J. Physiol. (1976), **256**, *pp.* 731–745
With 7 text-figures
Printed in Great Britain

THE RENAL BLOOD FLOW AND THE GLOMERULAR FILTRATION RATE OF ANAESTHETIZED DOGS DURING ACUTE CHANGES IN PLASMA SODIUM CONCENTRATION

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(*Received 2 October 1975*)

SUMMARY

1. The effects of acute changes in plasma Na concentration (P_{Na}) on renal blood flow (RBF) and glomerular filtration rate (GFR) were studied in anaesthetized greyhounds. Saline was infused at a constant rate (0·1 ml. kg^{-1} min^{-1}) either into a renal artery or into a systemic vein. Plasma Na concentration was altered by varying the Na concentration of the infused saline from 0·154 to 0·077, 0·616 or 1·232 M.

2. Blood pressure (B.P.), packed cell volume (PCV), concentration of plasma solids (PS) and the plasma concentration of H^+ and K (P_K) ions were measured but no attempt was made to contain their fluctuation.

3. An infusion of hypertonic saline into a renal artery usually led to an ipsilateral increase in RBF for 5–15 min, followed by a progressive fall. Over-all, mean values of RBF fell with P_{Na} throughout the range studied (120–190 m-mole $l.^{-1}$). Glomerular filtration rate rose with P_{Na} to reach maximal values at P_{Na} levels of 140–160 m-mole $l.^{-1}$, but fell thereafter. The combined fall in RBF and GFR, without change in filtration fraction, at P_{Na} values above 160 m-mole $l.^{-1}$ is consistent with an alteration in afferent arteriolar resistance. The fall in GFR despite a rise in RBF noted when P_{Na} was reduced below 140 m-mole $l.^{-1}$ requires an additional explanation.

4. Renal blood flow was independent of P_K; it was inversely related to $[H^+]$ and directly related to PS. Glomerular filtration rate was independent of PCV and P_K. It was also inversely related to $[H^+]$ and directly related to PS up to a value of 6 g 100 g^{-1} plasma, after which the relationship was reversed. These results suggest that the renal vascular responses to acute changes in P_{Na} may be mediated in part, at least, by concurrent change in PS and $[H^+]$.

INTRODUCTION

The blood flow to the kidney can be related to the rate of sodium reabsorption (Kramer & Deetjen, 1964). Since Nashat, Tappin & Wilcox (1975) have found P_{Na} to be an important determinant of Na reabsorption, one may speculate that it also determines blood flow. However, an acute increase in plasma Na has been reported to increase renal blood flow (Gazitua, Scott, Chou & Haddy, 1969; Young & Rostorfer, 1973) or to decrease it (Green & Farrah, 1949; Forgács, Châtel & Visy, 1969). The relationship between P_{Na} and GFR is no less confusing, for an acute increase in P_{Na} has been reported to increase GFR (Young & Rostorfer, 1973), to decrease it (Forgács *et al.* 1969) or not to change it consistently (Sadowski 1972*b*). Kady, Nashat, Tappin & Wilcox (1974) have recently observed that although a rise in P_{Na} from a low level (140 m-mole $l.^{-1}$) increased GFR, further rises in P_{Na} (above 155–160 m-mole $l.^{-1}$) progressively decreased it. The renal vascular responses to acute increase in P_{Na} are thus complicated. The conflicting findings must be related to the operation of other factors ignored in these experiments. In a previous paper, Nashat *et al.* (1975) observed that when P_{Na} was changed in the dog, there were accompanying changes in the packed cell volume and the plasma concentration of solids, H^+ and K ions. Clearly these are factors which need to be considered. It was the aim of the present study to investigate how an acute change in P_{Na} and the concomitant variations in the composition of the blood it imposes, affect RBF and GFR.

METHODS

Experiments were performed on thirty-six adult greyhounds anaesthetized with pentobarbitone Na. Isotonic saline (0·154 M-NaCl solution) was infused continuously either through a needle inserted into the left renal artery (twenty-six animals) or through a cannula in a femoral vein (ten animals). The infusion was given at a constant rate of 0·1 $ml.kg^{-1}\ min^{-1}$. The plasma Na concentration was altered by changing the Na concentration of the infused solution to 0·077, to 0·616, or to 1·232 M.

The glomerular filtration rate was estimated as the clearance of [^{125}I] Na diatrizoate (Hypaque) or [^{51}Cr]ethylene diamine tetra-acetic acid ([^{51}Cr]EDTA). Concentration of Na and K were measured by flame photometry, the concentration of H^+ with a glass electrode (Radiometer BMS 3), the packed cell volume with a microhaematocrit centrifuge and plasma solids by desiccation of a measured sample of plasma to constant weight. The weight of salts of measured ions was subtracted from the total weight of the plasma solids. Blood pressure was monitored with a mercury manometer connected to a cannula inserted into a femoral artery.

