Br. J. Pharmac. (1976), **58**, 81–88

THE EFFECT OF HIGH RATES OF VASOPRESSIN ADMINISTRATION ON RENAL POTASSIUM AND SODIUM EXCRETION DURING POTASSIUM LOADING IN THE SHEEP

A.M. BEAL

Department of Physiology, University of Queensland, St. Lucia, Queensland, Australia and the Agricultural Research Council Institute of Animal Physiology, Babraham, Cambridge

1 The influence of potassium loading on the renal excretion of sodium, potassium and solute during high rate vasopressin administration has been investigated in sheep.

2 Adrenalectomized sheep were infused with 0.43 M KCl at 2 ml/min for 2–2.5 hours. Coincident with the rise in plasma potassium concentration, the urinary excretion of sodium, potassium, solute and water was increased as was the reabsorption of solute-free water. The rates of urinary excretion of sodium and potassium, osmolal clearance (C_{Osm}) and solute-free water reabsorption ($T^c_{H_2O}$) for the first 50 min of potassium infusion were each found to be linearly related to the plasma potassium concentration.

3 After 50 min an infusion of vasopressin at 1 or 4 mu/min was superimposed on the potassium infusion for a period of 30 minutes. The administration of vasopressin was consistently associated with further augmentation of potassium excretion and clearance, of osmolal clearance and of solute-free water reabsorption to values above those anticipated from the pre-vasopressin regression lines for these parameters. Urinary sodium showed a coincident depression in the rate of excretion and clearance during the same period.

4 Thirty to fifty minutes after the cessation of vasopressin infusion the potassium and sodium excretions had returned to values which approximated the pre-vasopressin relations between plasma potassium and the urinary excretions of these ions.

5 Both rates of vasopressin infusion were equally effective in increasing the potassium clearance. Any differences in clearance between the two rates of vasopressin administration were not statistically significant.

6 The large increments in potassium excretion (averaging > 40%) were interpreted as indicating that, when vasopressin is present at high concentrations, the distal tubule is one site of action of the hormone in the nephron of sheep.

Introduction

It has been known for some time that, in addition to altering water reabsorption by the kidney, vasopressin can influence the rate of renal excretion of the monovalent ions, sodium, potassium and chloride. However, the degree to which vasopressin alters the renal excretion of these electrolytes varies considerably with the most consistent effects occurring during water diuresis. In the water-loaded dog vasopressin increases the rate of renal sodium excretion but frequently does not increase potassium excretion (Shannon, 1942; Anslow & Wesson, 1955; Ali, 1958; Brooks & Pickford, 1958; Chan & Sawyer, 1961; Perlmutt, 1961). A similar response to vasopressin has been observed in the rat (Sawyer, 1952; Chan, 1965) although in one report (Heller & Stephenson, 1950) increased excretion of potassium was associated with reduced sodium excretion. In contrast vasopressin administration to sheep undergoing water diuresis usually causes increased potassium excretion with the effects on sodium excretion being the more variable (Kinne, Macfarlane & Budtz-Olsen, 1961; Cross, Thornton & Twedell, 1963; Kuhn & Peeters, 1965). The renal electrolyte response has proved to be even less reliable when vasopressin was given to animals in anti-diuresis. Non-hydrated dogs have frequently shown no response at all whereas sheep in the same state have responded to vasopressin administration with increased excretion of sodium, potassium and chloride (Kinne *et al.*, 1961; Kuhn & Peeters, 1965).

Clearly vasopressin can increase the renal excretion of electrolytes but which ion or ions will be increased

cannot be reliably predicted. This variability of response suggests that vasopressin does not specifically control the renal excretion of any of these ions and that the effect is dependent on some factor or factors associated with the relative availability of the ions at the time of observation. In a recent study Scott & Morton (1976) found that high level vasopressin administration to sodium-loaded sheep invariably increased renal sodium excretion with little effect on potassium excretion. The object of the experiments described in this paper was to determine whether a potassium-loaded sheep would respond to vasopressin by increasing the renal excretion of potassium rather than that of sodium.

Methods

Experimental procedures

The experiments were performed on 4 Merino ewes weighing 30–35 kg and 4 Clun Forest ewes weighing 37–57 kg. All animals were bilaterally adrenalectomized in 2 separate operations and after the second operation the sheep were allowed a minimum recovery period of 4 weeks before being used for experiment. The adrenalectomized sheep were maintained with intramuscular injections of 1.5–2.0 mg deoxycorticosterone acetate (DOCA) and 8–15 mg cortisone given once daily at 17 h 00 min. The sheep were allowed 1000 g chaff daily with continual access to water and were provided with a salt lick composed of sodium bicarbonate, chloride and phosphate. At 17 h 00 min on the day before the experiment any uneaten food was removed but access to salt and water was maintained until the experiment started.

