered urea is reabsorbed by the renal tubules of man. Varley (1967) on the other hand reported a value of 40%. The fact that man should excrete more nitrogen in the form of urea compared to other animals shown in Table 19 is to be expected since there is convincing evidence that only ruminants are able to recycle urea to the rumen from the plasma thus reducing the amount to be excreted in the urine (Houpt, 1959; Houpt and Houpt, 1968) or in saliva (Hinderer, and Engelhardt, 1975).

In renal clearance studies, the only valid proof for active tubular reabsorption of a substance that is freely filtered is that the substance can appear in the urine in a concentration lower than the simultaneous plasma concentration. Evidence for active tubular urea reabsorption has been found in the elasmobranch kidney where the urea U/P ratios normally range from 0.1 to 0.5 (Schmidt-Nielsen, 1957). Only in 3 urine samples (out of a total of 23 samples in the control period) from one animal in this study was the urine urea concentration

Table 19: Comparison of the percentages of urea filtered reabsorbed and excreted in various species of mammals

Animal species	% Filtered Reabsorbed	% Filtered excreted	Source of information
Camel	60	40	Schmidt-Nielsen (1957)
Man	20	80	Schmidt-Nielsen (1957)
Man	40	60	Varley (1967)
Calves	50	50	Dalton (1968)
Sheep	40	60	Maloiy and Scott (1969)
Deer	40	60	Maloiy and Scott (1969)
Dik dik	55.3	44.7	This study

lower than the plasma urea concentration. All the other animals had urine concentrations greater than the plasma urea concentration. Though the observed lower urine concentrations would suggest active tubular urea reabsorption, the occurrence was too low and insignificant to stand firm in favour of an active reabsorption process; and, does not eliminate a possibility of experimental and analytical errors.

Variations in urea excretion rates are known to be independent of plasma urea concentrations and of glomerular filtration rate, but related to nitrogen intake and rate of growth. The very low urinary urea concentration in this one dik dik can therefore be explained on the fact that the animal was young and still growing so that it had to preserve urea for later protein synthesis. The other dik diks, however, were fully grown and had little reason to preserve urea. A similar observation was noted in a growing camel by Schmidt-Nielsen et al. (1957).

Dehydration in the dik diks was followed by a decrease in the amount of urea excreted in the urine. The percent urea filtered reabsorbed rose from 55.3% to 77.2% while the plasma urea concentration rose by 45%. The decrease in urea excretion was thus the result of an increased tubular permeability to urea (though this has not been fully established, it can not be excluded) and reabsorption. However, in one animal, there was an increase in the amount of urea excreted during dehydration.

This was most likely a reflection of increased protein catabolism (the plasma urea concentration also rose during this period). A similar increase in rate of urea excreted during dehydration was observed in Marsupial (Trichosurus vulpecula) (Reid and McDonald, 1968) and in the Llama (Hinderer and Engelhardt, 1975).

The observed increase in tubular urea reabsorption during dehydration is in agreement with the established fact that tubular reabsorption of filtered urea depends primarily on the reabsorption of water (Best, 1961; Rabinowitz and Gunther, 1972b; Guyton, 1976). It is thus likely that during antidiuresis (dehydration), when the water permeability and thus reabsorption of water in the distal tubule is increased, the permeability of urea is also increased.

Potassium and sodium loading increased urinary Urea-N excretion. The amount of filtered urea reabsorbed during potassium loading decreased to 49.0%. This enhancement of urinary urea excretion during osmotic diuresis has been described in other animals: sheep offered water with 1.5% NaCl resulted in a 37% increase in urinary excretion of Urea-N when compared to animals receiving tap water (Church et al. 1974). Schmidt-Nielsen et al. (1958) reported that fractional urea excretion increases as the U/P inulin ratio decreases but below a ratio of 10 it remains constant; Gans (1966) found that fractional urea excretion increases over the entire range of U/P inulin ratio.