The experimental procedure was detailed previously as the 'third series' of experiments in Nashat *et al.* (1976).

The following additional procedures were carried out in a number of experiments. In ten animals the left renal vein was catheterized and the renal venous concentra-

tions of a number of plasma constituents were measured. In these experiments renal blood flow was estimated from the clearance of [^{131}I] hippuran (Radiochemicals Ltd, Amersham, Bucks). Fifteen μc of the marker were injected I.V. during surgery, and 30 μc added to the solution of 1 part of 20 % mannitol and 2 parts of isotonic (0·154 M) saline which was infused continuously into a vein throughout the experiment at a rate of 1 ml. min^{-1}. The renal clearance was corrected for the extraction of hippuran, using plasma from samples of arterial and renal venous blood drawn simultaneously. Renal blood flow was calculated from the corrected clearance rate of hippuran and the value of arterial packed cell volume.

The clearance of ^{133}Xe from the kidney was used to estimate renal cortical blood flow in eight experiments. For this, the technique described previously (Nashat, Scholefield, Tappin & Wilcox, 1969) was used but was modified to allow repeated estimates of renal cortical blood flow at intervals of 3–5 min. In this time interval, only the slopes of the first two components of the complex exponential Xenon washout curve could be resolved. Neglecting the contribution of the slow third component introduced an error in the estimated flow to the outer cortex (component 1) of less than 5 %.

An electromagnetic flow-meter was used for displaying the time course of changes in renal blood flow in six experiments. A flow head was selected to cause an approximately 20 % constriction in the renal artery. It encircled the artery proximal to the point at which the infusion of saline was introduced. A pulsed-logic (Biotronics BL 610) flow-meter was used. Each flow transducer was previously calibrated using excised segments of renal artery perfused with blood with appropriate haematocrit. The 'zero adjustment' was made at the beginning and end of each experiment by occluding the artery distal to the transducer.

The values for renal blood flow presented in the pooled results were calculated from the clearance of hippuran. Results obtained within 15–20 min of the start of the hypertonic saline infusions were discarded. The other methods for measuring RBF were only used to illustrate individual experiments.

The value of P_{Na} in femoral arterial blood was taken to be the P_{Na} of blood at the right (untouched) kidney and at the left kidney during infusion of 0·154 M saline into its artery. The value at the left kidney while it received hypertonic saline was taken to be that measured in blood obtained from its vein. In experiments where renal venous samples were not available, the value was calculated from the formula described by Nashat *et al.* (1976) which assumes simple mixture of saline and plasma within the renal artery. It was found previously that calculated values of P_{Na} corresponded to values measured in the renal vein after 30 min of hypertonic saline infusion. The calculated values used in this study were limited to those obtained after this time interval.

Renal venous pressure was measured electromanometrically via a catheter inserted into the renal vein through its gonadal tributary. The tip of the catheter lay 1 cm from the hilus of the kidney.

All the cited values refer to a single kidney, average weight 84 ± 4 g (S.D.).

RESULTS

When the Na concentration of a saline solution infused into the renal artery was increased from 0·154 to 0·616 or 1·232 M, there was usually some increase in blood flow to that kidney for 5–15 min. This was, however, followed by a fall in flow which was progressive. Blood flow rate gradually returned towards its previous level when the infusion was changed back to 0·154 M. This was the commonest sequence of blood flow changes observed

to accompany the hypertonic saline infusion. However, sometimes the delayed fall in blood flow was not seen. An electromagnetic flowmeter record illustrating these changes in one experiment is shown in Fig. 1.

In one experiment, the infusion of 0·616 M-$NaHCO_3$ solution into a renal artery reduced the blood flow to that kidney.

The renal cortical blood flow followed the pattern described for the total renal blood flow. Fig. 2 shows the results of measurements of renal cortical blood flow made during five separate infusions of hypertonic saline in one dog. Flow was either unchanged or increased at first but was invariably reduced thereafter.