Before each experiment a catheter (Casper pattern: Rusch) was inserted into the urinary bladder. This procedure was assisted by the application of a topical anaesthetic solution ('Xylocaine' spray; Astra Chemicals Ltd., Watford) to the vulva and urethral orifice and by lubricating the tip of the catheter with sterile anaesthetic jelly ('Xylocaine' Gel; Astra Chemicals Ltd., Watford). Both jugular veins were cannulated under local anaesthesia (lignocaine 3% with adrenaline 1:50,000; Willows Francis) using the technique of Seldinger (1953). The sheep were then restrained on leather stretchers in a normal upright position with their feet just off the floor. All solutions were given by intravenous infusion at 2 ml/min into one jugular cannula with blood samples being collected from the other cannula into tubes or syringes heparinized with one drop of heparin (5000 iu/ml). Urinary collections were made according to standard clearance techniques; clearance periods were of 10 min duration with blood samples being taken mid-period. After collection of a sample of urine and plasma (control period) the animals were primed with 20 ml of a solution containing 5 g inulin and 6 g sodium para-amino hippurate (PAH)/100 ml given via the infusion cannula. The animals were now allowed a 2 h stabilization period during which a solution containing 1.5 g inulin and 0.6 g PAH/100 ml of 0.125 M NaCl was infused. At the end of this infusion three clearance collections were made. Thereafter a solution containing 1.5 g inulin and 0.6 g PAH/100 ml of 0.43 M KCl was infused for the remaining 2–2.5 h of experiment. After 50 min of KCl infusion, vasopressin (Pitressin; Parke Davis or arginine vasopressin; Sigma) was infused for 30 min at one of the following rates: (1) All four Merino sheep were given an infusion of 4 mu/min Pitressin (pressor units) after a loading injection of 10 mu. (2) Two of the Clun Forest sheep were infused with arginine vasopressin at 4 mu/min (pressor units) without any loading injection. (3) All four Clun Forest sheep were infused with arginine vasopressin at 1 mu/min without any loading injection.

Analytical procedures

The following analyses were performed on the samples of urine and plasma:

(1) Inulin was estimated in urine and plasma by either the method of Davidson & Sackner (1963) or the method of Heyrovsky (1956) adapted to the Technicon autoanalyzer by Dawborn (1965).

(2) PAH was estimated in urine and plasma by either the method of Smith, Finkelstein, Aliminosa, Crawford & Graber (1945) or the method of Bratton & Marshall (1939) as adapted for the Technicon autoanalyzer by Harvey & Brothers (1962).

(3) Osmolality was calculated from the freezing-point depression as measured with either an Advanced osmometer (Model 31 LAS) or a Fiske osmometer (Model G 62).

(4) Sodium and potassium were estimated in diluted urine and plasma with an E.E.L. flame photometer (Model A) using mixed standards in the appropriate concentration ranges for the samples.

Mathematical and statistical procedures

The values for the renal plasma clearances of inulin, PAH and electrolytes were calculated as follows:

$$\text{Plasma clearance} = \frac{\text{urinary excretion rate}}{\text{plasma concentration}}$$

Solute-free water reabsorption = osmolal clearance − urine flow rate.

As Beal & Harrison (1975) have observed the concentration of solutes in the urine collected from a bladder catheter does not alter as soon as the urine flow alters because there is a finite volume or 'dead-space' between the kidney and the exterior in the