4.5 Effect of salts-loading on glomerular filtration rate

The effects of salt loading on GFR has not been clearly defined in most animals. This is because it involves a combination of an increase in plasma osmolality and at the same time, an expansion of extracellular fluid (Skadhauge and Schmidt-Nielsen 1967). Salt-loading and saline drinking in the dik dik increased the GFR by 19% and 43% respectively. Increased GFR induced by salt loading was observed in camels by Schmidt-Nielsen et al. (1957). Maloiy (1972) observed a 50% increase in GFR and 103% in urine flow rate after salt loading in camels. He however pointed out that; since it also occurs in the rat (Chester-Jones, 1957) this response does not reflect a specific adaptation to the desert environment. Moreover,saline drinking in this study was noted to decrease the amount of filtered water reabsorbed from a control value of 99.1% to 97.2% in the dik dik.

Maloiy (1972) further suggested that hormonal mechanisms are involved in the changes in GFR during salt loading. If such hormonal mechanisms exist; there is a possibility that they are related to the natriuretic hormone whose existence however has been controversial. De Wardener (1973) speculated that a fall in extracellular volume causes release of the natriuretic hormone; and two years later other workers suggested that the natriuretic hormone is released when extracellular volume is expanded (e.g. by saline infusion)

(Vander, 1975). The latter hypothesis on its release would be more applicable to observations of the present experiments as there was noticeable increase in sodium excretion rates. Nevertheless more information about the natriuretic hormone has to be sought yet.

4.6 Saline drinking ability

Experiments to determine the ability of the dik dik to drink and survive on saline revealed that, this animal like sheep, cannot survive on saline water exceeding a concentration of 0.3 mole/l NaCl. They were able to drink saline from a concentration of 0.1 to 0.3 mole/l. At 0.3 mole/l NaCl some animals started developing unphysiological signs. Those which withstood concentrations above 0.3 mole/l (up to 0.5 mole/l), did so by restricting the saline intake which resulted in reduction in food consumption and later loss of body weight. Sheep offered saline as the only source of drinking water could only drink up to a concentration of 0.25 mole/l NaCl, beyond which all were affected (Church et al., 1974).

Maloiy (1972) noted that camels could drink and survive on saline solutions as concentrated as 0.6-0.9 mole/l NaCl (more concentrated than sea water); while the donkey could not withstand these high concentrations. Considering the dik diks urine concentrating ability, that exceeds all other East African mammals including camels (Maloiy, 1972); one would have expected the dik dik to be able to survive

on saline solutions or to withstand the highest concentrations of the saline, but, results from these experiments showed that adverse signs developed in some dik diks at 0.3 mole/l NaCl. Similar findings were reported for the sheep (Church et al., 1974). Those that could withstand 0.5 mole/l NaCl did so only by cutting down on the amount of saline intake. Compared with the camel the dik dik kidney is thus less capable of excreting NaCl (Maloiy, 1972).

Concluding Summary

From the results obtained in this study, it appears that:

1. The kindey of the dik dik antelope qualitatively handles electrolytes and urea in the same way as in other ruminants.

2. The glomerular filtration rate of the dik dik is relatively high but comparable to those of some domesticated species and man.

3. The dik dik responds to dehydration by decreasing glomerular filtration rate, increasing tubular water and urea reabsorption. These and other responses lead to excretion of a very highly concentrated urine. It is not surprising therefore that the dik dik has the highest urinary concentrating ability of all the East African ruminants so far studied. These factors may

most likely be responsible for enabling this species of antelopes to inhabit hot arid lands that are out of reach of many domestic and wild animals.

4. Though the dik dik may drink saline solutions exceeding 0.3 mole/l NaCl, it cannot withstand drinking these solutions for prolonged periods nor will it survive on them.

It is therefore concluded that the renal mechanisms for handling urea and electrolytes in the dik dik antelope are similar to those already reported for other species of ruminants previously studied in the laboratory under similar experimental conditions.

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A P P E N D I C E S

Appendix I: Daily excretion of sodium and potassium in the urine and faeces of dik diks receiving the maintainance ration.