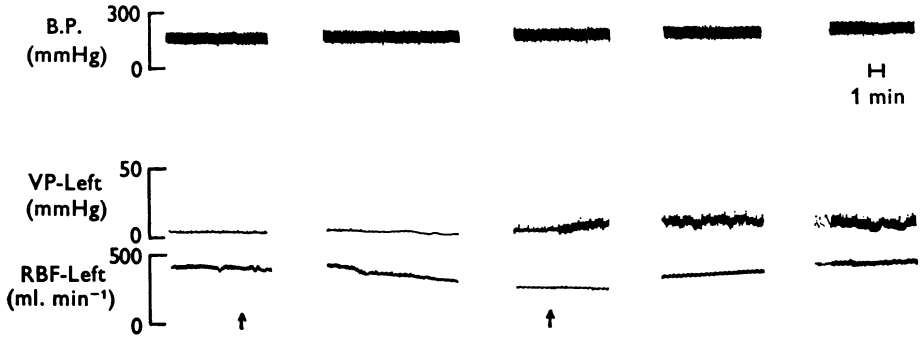

Fig. 1. Records from a single experiment showing from above downwards, systemic blood pressure (B.P.), left renal venous pressure (VP) and an electromagnetic flowmeter record of blood (RBF) through the left kidney. At the first arrow, the composition of saline infused into the left renal artery was changed from 0·154 to 1·232 M. It was changed back to 0·154 M at the second arrow. The rate of infusion was 0·1 ml. kg^{-1} min^{-1} throughout. A 1 min time interval is shown. The panels are separated by 11, 9, 8 and 5 min respectively. Note that the blood flow is slightly higher at the beginning of the second panel (420 ml. min^{-1}) than it is at the end of the first panel (390 ml. min^{-1}). In the third panel the blood flow is 250 ml. min^{-1} and recovers to 400 ml. min^{-1} by the 5th panel.

The response was not modified by cutting all the nerves seen to run to the renal hilum. Unlike hypertonic saline, an infusion of hypertonic dextrose solution led to a persistent increase in the cortical blood flow (Fig. 3). In five separate experiments the hypertonic saline was infused into the common carotid artery at 0·1 ml. kg^{-1} min^{-1}; flow through this vessel was increased throughout the period of the infusion and returned to the previous levels only when the infusion was stopped (Fig. 4).

Pooled results from experiments on ten dogs in which iso-, hypo- or hypertonic saline solutions were infused into one kidney are presented in Fig. 5. This Figure shows that renal blood flow is high at low levels of P_{Na}; it falls as P_{Na} rises to 140–160 m-mole l^{-1}. The peripheral vascular

resistance across the kidney calculated by dividing blood pressure by blood flow is seen to double within the range of P_{Na} values studied. Renal plasma flow varies with P_{Na} in similar fashion. Simultaneous measurements of glomerular filtration rate are seen to follow the more complicated pattern described previously (Nashat *et al.* 1976). Thus the filtration rate

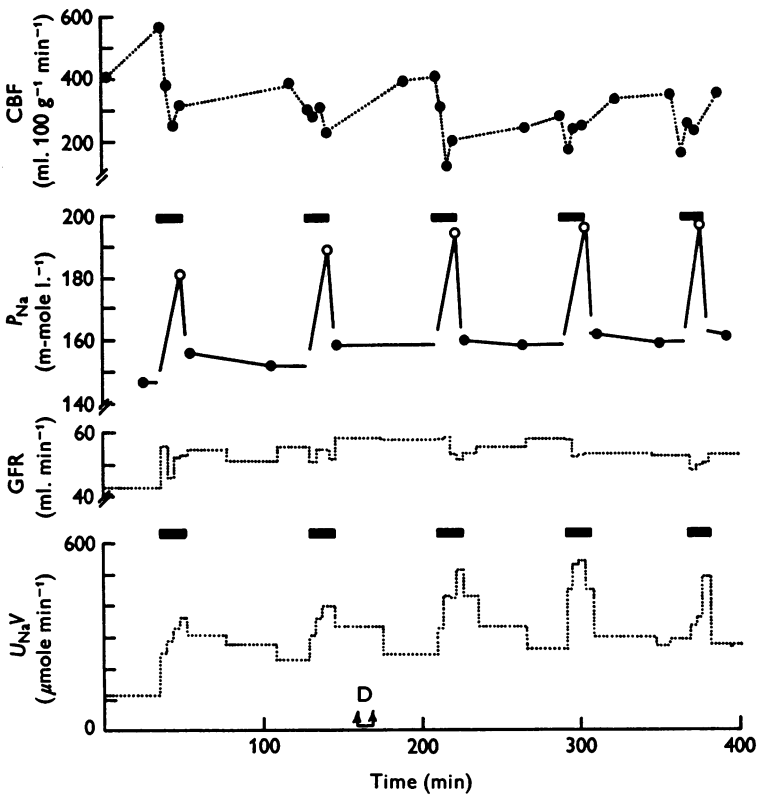

Fig. 2. Results from a single experiment showing from above downwards renal cortical blood flow (CBF), plasma Na concentration (P_{Na}), glomerular filtration rate (GFR) and Na excretion ($U_{Na}V$) plotted against time. During the periods marked by rectangles, hypertonic (1·232 M) saline was infused into the left kidney. All visible nerves converging on to the kidney were severed in the interval between the two arrows at D.

is low at P_{Na} values less than 140 m-mole l.$^{-1}$; it increases to a peak at P_{Na} values between 140 and 160 m-mole l.$^{-1}$ but declines at the higher levels. The filtration fraction is very low when P_{Na} is below 140 m-mole l.$^{-1}$; it rises at P_{Na} 140–160 m-mole l.$^{-1}$ and is unchanged thereafter.