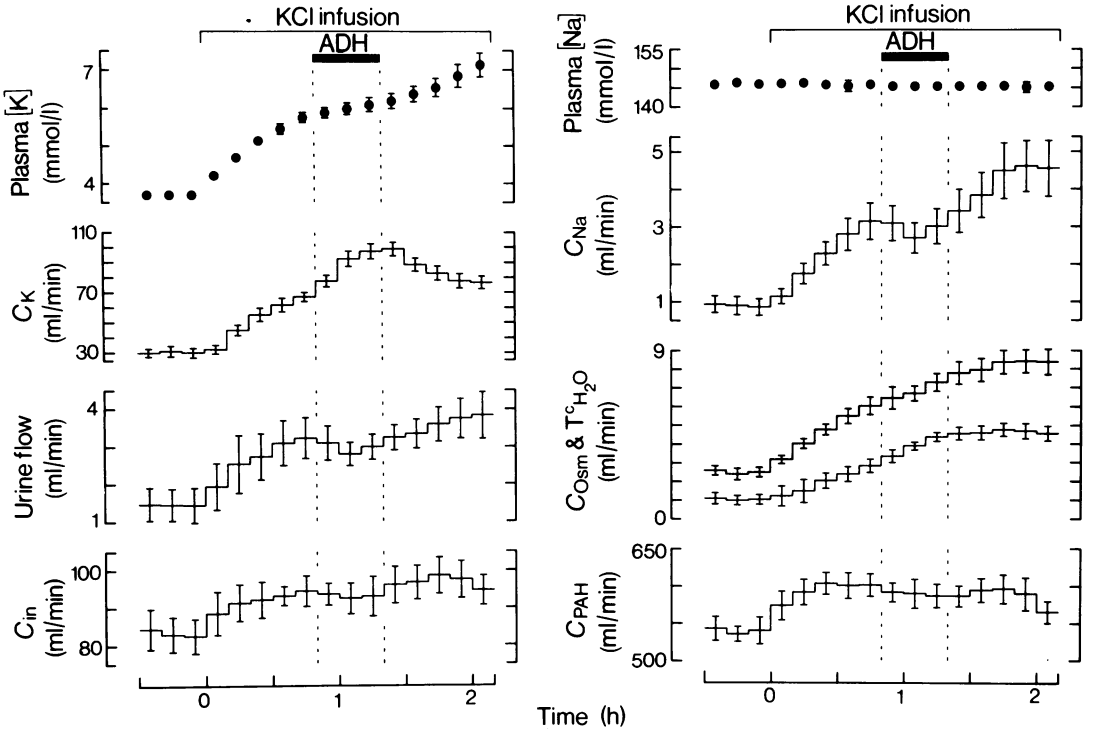

Figure 1 The concentrations of potassium and sodium in plasma, urine flow, solute-free water reabsorption ($T^c_{H_2O}$) and the clearance of potassium (C_K), sodium (C_{Na}), solute (C_{Osm}), inulin (C_{in}) and para-amino hippurate (PAH) (C_{PAH}) before, during and after vasopressin infusion (1 mu or 4 mu/min) into adrenalectomized sheep being potassium loaded at 860 μmol/minute. The solid bars indicate the period of vasopressin administration. Mean results are given; vertical lines show s.e. mean.

urinary tract and catheter. This 'dead-space' volume tends to cause errors in the measurement of rates of urinary excretion of solutes particularly when the urine collection times are short and the flow rate is changing rapidly. As the excretion rate of inulin is affected in a similar manner to the other urinary solutes, the excretion rates of potassium and sodium, the osmolal clearance and the solute-free water reabsorption were expressed as a ratio of the inulin clearance to prevent 'dead-space' errors from affecting the interpretation of these results. These parameters are presented in this form in Figures 2 and 3.

The slopes of linear regressions were compared by *t* test of regression coefficients. Analysis of covariance was applied to the potassium data for the period during which vasopressin was infused at 1 mu or 4 mu/minute. The covariates used in the analysis were the potassium clearances for the 2 periods immediately preceding vasopressin administration.

Results

As the infusion of vasopressin at 1 mu/min and 4 mu/min produced similar changes in renal function, all experiments have been summarized as a single treatment. During the infusion of potassium chloride the plasma potassium concentration was elevated and the concentration of sodium either remained unchanged or fell slightly. The concentrations of sodium and potassium in the urine rose as did the urine flow, resulting in increased excretions and clearances of sodium and potassium. These changes were associated with augmented osmolal clearance and solute-free water reabsorption. Coincident with the increased electrolyte excretion the inulin and PAH clearances also rose with the maximum rates of increase in these clearances occurring during the first 30 min of potassium infusion (Figure 1). Since the increases in potassium and sodium excretion rates,

