Influence of angiotensin II, ouabain and hydrostatic pressure on inulin and electrolyte concentration of fluid perfusing pig carotid arteries in vitro

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Summary

1. Angiotensin II was infused into isolated, perfused pig carotid arteries. The perfusate leaving the arteries was sampled into an Auto-analyzer system which continuously monitored its composition. Arterial pressure was recorded.

2. Low, subpressor doses of angiotensin II raised the perfusate potassium concentration, whereas high doses, which produced contraction, lowered perfusate potassium and sodium concentrations. Inulin and chloride concentrations did not change.

3. The elevation of perfusate potassium with low angiotensin II dosage was appreciable compared with that caused by high doses of ouabain.

4. Neurotransmitter blockade did not alter the low- and high-dose angiotensin II effects. In other sequential dose studies, valine5-angiotensin II and isoleucine5-angiotensin II did not differ in their effects on perfusate composition or arterial contraction.

5. Mechanically increased hydrostatic pressure lowered perfusate sodium concentration, so that increased arterial pressure might have contributed to this aspect of high-dose angiotensin II effects.

6. These effects of angiotensin II might have physiological significance in relation to arterial smooth muscle and to electrolyte homeostasis.

Key words: angiotensin, Auto-analyzer methods, carotid artery, hydrostatic pressure, ouabain, potassium, sodium, vascular smooth muscle.

Introduction

It has gradually been appreciated over the past decade that the pressor hormone angiotensin II, in addition to its indirect effect on electrolyte transport through aldosterone release (Kaplan & Bartter, 1962), is capable of a direct influence on Na+, water and possibly K+ transport in various biological tissues (Davies, Munday & Parsons, 1970; Leyssac, Østergaard-Christensen, Christiansen & Frederiksen, 1974; Healy & Elliott, 1976; Healy, Fraser & Young, 1976). These observations suggest that angiotensin II may help regulate electrolyte and water homeostasis.

Another site of action of angiotensin II upon electrolyte (Na+ and K+) transport which could be important might be the vascular tree. This possibility was previously suggested because of changes induced in arterial plasma electrolyte concentrations by angiotensin II (Healy, Elliott & Harrison, 1974). A number of vasoactive substances can affect Na+, K+ or water movement into or out of arteries (Muirhead, Goth & Jones, 1954; Edwards, 1977), including angiotensin II (Jamieson & Freidman, 1961; Friedman & Allardyce, 1962; Friedman & Friedman, 1964; Rorive, Hagemeijer & Schoffeniels, 1967; Türrker, Page & Khairallah, 1967; Guignard & Friedman, 1971; Jones, 1973), but no consistent pattern of the effects of angiotensin II has emerged. Further, with one exception (Jones, 1973), in all previous reports angiotensin II was used only in quantities very much greater than its physiological blood concentrations.

Our purpose therefore was to examine the effects of a wide range of doses of angiotensin II on the Na+, K+, Cl⁻ and inulin concentrations of fluid
perfusing an isolated artery. The results were compared with those produced by ouabain or increased hydrostatic pressure. Pig carotid arteries were employed and the perfusate composition was continuously monitored by a sensitive Auto-analyzer system.

**Methods**

15–20 min after pigs were killed by stunning and exsanguination at an abattoir carotid arteries were collected into the physiological perfusion medium (composition given below) at pH 7.4 and at 2–3°C. Arteries were used the same day, or refrigerated at 2°C and used within 48 h. Before use of the artery the adventitia was removed by gentle dissection in cold medium.

In preliminary studies, the Na+, K+ and water contents of the arteries were determined (a) cold, after overnight storage at 2°C, and (b) after 3 h perfusion with medium at 37°C and 60 mmHg pressure in medium in a perfusion box (see below). The procedure of Jones, Feigl & Peterson (1964) was used for tissue analysis.

**Studies on perfusate composition**

Carotid arteries (mean length 68 ± 3 mm, mean weight 1.6 ± SEM 0.1 g) were incubated in a perfusion box for 2 h in medium and for a further 1 h in mineral oil at 37°C and at 60 mmHg pressure before experiments. The arteries then remained in oil throughout the experiments. The perfusion box consisted of an inner artery chamber surrounded by an outer box through which warm water was circulated. Pressure in the artery was recorded electronically from an SE Laboratories transducer connected to the arterial inflow tube. The main supply of medium, kept at 37°C, was bubbled with O2 + CO2 (95:5). The perfusate flow rate was 0.29 ml/min, made up of 0.20 ml/min provided by an Auto-analyzer pump from the main supply of medium, and 0.09 ml/min from a separate roller pump (Ismatec) used to supply drugs dissolved in medium as required during experiments (Fig. 1). Regular testing before each experiment of all drug and control solutions used in the side infusion revealed no differences in their inulin, Na+, Cl− or K+ concentrations.