It was previously found that systemic blood pressure did not change with P_{Na}, but that there were significant changes in PCV, PS, [H$^+$] and

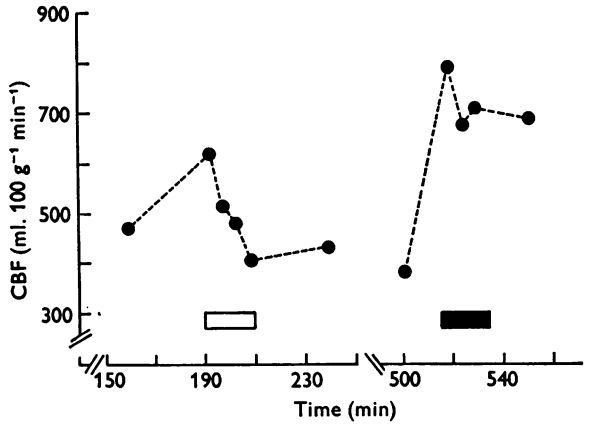

Fig. 3. Results obtained from a single experiment showing cortical blood flow (CBF) plotted against time. During the periods indicated by rectangles, hypertonic (1·232 M) saline (open rectangle) or hypertonic (2·23 M) dextrose (filled rectangle) were infused into the renal artery at identical rates of 0·1 ml.kg^{-1} min^{-1}.

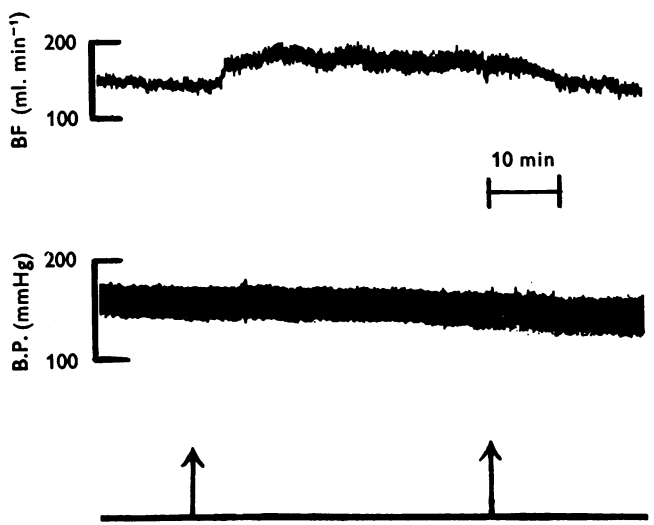

Fig. 4. Records from a single experiment showing from above downwards, an electromagnetic flow-meter record of blood flow (BF) in the common carotid artery and systemic blood pressure (B.P.). The composition of the saline infused into the common carotid artery was changed from 0·154 to 1·232 M at the first arrow and changed back to 0·154 M at the second arrow. The rate of the infusion was unchanged at 0·1 ml. kg^{-1} min^{-1}.

P_K (Nashat *et al.* 1976). Of these only PS and [H^+] were significantly related to RBF and GFR. Fig. 6 shows the relationships between RBF, GFR and PS for data obtained at P_{Na} levels above and below 150 m-mole $l.^{-1}$. Blood flow is seen to rise 2–3-fold as the plasma solids