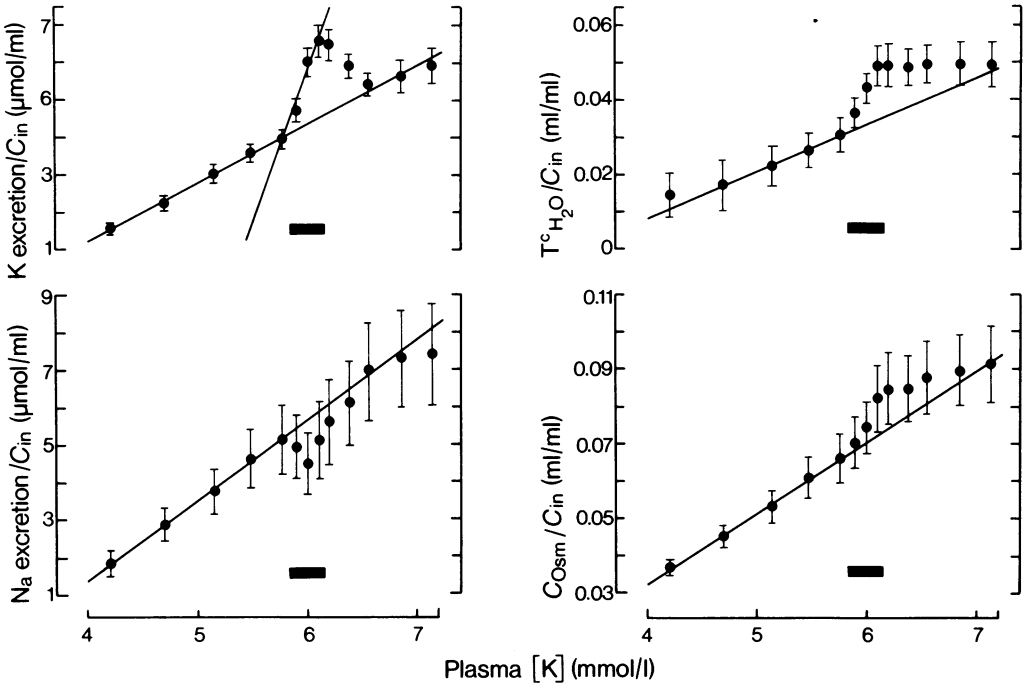

Figure 2 Regressions of urinary potassium excretion, urinary sodium excretion, solute-free water reabsorption ($T^c_{H_2O}$) and osmolal clearance (C_{Osm}) on the plasma potassium concentration before, during and after vasopressin infusion (1 mu or 4 mu/min) into adrenalectomized sheep being potassium-loaded at 860 µmol/minute. Each of the urinary parameters has been expressed as a ratio of the inulin clearance (C_{in}). The solid bars indicate the period of vasopressin administration. The calculated regression lines for the mean data for the 50 min (5 clearance periods) before vasopressin infusion are shown and are extended to higher plasma potassium concentrations as lines of prediction for the period during and after vasopressin infusion. Mean results are given; vertical lines show s.e. mean.

osmolal clearance and solute-free water reabsorption were obviously correlated with the progressive increases in plasma potassium concentration these parameters were plotted against the plasma potassium concentration and found to be linearly related to the plasma potassium (Figure 2).

The administration of vasopressin caused the urine flow to fall slightly in some experiments whereas in the remainder, flow continued to rise at a slower rate. The clearances of inulin and PAH also fell slightly in some experiments, usually, though not always, in the same experiments in which urine flow fell. After the vasopressin infusion had stopped the urine flow and the clearances of inulin and PAH resumed increasing and only started to fall at high plasma potassium concentrations.

During the infusion of vasopressin the urinary concentration and rate of excretion of potassium were further augmented and the rate of rise in plasma potassium concentration slowed, resulting in an increase in the slope for the regression of urinary potassium excretion on plasma potassium in all experiments. The regression lines for urinary potassium excretion on plasma potassium concentration for the periods before and during vasopressin infusion were compared in individual experiments by *t* test of regression coefficients and in all experiments the increase in slope during vasopressin administration was statistically significant (*P* ranged from 0.05 to 0.001). On cessation of vasopressin administration the urinary potassium concentration and excretion rate fell and the rate of rise in plasma potassium concentration increased again so that after 30–50 min the relation between potassium excretion and plasma concentration approximated that occurring before vasopressin infusion (Figures 2 and 3).

In contrast to potassium the concentration of sodium in the urine fell during vasopressin administra-

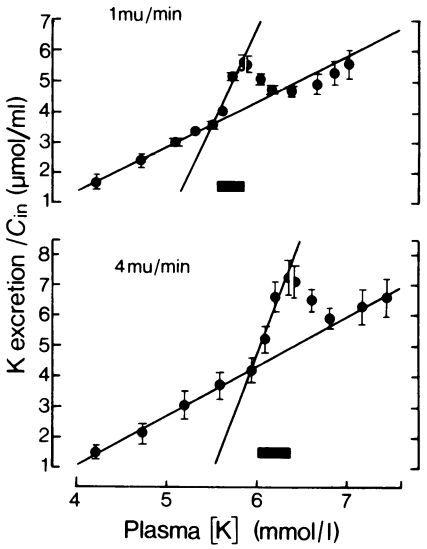

Figure 3 Regression of urinary potassium excretion on plasma potassium concentration before, during and after the infusion of vasopressin at 1 mu/min (4 sheep) and at 4 mu/min (6 sheep) into adrenalectomized sheep being potassium loaded at 860 μmol/minute. The data for potassium excretion are expressed as a ratio of the inulin clearance (C_{in}). The solid bars indicate the period of vasopressin administration. The calculated regression lines for the mean data for the 50 min before vasopressin infusion and for the 30 min during vasopressin infusion are shown. Mean results are given; vertical lines show s.e. mean.