Animal	Potassium excretion (nmole/day)			Sodium excretion (mmole/day)		
	Urine	Faeces	% in urine	Urine	Faeces	% in urine
A	32.6	10.9	74.9	2.6	8.4	23.6
	29.7	9.3	76.1	2.3	8.6	21.1
	38.7	14.6	72.6	3.9	9.2	29.7
	41.2	12.2	77.1	4.2	7.1	37.1
	26.9	12.1	68.9	3.5	7.5	31.8
	25.3	12.8	66.4	2.1	9.5	18.1
	39.2	12.3	76.1	1.9	9.2	17.1
	33.0	11.9	73.4	1.6	9.0	15.0
	32.9	13.2	71.3	4.1	8.7	32.0
	35.1	14.9	70.2	2.5	8.6	27.7
	34.4	12.5	73.3	2.2	8.4	20.7
	32.1	13.0	71.1	2.6	9.2	22.0
	30.9	11.5	72.8	2.7	9.0	23.0
	37.3	16.9	70.1	3.4	9.5	26.3
	32.1	14.2	69.3	3.6	7.8	31.5
	37.0	19.1	65.9	4.0	7.7	34.2
	38.4	8.3	82.2	2.3	8.9	20.5
	35.9	9.2	79.6	1.6	9.0	15.1
	39.2	12.6	75.6	3.5	9.5	26.9
	40.1	11.9	77.1	3.4	9.2	26.9
	$\bar{X}$=34.6	12.6	73.3	2.9	8.7	25.0
	±SD==4.5	2.5	4.2	0.8	0.7	6.4
	±SEM=1.0	0.6	0.9	0.2	0.2	1.5

Appendix I Continued

Animal	Potassium excretion (mmole/day)			Sodium excretion (mmole/day)		
	Urine	Faeces	% in urine	Urine	Faeces	% in urine
B	39.5	16.9	70.0	3.8	9.2	29.2
	29.7	11.5	72.0	3.9	9.5	29.3
	38.7	13.0	74.8	4.7	9.0	34.3
	47.2	12.3	79.3	2.2	8.9	19.8
	26.9	14.6	64.8	3.5	5.7	38.0
	35.3	15.2	69.9	4.1	7.8	34.4
	39.2	11.9	76.7	4.6	13.5	25.4
	36.6	12.6	74.4	4.9	9.0	35.2
	32.9	12.5	72.4	2.1	9.2	18.5
	35.1	13.4	72.3	4.0	11.4	25.9
	34.4	12.3	73.6	4.3	8.6	33.3
	32.1	15.2	67.8	3.9	8.7	30.9
	35.9	9.4	81.0	2.7	12.0	21.2
	37.3	10.9	77.3	2.9	9.2	23.9
	$\bar{X}$=35.8	13.1	73.3	3.7	9.4	28.5
	±SD= 4.8	2.0	4.4	0.9	1.8	6.2
	±SEM= 1.4	0.5	1.2	0.2	0.5	1.7
C	28.6	12.6	69.4	0.4	13.7	3.0
	24.6	16.2	60.3	0.5	11.2	4.2
	15.3	14.3	51.6	0.7	10.6	6.2
	21.2	9.2	69.7	0.4	9.4	4.0
	32.4	8.9	78.4	0.5	14.0	3.4
	32.3	11.5	73.7	0.6	16.2	3.5
	21.1	12.0	63.7	0.4	10.1	3.8
	19.6	13.2	59.7	0.3	11.5	2.5
	24.5	16.2	60.2	0.6	9.2	6.1
	28.7	8.2	77.7	0.2	8.1	2.4
	26.6	9.2	74.3	0.4	13.7	2.8
	27.4	10.4	72.4	0.6	11.6	4.9