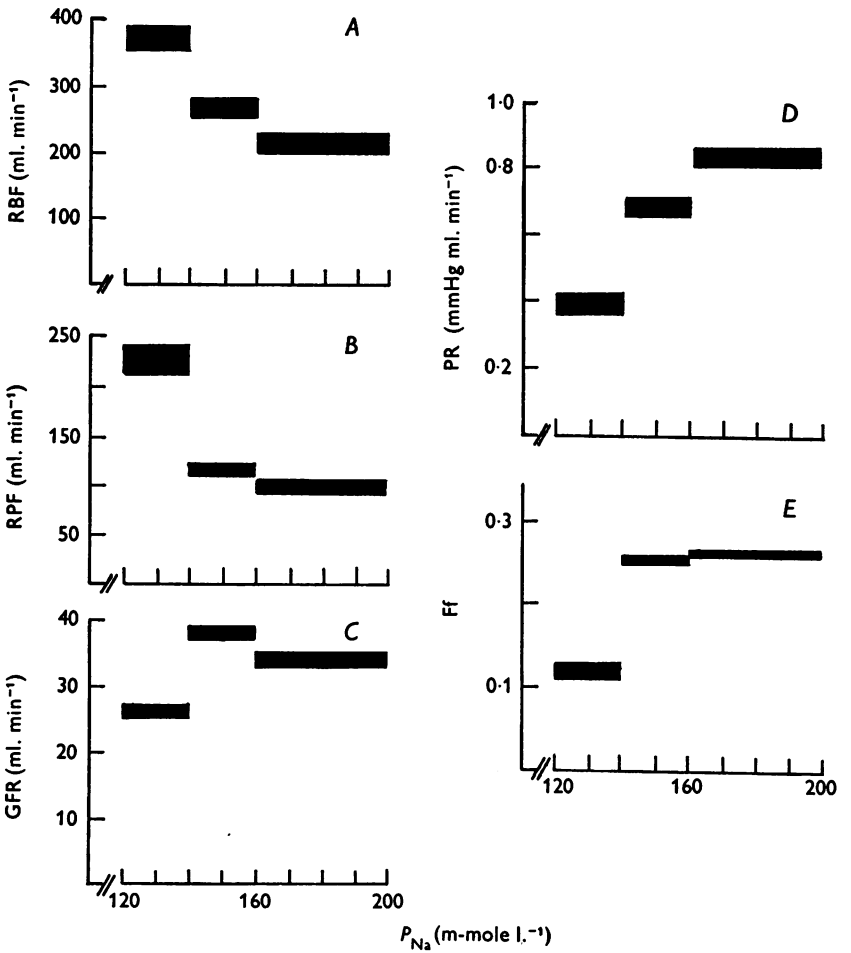

Fig. 5. Composite graph summarizing the relation between plasma sodium concentration and (*A*) renal blood flow, (*B*) renal plasma flow, (*C*) glomerular filtration rate, (*D*) renal peripheral resistance and (*E*) filtration fraction.

The width of the blocks indicates ranges of P_{Na} (120–140, 140–160 and 160–190 m-mole. 2^{-1}) while their height indicates the mean plus and minus one S.E. of mean of values obtained within that range. The data were obtained from ten experiments. The number of observations for the successive P_{Na} intervals are 30, 75 and 57.

The differences between the blocks in each panel are highly significant ($P < 0{\cdot}001$), except for the last two blocks in panel *E*.

concentration increased from 4 to 5·75 g $100\,g^{-1}$. This increase was similar at both ranges of P_{Na}. Over-all, there was a significant dependence of GFR on the concentration of plasma solids at both P_{Na} ranges. Data obtained in experiments using haemodialysis (Nashat *et al.* 1976) were included in Fig. 6 to extend the relationship to higher levels of PS. It is apparent that

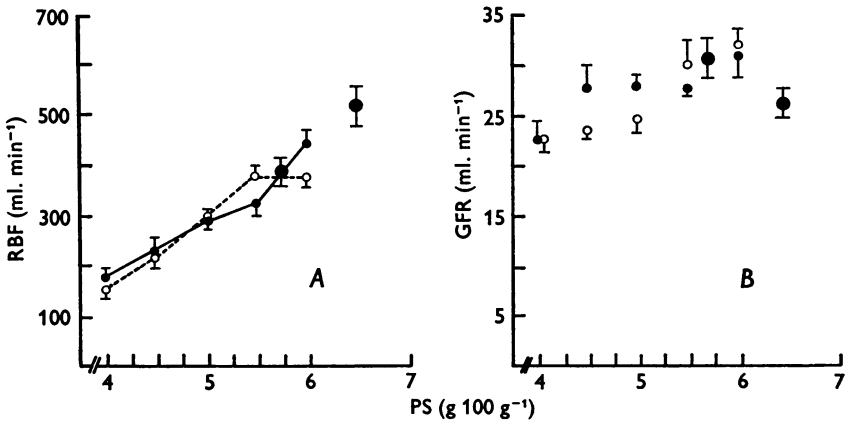

Fig. 6. A composite graph relating the renal blood flow (in *A*) and the glomerular filtration rate (in *B*) to the concentration of plasma solids. Mean values and 1 S.E. of mean are shown for results obtained when the plasma Na concentration was below 150 m-mole $l.^{-1}$ (filled circles and continuous lines) and above 150 m-mole, $l.^{-1}$ (open circles and interrupted lines). The regression equations and data for the relationships shown are as follows.