tion in 8 of the experiments and the excretion of sodium decreased in all experiments to values below those expected from the pre-vasopressin regression of sodium excretion on plasma potassium concentration. The extent of this fall in urinary sodium excretion was variable and on a molar basis, the decline in sodium excretion was never greater and was frequently less than the increment in potassium excretion for the same clearance period. After the vasopressin infusion had ended the rate of sodium excretion rose to such an extent that the pre-vasopressin relation between urinary sodium excretion and plasma potassium concentration appeared to be re-established (Figure 2).

Superficially the increase in urinary potassium excretion in the group receiving 1 mu/min vasopressin appeared to be smaller than that for the sheep receiving 4 mu/min (Figure 3). However, when the ratios of potassium clearance/inulin clearance for the 3 clearance periods of vasopressin infusion were compared by analysis of covariance, no significant differences were found between the 2 rates of vasopressin infusion ($F_{2:6}=4.32$, 0.31, 0.02 respectively).

Discussion

As Thorn (1968) observed, one of the difficulties in the interpretation of the effect of neurohypophysial hormones on renal electrolyte excretion has been that the status of water and salt metabolism of the experimental animals has not been well defined or controlled. Although the overall water and mineral balances of the sheep in the present investigation were not uniform, the animals were all in positive potassium balance as a result of the potassium infusion. In the intact animal hyperkalaemia has been shown to increase aldosterone release from the adrenal gland (Funder, Blair-West, Coghlan, Denton, Scoggins & Wright, 1969). By performing the present experiments on adrenalectomized sheep the possible intervention of endogenous adrenal steroids released as a result of the potassium infusion was prevented. As judged from salivary sodium/potassium ratios the effect of the DOCA maintenance injection reaches maximum and returns to sodium-replete ratios within 6–8 h of injection (Beal, Budtz-Olsen, Clark, Cross & French, 1975) so that during these experiments which started 18–20 h after the maintenance injection the concentrations of circulating steroids from exogenous sources would be expected to be low and falling relatively slowly.

The increase in plasma potassium concentration during the infusion of potassium chloride into the sheep was always associated with increased urinary excretion of both sodium and potassium. The rate of excretion of each ion was found to be linearly related to the plasma potassium concentration provided that renal function is not altered by other factors. Micropuncture studies in rat and dog have shown that during potassium loading, the reabsorption of sodium and water in the proximal tubule is depressed thus providing an explanation for the natriuretic diuresis observed in hyperkalaemia (Malnic, Klose & Giebisch, 1966; Watson, 1966; Brandis, Keyes & Windhager, 1970). Observations in potassium-infused sheep although less direct, suggest that the same explanation is tenable for the increase in urinary sodium excretion in this species also (Beal, Budtz-Olsen, Clark, Cross & French, 1973; Beal & Harrison, 1975).

The infusion of vasopressin resulted in a significant increase in the excretion of potassium and a coincident decrease in the excretion of sodium. The site of action of vasopressin on water permeability and electrolyte transport appears to be restricted to the nephron segments distal to the loop of Henle. In dogs and rats vasopressin does not alter the water permeability of

the proximal convoluted tubule (Clapp, Watson & Berliner, 1963; Gertz, Kennedy & Ullrich, 1964; Ullrich, Rumrich & Fuchs, 1964) or the loop of Henle (Wirz, 1956; Gottschalk, 1961; Morgan & Berliner, 1968). Likewise Davis, Knox & Berliner (1967) found no evidence of sodium reabsorption in the proximal tubule being altered by vasopressin although some earlier reports suggest that vasopressin might stimulate sodium reabsorption in this segment (Clapp *et al.*, 1963; Gottschalk, cited by Gertz *et al.*, 1964). In the rat various lines of evidence indicate that the distal convoluted tubule is one site of action of vasopressin on water reabsorption (Wirz, 1956; Gottschalk & Mylle, 1959; Darmady, Durant, Matthews & Stranack, 1960) but in other species such as dog, monkey and *Meriones* the distal tubule does not show the same responsiveness to the hormone (Clapp & Robinson, 1966; Bennett, Brenner & Berliner, 1968; Rouffignac, Lechene, Guinnebault & Morel, 1969). The collecting duct is therefore the only unequivocal site of action of vasopressin on water permeability in the mammalian kidney. Although the infusion of a hyperosmotic solution into sheep would be expected to raise plasma vasopressin concentrations, maximum antidiuretic activity had not been achieved in most experiments as is evidenced by the increment in solute-free water reabsorption resulting from the administration of vasopressin being larger than the corresponding increase in osmolal clearance. However, much of the increment in solute-free water reabsorption clearly results from the addition of solute to the tubular fluid. When vasopressin was infused renal potassium excretion was significantly augmented. Under some conditions particularly potassium loading, secretion of potassium occurs in the collecting duct although in the rat, it adds no more than a small percentage of the total potassium excretion (Hierholzer, 1961; Malnic *et al.*, 1966; Diezi, Michoud, Aceves & Giebisch, 1973). In the present investigation the size of the increment in potassium excretion which averaged over 40% in excess of the rate predicted from the pre-vasopressin regression line (Figure 2) indicates that unless the collecting duct of the sheep has a much greater capacity to secrete potassium than that of the rat, the main site for this effect must be the distal tubule as no other segment of the nephron has the secretory capability consistent with such an increase in potassium excretion.