Appendix I continued

Animal	Potassium excretion (mmole/day)			Sodium excretion (mmole/day)		
	Urine	Faeces	% in urine	Urine	Faeces	% in urine
C	24.9	15.2	62.1	0.5	11.5	4.2
	19.3	15.6	55.3	0.6	10.3	5.5
	$\bar{X}$=24.4	12.3	66.5	0.5	11.7	4.1
	±SD= 5.0	2.7	8.2	0.15	2.2	1.2
	±SED= 1.2	0.6	2.0	0.03	0.5	0.3
D	33.9	10.4	76.5	2.4	6.2	27.9
	36.0	11.1	78.1	2.0	4.6	30.3
	31.2	8.2	79.1	1.8	5.7	24.0
	26.4	9.0	74.5	1.9	5.2	26.7
	29.3	9.9	74.7	2.6	5.9	30.5
	25.8	12.4	67.5	2.9	3.2	47.5
	34.5	13.5	71.8	3.4	2.8	54.8
	37.6	7.2	83.9	3.7	4.4	45.6
	32.0	8.4	79.2	2.7	4.5	37.5
	31.8	9.2	77.5	2.9	4.9	37.1
	36.1	9.1	79.8	2.8	6.2	31.1
	26.4	7.6	77.6	2.7	6.4	29.6
	38.0	8.0	82.6	3.0	5.3	36.1
	32.9	8.9	78.9	3.1	5.5	36.0
	36.2	7.5	82.8	2.8	4.8	36.8
	30.3	8.4	78.3	4.1	4.4	48.2
	$\bar{X}$=32.4	9.3	77.7	2.8	5.0	36.2
	±SD= 3.9	1.7	4.1	0.6	1.0	8.7
	±SEM 1.0	0.4	0.1	0.15	0.2	2.1

Appendix II : The amount of potassium filtered at the glomerulus, the amount reabsorbed or secreted in the tubules and their respective percentages.

Animal and treatment	Potassium conc. (mmole/l)		Urine flow rate (ml/min)	Clearance (ml/min.)		Potassium (µ-mole/min.)		% K filtered reabsorbed (+) or excreted secreted (-)
	Plasma	Urine		Creatinine	Potassium	Filtered	Excreted	
Control	3.4	260	0.05	7.8	1.9	26.5	13.0	50.9+
A	4.2	342	0.04	8.1	3.1	34.0	13.7	59.7+
	3.6	290	0.06	6.0	3.2	21.6	17.4	19.4+
	3.0	310	0.05	6.8	2.8	20.7	15.5	25.1+
	3.3	330	0.06	7.8	2.8	25.7	19.8	22.9+
	4.0	260	0.06	7.2	2.6	28.8	15.8	45.8+
	3.8	300	0.05	6.9	3.9	26.2	15.0	42.7+
	3.4	280	0.06	7.4	2.5	25.2	16.8	33.3+
	4.0	320	0.05	7.0	4.0	28.0	16.0	42.8+
B	3.4	370	0.05	8.7	3.3	29.6	18.5	37.5+
	3.0	260	0.05	5.7	2.1	17.1	13.0	23.9+
	3.8	440	0.04	9.9	4.6	37.6	17.6	53.2+
	2.2	340	0.04	8.0	4.6	17.6	13.6	22.7+
	2.8	350	0.03	5.1	2.5	14.3	10.5	26.5+
	3.6	360	0.06	11.9	2.9	42.8	18.0	57.9+
	3.9	280	0.06	9.6	2.2	37.4	16.8	55.0+
	4.0	360	0.04	8.4	3.0	33.6	14.4	57.1+
	2.6	290	0.05	9.9	3.3	25.7	14.5	43.5+
$\bar{X}$	3.4	319.0	0.05	7.9	3.1	27.4	15.5	40.0
±SD	0.5	47.4	0.009	1.6	0.8	7.6	2.3	13.9
±SEM	0.13	11.8	0.002	0.4	0.2	1.9	0.6	3.5

Appendix II continued

Animal and treatment	Potassium conc. (mmole/l)		Urine flow rate (ml/min)	Clearance (ml/min.)		Potassium (µ-mole/min.)		% K filtered reabsorbed (+) or excreted secreted (-)
	Plasma	Urine		Creatinine	Potassium	Filtered	Excreted	
Potassium	3.9	228	0.06	4.7	3.5	18.3	13.7	25.1+
loading	5.1	348	0.05	5.9	3.4	30.1	17.4	42.2+
0.3 mole/l	3.8	408	0.06	7.2	6.8	27.4	24.5	10.6+
	3.2	402	0.05	6.8	6.3	21.8	20.1	7.8+
C	4.6	450	0.10	12.8	9.8	58.9	45.0	23.6+
	4.2	366	0.11	9.4	9.6	39.5	40.5	2.0-
	3.6	288	0.10	8.6	8.0	31.0	28.8	7.1+
	5.0	264	0.10	8.0	5.3	40.0	26.4	34.0+
	5.2	402	0.10	12.2	7.7	63.4	40.2	36.6+
	4.6	486	0.11	14.1	11.6	64.9	53.5	17.6+
	4.1	340	0.09	7.6	7.5	31.2	30.6	1.9+
	3.8	420	0.10	9.9	11.3	37.6	43.0	12.6-
$\bar{X}$	4.3	366.8	0.09	8.9	7.5	38.7	32.0	18.4+
±SD	0.6	77.0	0.02	2.8	2.7	15.7	12.4	13.8
±SEM	0.2	25.6	0.006	0.9	0.8	5.2	4.0	4.4
Potassium Loading	4.2	180	0.17	6.4	7.3	26.9	30.6	12.6-
0.5 mole/l	1.6	220	0.20	11.8	27.5	18.9	44.0	57.0-
	2.4	160	0.22	8.9	14.7	21.4	35.2	64.5-
	2.6	230	0.12	8.4	15.0	21.8	39.1	44.2-
	3.4	330	0.13	9.3	12.6	31.6	42.9	26.3-