About 60 mmHg pressure was achieved in the arteries by the use of 10–15 cm of fine-bore Auto-analyzer pump tubing connected to the arterial outflow. This tube led to a T-piece, from which 0.23 ml of the fluid emerging/min was continuously sampled into an Auto-analyzer system, the remaining 0-06 ml/min running to waste.

The sample stream was diluted with Li2SO4 solution and passed to a dual-channel flame photometer for continuous Na+ and K+ readings. The residual stream not used in flame photometry was separated from bubbles and divided into two (Fig. 1), one part passing to a second Auto-analyzer pump for inulin determination by a diphenylamine procedure (Walser, Davidson & Oroff, 1953) and the other part passing to a third Auto-analyzer pump for Cl− estimation by a mercuric thiocyanate/ferric nitrate method (Technicon, 1963). The colours developed in inulin and Cl− determination methods were read in flow cells in separate spectrophotometers. All readings were

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**Fig. 1. Flow diagram for the artery perfusion and the Auto-analyzer system.** Perfusion medium at 37°C, gassed with O2 + CO2 (95:5) (lower right), is pumped to the artery in the perfusion box, a separate side infusion for drug administration joining it. Resistance on arterial outflow is achieved with fine-bore tubing. The perfusate passes to pump 1, is diluted with Li2SO4 solution, and fed to a dual-channel Na+/K+ flame photometer (EEL240). The residual stream passes to pumps 2 and 3 and subsequently to spectrophotometers for inulin and Cl− analysis. Arterial pressure is recorded with the aid of a transducer. Pumps 1–3 are Technicon Mk.I Auto-analyzer pumps. The side infusion pump is an Ismatec roller pump.
continuously charted by electronic recorders. Time delays in the system were corrected for in the analysis. All four substances were not always measured, partly because inulin and Cl\(^-\) were omitted in earlier studies and partly because of analysis.

The perfusion medium saline used throughout contained (mmol/l): Na\(^+\), 145; Cl\(^-\), 136; K\(^+\), 5-8; H\(_2\)PO\(_4\), 1-2; SO\(_4\)^{2-}, 1-2; HCO\(_3\), 25; Mg\(^{2+}\), 1-2; Ca\(^{2+}\), 1-6; glucose, 5-5; 1 g of inulin/100 ml was added. The following groups of experiments (A-F) were performed.

**Control group A.** Control studies were carried out over 40 min without drugs in 12 arteries, the number of estimations of each substance appearing in the Results section. Nine more control studies over 60 min were also done, in all of which the four perfusate components and arterial pressure were monitored as a basis of comparison for 60 min studies.

**Effect of ouabain (group B).** This was used as a test substance, which might influence perfusate K\(^+\) content by causing arterial K\(^+\) loss (Friedman & Friedman, 1974). Perfusate Na\(^+\) and K\(^+\) concentrations and arterial pressure were followed in 40 min experiments, ouabain being given from minute 13 to minute 21 in a dose at the artery of 10\(^{-6}\) mol/l (seven arteries) and 10\(^{-3}\) mol/l (six other arteries). Perfusate inulin concentrations were monitored in four additional arteries treated with 10\(^{-3}\) mol of ouabain/l.

**Effect of angiotensin II (group C).** In 40 min experiments valine\(^5\)-angiotensin II amide (Hypertensin, Ciba) was given for 8 min from minutes 13 to 21 in doses of 10\(^{-11}\) mol/l (14 arteries), 10\(^{-7}\) mol/l (11 arteries) and 10\(^{-5}\) mol/l (12 arteries). The numbers of experiments in which various components of the medium could be followed are shown in the Results section.

**Effect of valine\(^5\)-angiotensin II with neurotransmitter blockade (group D).** To exclude possible mediation of the results with group C by neurotransmitters derived from residual nervous tissue in the artery walls, further 40 min studies were done in which 10\(^{-4}\) mol of dibenzyline/l, 10\(^{-4}\) mol of propranolol/l and 10\(^{-5}\) mol of atropine/l were infused in medium for 15 min before and without interruption throughout the experiments. Valine\(^5\)-angiotensin II was infused from minutes 13 to 21 as before in doses of either 10\(^{-11}\) (n = 6) or 10\(^{-5}\) (n = 6) mol/l. Perfusate Na\(^+\), K\(^+\) and inulin concentrations and arterial pressure were successfully monitored in all studies.