The fall in renal sodium excretion during vasopressin infusion may be explained by one of a number of mechanisms. The inulin clearance fell slightly in some experiments during vasopressin infusion. However, it is doubtful if this represents a real fall in glomerular filtration rate (GFR) since in most cases the urine flow fell also and the urinary inulin concentration rose after a short delay which suggested that this fall in inulin clearance was a 'dead-space' effect resulting from a fall in urine flow during short urine collection periods. Expression of the sodium excretion as a ratio of the inulin clearance should correct for this artifact. In other experiments the inulin clearance was not depressed indicating that the fall in sodium excretion rate was not dependent on a fall in GFR. Since the fall in urinary sodium excretion was not due to a fall in GFR the lowering of sodium excretion during vasopressin infusion must be the result of increased reabsorption of sodium in the nephron. If vasopressin acts directly on the sodium pump of the cortical collecting duct as some evidence suggests (Morgan & Berliner, 1968; Helman, Grantham & Burg, 1971; Frindt & Burg, 1972) the fall in sodium excretion may be due to increased active reabsorption in this segment. However, if Ullrich, Baldamus, Uhlich & Rumruch (1969) are correct in their conclusion that vasopressin increases the sodium permeability of the collecting duct rather than affecting active transport, the reduction in sodium excretion may result from the influx of potassium into the tubule reducing the potential difference across the tubule thus increasing the ease with which sodium could be reabsorbed from this segment. These arguments may extend to the distal tubule of the sheep as well but as yet no direct measurements of the effect of vasopressin on water permeability or sodium transport in the nephron have been reported for this species. The situation is obviously confused by the continuing increase in plasma potassium concentration causing ever increasing amounts of sodium to be rejected in the proximal segment of the nephron.

Following the cessation of vasopressin infusion there was an obvious return of the relationship between plasma potassium concentration and the excretions of sodium and potassium to the condition which existed before vasopressin administration although the continuous fall in steroid levels throughout the experiment may have led to a slight change in this relationship (Figure 2). At still higher plasma potassium levels both potassium and sodium excretion began to fall as the haemodynamic state of the kidney was affected by the high plasma potassium concentration.

The effects on urinary potassium excretion of Pitressin and arginine-vasopressin were of similar magnitude which agrees with the observation of Macfarlane, Kinne, Walmsley, Siebert & Peter (1967) that arginine-vasopressin, lysine-vasopressin and Pitressin were of equal effect in the adult sheep. Although the two rates of infusion of vasopressin used in these experiments were clearly pharmacological the similarity of the response to these dose rates suggests that they were both supramaximal and that administration of vasopressin at more physiological rates would also augment urinary potassium excretion during potassium loading. The results obtained in this work support the thesis that relative availability of

sodium and potassium is one important determinant of the pattern of change in renal excretion of these ions during vasopressin administration.

I wish to thank Mrs M. Ford and Mr P. Burrow for their technical assistance with these experiments.

References

ALI, M.M. (1958). A comparison of some activities of arginine-vasopressin and lysine-vasopressin on kidney functions in conscious dogs. *Brit. J. Pharmac. Chemother.*, **13**, 131–137.

ANSLOW, W.P. & WESSON, L.G. (1955). Some effects of pressor-antidiuretic and oxytocic fractions of posterior pituitary extract on sodium, chloride, potassium and ammonium excretion in the dog. *Am. J. Physiol.*, **182**, 561–566.

BEAL, A.M. & HARRISON, F.A. (1975). Renal function in sheep during infusion of alkali metal ions into the renal artery. *J. Physiol., Lond.*, **245**, 137–162.