Appendix II continued

Animal and treatment	Potassium conc. (mmole/l)		Urine flow rate (ml/min)	Clearance (ml/min.)		Potassium (µ-mole/min.)		% K filtered absorbed (+) or excreted secreted (-)
	Plasma	Urine		Creatinine	Potassium	Filtered	Excreted	
	1.8	340	0.10	7.3	18.9	13.1	34.0	61.5
	2.0	220	0.18	8.7	19.8	17.4	39.6	56.1
	4.0	310	0.19	7.5	14.7	30.0	58.9	49.1
	1.6	180	0.17	10.2	19.1	16.3	30.6	46.7
	2.2	240	0.20	11.6	21.8	25.5	48.0	46.9
$\bar{X}$	2.6	241.0	0.17	9.0	17.1	22.3	40.3	46.4
±SD	1.0	64.5	0.04	1.8	5.5	6.1	8.7	16.2
±SEM	0.3	21.5	0.01	0.6	1.8	2.0	2.9	5.3

Appendix III: Individual did dik body weights, food intake, urine volume and osmolality during water restriction.

Animal and days after restriction	Body weight (kg)	Food intake (g/day)	Urine volume (ml/day)	Urine osmolality (mOsm/kg H_2O)
A 0	4.7	150	140	1650
1		138	120	1720
2	4.6	140	103	1930
3		137	93	1820
4	4.4	112	67	1790
5		83	70	1980
6	4.1	80	58	1810
7		98	40	1820
8	4.0	81	59	2010
9		101	38	2210
10	3.9	72	50	1990
11		78	49	2100
12	3.9	79	48	2180
13		59	63	2270
14	3.8	50	50	2190
15		53	58	2280
16	3.8	75	48	2310
17		68	41	2190
18	3.6	73	46	2220
19		59	52	2260

Appendix III continued

Animal and days after water restriction	Body weight (kg)	Food intake (g/day)	Urine volume (ml/day)	Urine Osmolality (mOsm/kg H_2O)
20	3.5	53	42	2400
21		56	57	2380
22	3.5	56	54	2340
B 0	4.4	138	176	1460
1		132	169	1500
2	4.4	125	150	1540
3		98	107	1620
4	4.2	85	85	1600
5		92	81	1660
6	4.2	87	94	1570
7		91	79	1730
8	3.9	77	75	1870
9		77	89	1800
10	3.8	81	93	1770
11		83	80	1890
12	3.8	72	87	1630
13		74	80	1770
14	3.8	67	88	1860
15		71	83	1790
16	3.6	66	75	1850

Appendix III continued

Animal and days after water restriction	Body weight (kg)	Food intake (g/day)	Urine volume (ml/day)	Urine Osmolality (mOsm/kg H_2O)
17		76	79	1720
18	3.5	57	65	1960
19		61	60	2130
20	3.4	66	71	1970
21		58	77	2170
22	3.3	63	77	2160
C 0	4.5	173	53	3020
1		171	52	3030
2	4.5	171	42	3150
3		168	34	2980
4	4.5	164	36	3100
5		145	26	3400
6	4.4	143	30	3260
7		134	34	3320
8	4.4	143	25	3170
9		144	21	3430
10	4.2	121	25	3640
11		125	22	3420
12	4.2	93	23	3420
13		105	27	3500
14	4.1	83	20	3800