For RBF

$P_{Na} < 150$: RBF = 99·2PS − 205 ($r = 0{\cdot}49$; $n = 61$; $P < 0{\cdot}001$).
$P_{Na} > 150$: RBF = 90·4PS − 187 ($r = 0{\cdot}65$; $n = 71$; $P < 0{\cdot}001$).
All results: RBF = 98·6PS − 214 ($r = 0{\cdot}61$; $n = 132$; $P < 0{\cdot}001$).

For GFR

$P_{Na} < 150$: ($r = 0{\cdot}09$; $n = 61$; n.s.).
$P_{Na} > 150$: ($r = 0{\cdot}15$; $n = 71$; n.s.).
All results: GFR = 1·7PS + 18·4 ($r = 0{\cdot}18$; $n = 132$; $P < 0{\cdot}05$).

The two large circles in each panel represent the mean values (± 1 S.E. of mean) of data obtained from fourteen experiments where haemodialysis was employed (Nashat *et al.* 1975). These data are not included in the calculations of regression coefficients given above.

an increase in PS above 6 is associated with a further rise in RBF but a fall in GRF. A fall in both RBF and GFR accompanied an increase in the plasma H^+ concentration (Fig. 7). There was an insufficient range of values of plasma H^+ concentration at low levels of P_{Na} to allow division of results into two groups. Neither RBF nor GFR were significantly dependent on P_K ($r = 0{\cdot}09$; $P > 0{\cdot}1$). The glomerular filtration rate was also

independent of PCV ($r = 0{\cdot}09$; $P > 0{\cdot}1$). Since packed cell volume was used to calculate values of RBF, the relationship between these two variables could not be assessed.

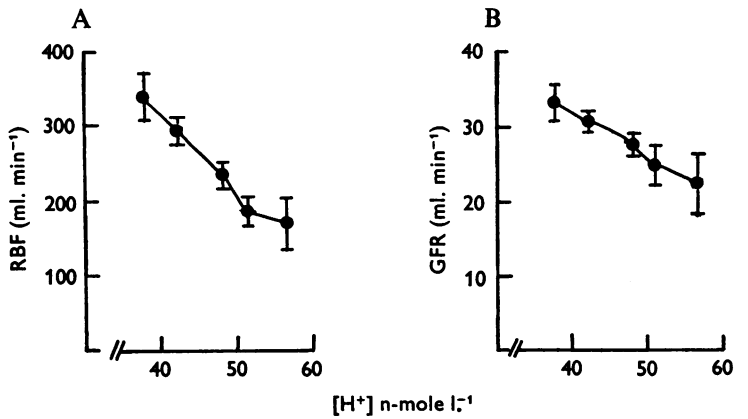

Fig. 7. A composite graph relating the renal blood flow (in *A*) and the glomerular filtration rate (in *B*) to the plasma concentration of H^+. Mean values ± 1 S.E. of mean are shown. The regression equations and data for the relationships shown are as follows:

$$\text{RBF} = -8{\cdot}09\,[H^+] + 621{\cdot}8\ (r = -0{\cdot}40;\ n = 132;\ P < 0{\cdot}001);$$
$$\text{GFR} = -0{\cdot}419\,[H^+] + 48{\cdot}2\ (r = -0{\cdot}28;\ n = 132;\ P < 0{\cdot}01)$$

DISCUSSION

The pooled results show that the mean value of the renal blood flow fell as the P_{Na} increased in the range 120–190 m-mole $l.^{-1}$. The results of individual experiments, however, indicate that the response to an acute increase in P_{Na} was time-dependent and often biphasic. On substituting a hypertonic for an isotonic saline infusion into the renal artery, there was a transient increase in the renal blood flow which was followed by a progressive fall. The reduction in flow was reversed when the infusion was switched back to isotonic saline. Changes in renal cortical blood flow followed a similar course. The infusion of hypertonic saline into the renal artery produced only a transient rise in renal cortical blood flow, followed by a progressive fall. In contrast, the rise in renal cortical blood flow produced by hypertonic dextrose was sustained throughout the period of the infusion and for 20 min thereafter. The infusion of hypertonic saline into the carotid artery always increased blood flow.

Most vascular beds respond to an increase in plasma osmolarity by sustained vasodilatation (Mellander, Johansson, Gray, Johnsson, Lundvall

& Ljung, 1967) and Fig. 3. Initially the renal cortical circulation reacts in similar fashion. But in contrast to the behaviour characteristic of other vascular beds, when the plasma osmolarity is raised by sodium chloride, the dilatation of the renal vessels appears to be overcome by a slowly developing vasoconstriction. These findings agree with those recently reported by Sadowski (1972*a*). He also proposed that the renal vascular response to an infusion of hypertonic saline is the summation of two opposite effects: a non-specific vasodilatation and a vasoconstriction characteristic for the 'normally functioning' kidney. The time-dependence of the renal vascular response could account, in part, for the conflicting reports of the effects of hypertonic saline infusion on renal blood flow (Green & Farrah, 1949; Forgács *et al.* 1969; Gatizua *et al.* 1969; Young & Rostorfer, 1973).