BEAL, A.M., BUDTZ-OLSEN, O.E., CLARK, R.C., CROSS, R.B. & FRENCH, T.J. (1973). Renal and salivary responses to infusion of potassium chloride, bicarbonate and phosphate in Merino sheep. *Q. Jl exp. Physiol.*, **58**, 251–265.

BEAL, A.M., BUDTZ-OLSEN, O.E., CLARK, R.C., CROSS, R.B. & FRENCH, T.J. (1975). Changes in renal haemodynamics and electrolyte excretion during acute hyperkalaemia in conscious adrenalectomized sheep. *Q. Jl exp. Physiol.*, **60**, 207–221.

BENNETT, C.M., BRENNER, B.M. & BERLINER, R.W. (1968). Micropuncture study of nephron function in the Rhesus monkey. *J. clin. Invest.*, **47**, 203–216.

BRANDIS, M., KEYES, J. & WINDHAGER, E.E. (1970). Potassium-induced inhibition of proximal tubular fluid reabsorption. *Physiologist, Wash.*, **13**, 154.

BRATTON, A.C. & MARSHALL, E.K. (1939). A new coupling component for sulphanilamide determination. *J. biol. Chem.*, **128**, 537–550.

BROOKS, F.P. & PICKFORD, M. (1958). The effect of posterior pituitary hormones on the excretion of electrolytes in dogs. *J. Physiol., Lond.*, **142**, 468–493.

CHAN, W.Y. (1965). Effects of neurohypophysial hormones and their deamino analogues on renal excretion of sodium, potassium and water in rats. *Endocrinology*, **77**, 1097–1104.

CHAN, W.Y. & SAWYER, H. (1961). Saluretic actions of neurohypophysial peptides in conscious dogs. *Am. J. Physiol.*, **201**, 799–803.

CLAPP, J.R. & ROBINSON, R.R. (1966). Osmolality of distal tubular fluid in the dog. *J. clin. Invest.*, **45**, 1847–1853.

CLAPP, J.R., WATSON, J.F. & BERLINER, R.W. (1963). Osmolality, bicarbonate concentration and water reabsorption in proximal tubule of the dog nephron. *Am. J. Physiol.*, **205**, 273–280.

CROSS, R.B., THORNTON, W.M. & TWEDELL, E.D. (1963). The effect of vasopressin on water and electrolyte excretion by the sheep. *Aust. J. exp. Biol. med. Sci.*, **41**, 629–636.

DARMADY, E.M., DURRANT, J., MATTHEWS, E.R. & STRANACK, F. (1960). Location of ^{131}I Pitressin in the kidney by autoradiography. *Clin. Sci.*, **19**, 229–241.

DAVIDSON, W.D. & SACKNER, M.A. (1963). Simplification of the anthrone method for determination of inulin in clearance studies. *J. lab. clin. Med.*, **62**, 351–356.

DAVIS, B.B., KNOX, F.G. & BERLINER, R.W. (1967). The effect of vasopressin on proximal tubule sodium reabsorption in the dog. *Am. J. Physiol.*, **212**, 1361–1364.

DAWBORN, J.K. (1965). Application of Heyrovsky's inulin method to automatic analysis. *Clin. Chim. Acta*, **12**, 63–66.

DIEZI, J., MICHOUD, P., ACEVES, J. & GIEBISCH, G. (1973). Micropuncture study of electrolyte transport across papillary collecting duct of the rat. *Am. J. Physiol.*, **224**, 623–634.

FRINDT, G. & BURG, M.B. (1972). Effect of vasopressin on sodium transport in renal cortical collecting tubules. *Kidney Int.*, **1**, 224–231.

FUNDER, J.W., BLAIR-WEST, J.R., COGHLAN, J.P., DENTON, D.A., SCOGGINS, B.A. & WRIGHT, R.D. (1969). Effect of plasma [K^+] on the secretion of aldosterone. *Endocrinology*, **85**, 381–384.

GERTZ, K.H., KENNEDY, G.C. & ULLRICH, K.J. (1964). Mikropunktionuntersuchungen über die Flüssigkeitsrückresorption aus den einzelnen Tabulusabschnitten bei Wasserdiurese (diabetes insipidus). *Pflügers Arch. ges. Physiol.*, **278**, 513–519.

GOTTSCHALK, C.W. (1961). Micropuncture studies of tubular function in the mammalian kidney. *Physiologist, Wash.*, **4**, 35–55.

GOTTSCHALK, C.W. & MYLLE, M. (1959). Micropuncture study of the mammalian urinary concentrating mechanism: evidence for the countercurrent hypothesis. *Am. J. Physiol.*, **196**, 927–936.