Appendix III continued

Animal and days after water restriction	Body weight (kg)	Food intake (g/day)	Urine volume (ml/day)	Urine osmolality (mOsm/kg H_2O)
15		90	23	3760
16	4.0	90	25	3890
17		96	25	3870
18	3.9	80	25	4060
19		87	26	4180
20	3.9	85	25	4200
21		95	20	4120
22	3.9	88	23	4190
D 0	4.2	126	117	1540
1		122	112	1620
2	4.1	120	108	1840
3		118	99	2130
4	4.0	123	91	2520
5		99	76	2530
6	4.0	99	64	2710
7		87	48	2600
8	3.9	96	38	2830
9		87	42	2830
10	3.8	94	33	3200
11		80	38	3210

Appendix III continued

Animal and days after water restriction	Body weight (kg)	Food intake (g/day)	Urine volume (ml/day)	Urine osmolality (mOsm/kg H_2O)
12	3.6	89	31	3110
13		93	33	3150
14	3.5	77	31	3140
15		82	41	3600
16	3.4	71	36	3540
17		77	37	3630
18	3.5	68	32	3490
19		75	41	3770
20	3.6	62	36	3600
21		71	33	3480
22	3.6	70	34	3550

Appendix IV: The amount of sodium filtered at the glomerulus and percentage reabsorbed in the renal tubules and the amount excreted in urine of dik dik.

Animal and treatment	Sodium conc. (mmole/l)		Urine flow rate (ml/min)	Clearance (ml/min)		Sodium (µ-mole/min)		Percent sodium filtered reabsorbed
	Plasma	Urine		Creat-inine	Sodium	Fil-tered	Excr-eted	
Contol A	118	16	0.04	7.8	0.005	920.4	0.64	99.93
	120	18	0.08	8.1	0.012	972.0	1.44	99.85
	124	18	0.06	6.0	0.008	744.0	1.08	99.85
	110	12	0.04	6.9	0.004	759.0	0.48	99.93
	118	18	0.06	5.8	0.009	684.4	1.08	99.84
	106	18	0.05	7.2	0.008	763.2	0.90	99.88
	122	12	0.07	6.9	0.006	841.8	0.84	99.90
	120	24	0.05	5.4	0.010	648.0	1.20	99.81
	118	28	0.08	7.0	0.019	826.0	2.24	99.72
	112	19	0.05	8.7	0.008	974.4	0.95	99.90
D	106	19	0.07	5.7	0.012	604.2	1.33	99.78
	118	21	0.04	9.9	0.007	1168.2	0.84	99.94
	118	24	0.05	8.0	0.010	944.0	1.20	99.87
	128	20	0.07	5.1	0.011	652.8	1.40	99.78
	126	29	0.06	5.9	0.014	743.4	1.74	99.76
	116	38	0.07	9.6	0.022	1065.6	2.66	99.76
	112	12	0.06	8.4	0.006	940.8	0.72	99.72
	122	10	0.08	5.9	0.006	719.8	0.80	99.88
$\bar{X}$	117.4	19.7	0.06	7.1	0.01	833.5	1.19	99.85
±SD	6.2	7.7	0.02	1.4	0.004	156.7	0.55	0.06
±SEM	1.5	1.9	0.004	0.3	0.001	36.4	0.12	0.01