In the present experiments, a fall in P_{Na} produced by infusion of hypotonic saline into the renal artery led to an increase in RBF. An increase in RBF was also observed by Wilcox (1974) when he reduced P_{Na} by exchange transfusion of blood for iso-oncotic dextran in salt-free solution, or by dialysis of blood against a solution of low sodium concentration. These findings conflict with those of Gazitua *et al.* (1969) who noted a reduction in renal blood flow when P_{Na} was reduced by the infusion of hypo-osmotic solutions of saline, dextrose or urea into the renal artery. The difference might be ascribed to the rates of infusion used. Gazitua *et al.* (1969) infused the hypo-osmotic solutions at a rate equivalent to 20% of the renal blood flow whereas the rate of saline infusion in the present experiments was only about 1% of the RBF. Gazitua *et al.* (1969) observed that acetylcholine injected into the renal artery could not fully reverse the increased renal resistance produced by their infusion. This may suggest that a mechanical hindrance due to swelling of red cells or endothelial cells consequent upon the considerable fall in plasma osmolarity may have contributed to their findings. Such passive changes in resistance could easily have concealed the more subtle effects of P_{Na} itself.

The fall in both RBF and GRF, without a change in the filtration fraction observed when P_{Na} exceeded 160 m-mole $l.^{-1}$ is consistent with a rise in resistance to flow through the afferent arterioles. It is tempting to explain this by invoking the 'tubulo-glomerular-feed-back' mechanism described by Schnermann, Wright, Davis, Stackelberg & Grill (1970). These authors have shown that in micropuncture experiments in rats a nephron's GFR varied inversely with the amount of Na available for reabsorption at its macula densa segment. The explanation assumes that a rise in P_{Na} is reflected as an increase in the concentration or load of Na available for reabsorption at the macula densa region. Giebisch, Klose &

Windhager (1964) showed in micropuncture studies in rats that the ratios of tubular fluid to plasma sodium concentration, at the end of the proximal and the beginning of the distal tubule were not changed when P_{Na} was raised by infusions of hypertonic saline. A rise in P_{Na} may thus be taken to increase the Na concentration at the macula densa.

The rise in RPF but fall in GFR observed when P_{Na} was reduced below 140 m-mole l^{-1} could not be ascribed simply to a lowering of afferent arteriolar resistance and additional mechanisms must be considered. A divergence of the GFR from the RPF might theoretically be caused either by a reduction in the mean glomerular hydrostatic permeability, or in the net filtering force.

Although there is no direct evidence that glomerular permeability is reduced at low levels of P_{Na}, it is conceivable that there is an alteration of the geometry of the glomerula structures, caused by changes in plasma osmolarity. Recently an alteration in glomerular permeability has been invoked by Blantz, Rector & Seldin (1974) to account for some of the rise in GFR provoked by an infusion of hyperoncotic albumin solution in rats.

A fall in net filtering force at low levels of P_{Na} would be anticipated if the observed fall in renal vascular resistance were predominantly post-glomerular. However, any fall in efferent arteriolar tone is hard to reconcile with the paucity of smooth muscle fibres seen in the walls of the majority of efferent renal vessels (*vide* Nashat, 1974). This does not exclude the possibility that a fall in mean efferent arteriolar resistance could have been achieved by a redistribution of the blood flow to nephrons with intrinsically low levels of post-glomerular vascular resistance. Alternatively, a fall in net filtering force could be explained if there were a rise in intratubular pressure. But at this level of P_{Na} the tubular reabsorption of Na was maximal and the urine volume slight (Wilcox, 1974; Nashat *et al.* 1976); a rise in intratubular pressure is thus unlikely. Finally, a fall in net filtering force could be explained if the plasma oncotic pressure had risen. But there were no significant changes ($P > 0{\cdot}1$) in PS at this level of P_{Na}, indicating that the plasma protein concentration had not changed. Thus present evidence does not allow a clear explanation for the divergence between GFR and RPF seen at low levels of P_{Na}.