HARVEY, R.D. & BROTHERS, A.J. (1962). Renal extraction of paraamino-hippurate and creatinine measured by continuous *in vivo* sampling of arterial and renal vein blood. *Ann. N.Y. Acad. Sci.*, **102**, 46–54.

HELLER, H. & STEPHENSON, R.P. (1950). Effect of posterior pituitary extract and its fractions on renal electrolyte excretion. *Nature, Lond.*, **165**, 189.

HELMAN, S.I., GRANTHAM, J.J. & BURG, M.B. (1971). Effect of vasopressin on electrical resistance of renal cortical collecting tubules. *Am. J. Physiol.*, **220**, 1825–1832.

HEYROVSKY, A. (1956). A new method for the determination of inulin in plasma and urine. *Clin. Chim. Acta*, **1**, 470–474.

HIERHOLZER, K. (1961). Secretion of potassium and acidification in collecting ducts of mammalian kidney. *Am. J. Physiol.*, **201**, 318–324.

KINNE, R., MACFARLANE, W.V. & BUDTZ-OLSEN, O.E. (1961). Hormones and electrolyte excretion in the sheep. *Nature, Lond.*, **192**, 1084–1085.

KUHN, E. & PEETERS, G. (1965). Influence de l'arginine vasopressin sur l'excrétion d'électrolytes chez le mouton. *Archs int. Pharmacodyn. Thér.*, **155**, 455–458.

MACFARLANE, W.V., KINNE, R., WALMSLEY, C.M., SIEBERT, B.D. & PETER, D. (1967). Vasopressin and the increase in water and electrolyte excretion by sheep, cattle and camels. *Nature, Lond.*, **214**, 979–981.

MALNIC, G., KLOSE, R.M. & GIEBISCH, G. (1966). Micropuncture study of distal tubular potassium and sodium transport in the rat kidney. *Am. J. Physiol.*, **211**, 529–547.

MORGAN, T. & BERLINER, R.W. (1968). Permeability of the loop of Henle, vasa recta and collecting duct to water, urea and sodium. *Am. J. Physiol.*, **215**, 108–115.

PERLMUTT, J.H. (1961). Renal activity of vasopressin in anesthetized dogs. *Am. J. Physiol.* **200**, 400–404.

ROUFFIGNAC, C. DE, LECHENE, C., GUINNEBAULT, M. & MOREL, F. (1969). Etude par microponction de l'élaboration de l'urine. III Chez le mérion non diurétique et en diurése par le mannitol. *Nephron*, **6**, 643–666.

SAWYER, W.H. (1952). Posterior pituitary extracts and excretion of electrolytes by the rat. *Am. J. Physiol.*, **169**, 583–587.

SCOTT, D. & MORTON, J.J. (1976). Changes in urinary water and electrolyte excretion in sodium-loaded sheep in response to intravenous infusion of arginine vasopressin. *Q. Jl exp. Physiol.*, **61**, 57–70.

SELDINGER, S.I. (1953). Catheter replacement of the needle in percutaneous arteriography. *Acta Radiologica*, **39**, 368–376.

SHANNON, J.A. (1942). The control of renal excretion of water. *J. exp. Med.*, **76**, 387–399.

SMITH, H.W., FINKELSTEIN, N., ALIMINOSA, L., CRAWFORD, B. & GRABER, M. (1945). Renal clearances of substituted hippuric acid derivatives and other aromatics in man. *J. clin. Invest.*, **24**, 388–404.

THORN, N.A. (1968). The influence of the neurohypophysial hormones and similar polypeptides on the kidneys. In *Neurohypophysial Hormones and Similar Polypeptides, Handb. exp. Pharmac.* Vol. 23, ed. Berde, B. pp. 372–442. Berlin, Heidelberg & New York: Springer-Verlag.

ULLRICH, K.J., RUMRICH, G. & FUCHS, G. (1964). Wasserpermeabilität und transtubulärer Wasserfluss corticaler Nephronabschnitte bei verschiedener Diuresezuständen. *Pflügers Arch. ges. Physiol.*, **280**, 99–119.

ULLRICH, K.J., BALDAMUS, C.A., UHLICH, E. & RUMRICH, G. (1969). Influence of ionic calcium and antidiuretic hormone on transtubular sodium transport in the rat kidney. *Pflügers Arch.*, **310**, 369–376.

WATSON, J.F. (1966). Potassium reabsorption in the proximal tubule of the dog nephron. *J. clin. Invest.*, **45**, 1341–1348.

WIRZ, H. (1956). Der osmotische Druck in den corticalen Tubuli der Ratteniere. *Helv. Physiol. Pharmac. Acta*, **14**, 353–362.

(Received January 28, 1976. Revised March 24, 1976.)