Appendix IV continued

Animal and treatment	Sodium conc. (mmole/l) Plasma	Urine	Urine flow rate (ml/min)	Clearance (ml/min) Creat-inine	Sodium	Sodium (µ-mole/min) Filt-ered	Excr-eted	Percent sodium filtered reabsorbed
Potassium M	124	7	0.06	4.7	0.003	582.8	0.42	99.93
loading	126	26	0.05	5.9	0.010	743.4	1.30	99.83
(0.3 mole/l)	120	68	0.06	7.2	0.034	864.0	4.08	99.53
	116	74	0.05	6.8	0.032	788.8	3.70	99.53
	124	27	0.10	12.8	0.022	1587.2	2.70	99.83
	126	13	0.11	9.4	0.011	1203.2	1.43	99.88
R	118	9	0.10	8.6	0.008	1014.8	0.90	99.91
	124	49	0.10	8.0	0.040	992.0	4.90	99.50
	116	30	0.10	12.2	0.026	1415.2	3.00	99.78
	120	35	0.11	14.1	0.032	1692.0	3.85	99.77
	122	28	0.09	7.6	0.021	927.2	2.52	99.93
	118	37	0.10	9.9	0.031	1168.2	3.70	99.68
$\bar{X}$	121.3	33.6	0.09	8.9	0.023	1081.6	2.7	99.75
±SD	11.0	21.6	0.02	2.8	0.012	343.0	1.4	0.16
±SEM	3.6	7.0	0.006	0.9	0.004	114	0.5	0.05
Potassium M	124	110	0.17	6.4	0.151	793.6	18.70	97.64
loading	120	40	0.20	11.8	0.067	1416.0	8.00	99.44
(0.5 mole/l)	124	60	0.22	8.9	0.106	1103.6	13.20	98.80
	118	80	0.17	8.4	0.115	991.2	13.60	98.63
	120	100	0.13	9.3	0.108	1116.0	13.00	98.84
	126	40	0.10	7.3	0.032	919.8	4.00	99.57
R	124	60	0.18	8.7	0.087	1078.8	10.80	99.00
	122	100	0.19	7.5	0.156	915.0	19.00	97.92
	120	90	0.17	10.2	0.128	1224.0	15.30	98.75
	126	50	0.20	11.6	0.080	1461.6	10.00	99.34
$\bar{X}$	122.4	73.0	0.17	9.0	0.103	1102.0	12.6	98.85
±SD	2.8	26.3	0.04	1.8	0.04	2158	4.6	0.6
±SEM	0.9	8.7	0.01	0.6	0.01	71.6	1.4	0.2

Appendix V: The day-to-day changes in drinking rate and NaCl intake during 0.4 mole/l saline drinking experiment.

Days after start of experiment	Fluid intake (ml/day)	NaCl intake (mmole/day)	Urine osmolality (mOsm/kg H_2O)
1	290	116.0	1320
2	550	220.0	1160
3	682	272.8	1050
4	510	204.0	1250
5	715	286.0	1180
6	420	168.0	1390
7	355	142.0	1570
8	275	110.0	1700
9	210	84.0	2250
10	145	58.0	1420
11	119	44.4	2550
12	65	26.0	2550
13	50	20.0	2620
14	45	18.0	2700
15	48	19.2	2690

Appendix VI: The effects of NaCl intake on drinking rate, urine osmolality, electrolytes, urea and creatinine concentrations.

Animal and treatment	Fluid intake (ml/day)	NaCl taken in by drinking (mmole/day)	Osmolality (mOsm/kg H_2O)	Concentration (mmole/l)			Creatinine conc. (mg/100 ml)
				Sodium (mmole/l)	Potassium (mmole/l)	Urea (mmole/l)	
B							
H_2O ad. lib.	233.0 ± 28		2015.0 ± 460	10.3 ± 1.8	320.0 ± 88.8	785.0 ± 67	341.8 ± 70.3
0.1 mole/l NaCl	234 ± 32	23.4 ± 4.2	1794 ± 155	85.8 ± 45	218 ± 35	914 ± 42	253 ± 42
0.2 mole/l NaCl	294.7 ± 33	58.9 ± 11	1665 ± 102	246.6 ± 114	186 ± 28	646.5 ± 35	89.6 ± 17
0.3 mole/l NaCl	642 ± 210	192.8 ± 34	866 ± 185	243.3 ± 12	84 ± 12	410.6 ± 182	21.6 ± 11.4
A							
H_2O ad lib.	270 ± 37		1590 ± 114	11.6 ± 6	254.0 ± 61	746.1 ± 36	236.6 ± 9
0.1 mole/l NaCl	274.3 ± 39	27.4 ± 8	1681 ± 121	113.3 ± 52	207.1 ± 45	602.6 ± 41	124.4 ± 40
0.2 mole/l NaCl	301.0 ± 38	60.2 ± 11	1424.4 ± 130	290.0 ± 73	153.3 ± 42	307.0 ± 29	65.4 ± 15
0.3 mole/l NaCl	650.9 ± 49	195.3 ± 26	1357.7 ± 149	315.5 ± 93	68.6 ± 7	90.2 ± 11	161.9 ± 21
0.4 mole/l NaCl	938.0 ± 61	391.2 ± 53	924 ± 169	358.0 ± 87	32.0 ± 6	122.2 ± 13	25.5 ± 4

Appendix VII: Calculated P values between the control data and data of the different treatments, using Student's t-test, for various parameters.