Nashat *et al.* (1976) have reported that an infusion of hypertonic saline not only raises P_{Na} but also provokes a fall in PCV and PS and a rise in $[H^+]$ and P_K. In this study RBF and GFR were found to depend upon PS and $[H^+]$. A possible role of these two variables in mediating the renal vascular responses that follow a rise in P_{Na}, must therefore be considered. Fig. 6 clearly relates RBF to the concentration of PS but also shows RBF to be the unique function of PS even when P_{Na} varies. This latter finding

makes it impossible to isolate an action of P_{Na} on RBF which could not be accounted for by the changes that it provokes in PS. Thus the fall in RBF shown in Fig. 5 at high levels of P_{Na} might, in fact, be due to the observed fall in PS. If P_{Na} were exerting an independent influence on RBF the relationship between RBF and PS would have been expected to be separate at the two levels of P_{Na}. Overall, the GFR was also dependent on PS. The data, however, were not sufficient to define significant relations between GFR and PS at different levels of P_{Na} and could not therefore be analysed further. The fact that both GFR and RBF are related to PS within a wide range suggests that the concentration of PS preferentially influences afferent arteriolar resistance. The 'tubulo-glomerular feed-back hypothesis' could explain a link between afferent arteriolar tone and the concentration of PS. The plasma protein concentration of peritubular capillary blood is held to modulate proximal tubular Na reabsorption (Windhager, Lewy & Spitzer, 1969) and might thus determine the load of sodium available for reabsorption at the macula densa segment. Failure of the GFR to rise with the RBF at the highest level of PS may simply indicate that the rise in colloid osmotic pressure within the glomerular capillaries has exceeded any effect plasma proteins exert on GFR by afferent arteriolar dilatation.

These observations are consonant with earlier findings which could be interpreted as showing that RBF increases progressively with PS while GFR increases only to a limiting value. Thus the infusion of hyperoncotic albumin or dextran was found to increase RBF in the normal man and dog but to have inconsistent effects on GFR (Cargill, 1948; Barker, Clark, Crosley & Cummins, 1949; Elpers & Selkurt, 1963; Navar, Baer, Wallace & McDaniel, 1971). Low levels of plasma proteins and reduced rates of RBF and GFR have often been recorded in patients with cirrhosis of the liver, nephrotic syndrome or malnutrition (Epstein, Berk, Hollenberg, Adams, Chalmers, Abrams & Merrill, 1970; Klahr & Alleyne, 1973). In such patients an infusion of hyperoncotic albumin was reported to restore RBF and GFR (Eder, Chinard, Greil, Cotzias, Hiller, Van Slyke & Lauson, 1948; Patek, Mankin, Colcher, Howell & Earle, 1948). In the present experiments the concentration of plasma solids varied directly with PCV ($r = 0{\cdot}3$, $n = 541$; $P < 0{\cdot}001$), suggesting that the variations in PS in these circumstances indicate converse changes in blood volume. The relation between blood volume and plasma protein concentration in these experiments was presumably the opposite of that occurring when protein was added to or lost from the circulation. Yet in both circumstances RBF and GFR depended on the concentration of plasma proteins. This appears to relate the renal response to the concentration of plasma proteins rather than to the blood volume. The dependence of RBF on the plasma protein

concentration observed in the totally isolated perfused kidney supports this contention (Nizet, 1968; Little & Cohen, 1974).

The association of a metabolic acidosis with high levels of plasma Na has been discussed previously (Nashat *et al.* 1976). The substantial fall in both RBF and GFR with increasing plasma hydrogen ion concentration is an interesting finding but one for which no clear explanation can be offered at present. Hydrogen ions have not only highly complex and often contradictory actions on resistance to flow through different vessels (Friedman & Friedman, 1963) but also profound influences on tubular function (Sartorius, Roemmelt & Pitts, 1949).

The fall in GFR observed at high levels of P_{Na} might be held to limit sodium excretion and thus to contravene the kidney's acknowledged role in homoeostasis. However, at high P_{Na}, Na excretion was no longer dependent on GFR and a substantial increase in $U_{Na}V$ occurred despite the fall in GFR (Nashat *et al.* 1976). These facts testify to the overriding importance of changes in sodium reabsorption in this condition. It is conceivable that the increased renal vascular resistance, despite reducing the GFR, can still contribute to the natriuresis. Windhager *et al.* (1969) found that a reduction in renal plasma flow limits reabsorption in the proximal tubule of a single nephron. Analysis of our data shows a clear dependence of fractional reabsorption of Na on renal blood flow even before P_{Na} is altered ($r = 0{\cdot}42$; $n = 61$; $P < 0{\cdot}001$). Whether the reduced blood flow during hypernatraemia is the cause or the consequence of reduced sodium reabsorption remains an intriguing speculation.

The authors wish to thank Dr N. N. Kady for much valuable help and Mr F. R. Scholefield for expert technical assistance. This work was supported in part by an M.R.C. grant to F. S. Nashat.

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