Parameter	Treatment	Mean ($\bar{X}$)	± SEM	df	P
Urine flow rate (ml/min)	Control	0.006	0.005	23	
	Dehydrated	0.03	0.002	46	2.01×10^{-4}
	K loading	0.09	0.004	34	3.78×10^{-4}
	Na loading	0.07	0.005	34	1.68×10^{-1}
	H_2O loading	0.05	0.003	34	3.71×10^{-1}
Urine Osmolality (mOsm/kg H_2O)	Control	1989.3	103.0	43	
	Dehydrated	2738.1	136.6	84	1.64×10^{-3}
	K loading	1328.6	60.0	52	1.59×10^{-3}
	H_2O loading	1975.9	115.0	52	8.71×10^{-1}
	Saline drinking	1408.3	68.0	64	3.52×10^{-2}
Plasma osmolality (mOsm/kg H_2O)	Control	322.0	1.4	19	
	Dehydrated	322.4	3.7	38	1.41×10^{-2}
	K loading	324.0	2.8	37	8.95×10^{-1}
	Saline loading	328.0	3.4	37	8.16×10^{-1}
	H_2O loading	324.0	1.9	38	9.42×10^{-1}
	Saline drinking	325.0	4.9	38	7.57×10^{-1}

Appendix VII continued

Parameter	Treatment	Mean X($\bar{X}$)	± SEM	df	P
Plasma urea conc. (mmole/l)	Control	15.4	0.8	20	
	Dehydrated	22.4	0.9	38	7.49×10^{-6}
	K loading	11.1	0.5	33	7.24×10^{-1}
	Na loading	14.3	1.1	33	7.43×10^{-1}
Glomerula fi filtration rate (ml/min /100 kg b.wt.)	Control	182.6	11.7	23	
	Dehydrated	141.7	11.4	46	3.45×10^{-2}
	K loading	225.9	12.7	34	4.21×10^{-2}
	Na loading	206.8	12.0	34	1.13×10^{-1}
	H_2O loading	182.6	11.7	34	8.69×10^{-1}
Percent filtered urea reabsorbed (%)	Control	55.3	6.2	16	
	Dehydrated	77.2	1.8	35	1.4×10^{-3}
	K loading	49.0	3.2	27	4.53×10^{-1}
	Na loading	48.6	3.6	27	6.77×10^{-1}
	H_2O loading	54.4	5.1	27	9.30×10^{-1}
Percent filtered sodium reabsorbed (%)	Control	99.85	0.01	17	
	0.3 mole/l K loading	99.75	0.05	28	4.32×10^{-1}
	0.5 mole/l K loading	98.85	0.20	28	1.9×10^{-2}

Appendix VII continued

Parameter	Treatment	Mean ($\bar{X}$)	± SEM	df	P
Potassium excreted (μ-mole/min)	Control	15.5	0.6	17	
	0.3 mole/l K loading	32.0	4.0	28	6.39×10^{-6}
	0.5 mole/l K loading	40.3	2.9	28	5.06×10^{-11}
Sodium excreted (μ-mole/min)	Control	1.2	0.1	17	
	0.3 mole/l K loading	2.7	0.5	28	3.26×10^{-4}
	0.5 mole/l K loading	12.6	1.4	28	1.07×10^{-11}
Urea excreted (μ-mole/min)	Control	48.8	4.5	16	
	Dehydrated	24.9	2.1	35	2.93×10^{-5}
	K loading	50.3	3.8	27	9.86×10^{-2}
	Na loading	49.1	3.1	27	8.96×10^{-2}
	H_2O loading	49.6	3.4	27	9.1×10^{-1}