**Effect of isoleucine\(^5\)-angiotensin II: sequential dose studies (group E).** Circulating angiotensin II in pigs is isoleucine\(^5\)-angiotensin II (Riniker, 1964), but this was not used throughout because of expense. Some was used to see if its action differed from that of valine\(^5\)-angiotensin II. The two forms of angiotensin II were compared in sequential dose studies, in which, after a 15 min control period, 10\(^{-12}\), 10\(^{-11}\), 10\(^{-9}\), 10\(^{-7}\), 10\(^{-5}\) and 10\(^{-4}\) mol of angiotensin II/l doses were given successively for 5 min each. Ten studies were done with valine\(^5\)-angiotensin II and 12 with isoleucine\(^5\)-angiotensin II (Calbiochem). Perfusate inulin, Na\(^+\), K\(^+\) and Cl\(^-\) concentrations and arterial pressure were successfully followed in all studies.

**Effect of passive stretch (group F).** Because angiotensin II sometimes increased arterial pressure, 40 min studies were also done to determine if a rise in hydrostatic pressure *per se* could affect perfusate composition. For these, arterial pressure was raised by partial clamping of perfusate outflow from minutes 13 to 21, corresponding to the time of angiotensin II pressor responses. Fourteen studies were done in eight arteries, the number of measurements of the components of the medium being shown in the Results section.

**Calculation of results**

A line was drawn on the chart joining standard readings at the start and finish of the recordings. A line parallel to this was drawn through the reading of the substance in question, results being estimated then at intervals of 2 min 40 s, or of 1 min in sequential dose studies. Results were expressed as positive or negative changes (or zero) about this line. In addition, the five readings in the first 11 min were regarded as controls (15 readings in 15 min in group E), and the mean of those readings was used as a final correction to all data throughout the experiments.

Standard statistical methods were used (Snedecor & Cochran, 1967), mean and SEM being calculated from the charts at the intervals referred to above. In the control groups, significant changes from zero were sought by *t*-test. In treated groups, meaningful differences were sought by comparing the average results from minutes 19 to 40 (or 60) in experiments with the corresponding average control result over that period. The data were analysed by *t*-test, or where variance ratios differed significantly (group B) by Wilcoxon's signed rank test. Further confirmation of changes in treated groups was sought over the time periods referred to above.
by comparison of the number of positive, zero and negative results in treated groups compared with controls, for which Bartholomew’s modification of the $\chi^2$-test was used (Bartholomew, 1959).

**Results**

**Artery composition (Table 1)**

Warming the arteries to $37^\circ$C caused a significant loss of Na$^+$ and gain in K$. As previous data on pig carotid arteries were not available, the composition of dog carotid artery (Jones et al., 1964) is shown in Table 1 for comparison.

**Studies on perfusate composition**

The system of auto-analysis used was tested thoroughly and found stable, as indicated by the control results below. Na$^+$ concentration in the medium could be varied up to 5 mmol/l without the problem arising of interference with K$^+$ readings (Anand, Lott, Grannis & Mercier, 1973). Changes in concentration of 0.5% in the medium could readily be detected. At this value, quantification was accurate for inulin but electrolyte changes were slightly underestimated. 1–5% changes in all substances could be quantified accurately. Static and dynamic response times for readings to reach a new equilibrium, as defined by Moody & Thomas (1974), were less than 2 min for a 1% change in concentration for all four substances.

**Control groups.** The results of these are shown on Figs. 2–5 as shaded areas, which embrace ±SEM about the mean values. No significant changes occurred in perfusate composition or arterial pressure. Absolute mean initial arterial pressure was $64 \pm 2$ and $66 \pm 3$ mmHg in the two control series, and no mean initial pressure (range $58 \pm 2 - 64 \pm 2$ mmHg) in treated groups differed significantly from these.

**Effect of ouabain.** Both doses raised perfusate K$^+$ (Fig. 2), the low dose by a mean (19–60 min) of $+0.032 \pm 0.005$ mmol/l, the high dose by $+0.094 \pm 0.006$ mmol/l. Both increments were significant ($P < 0.001$ on Wilcoxon’s and modified $\chi^2$-tests) and differed significantly from each other ($P < 0.001$). Perfusate Na$^+$ did not change significantly with either of the ouabain doses, nor did inulin concentration in the additional high-dose studies. Both doses were pressor, the high dose in a biphasic manner (Fig. 2).

**Effect of valine$^5$-angiotensin II.** With valine$^5$-angiotensin II at $10^{-11}$ mol/l (Fig. 3, Table 2) the...
Effect of angiotensin on perfused artery electrolytes

Effect of ouabain for 8 min

**FIG. 2.** Effect of two doses of ouabain (—, 10^-6 mol/l, n = 7; —, 10^-3 mol/l, n = 6) infused from minute 13 to minute 21 on changes in perfusate K^+ concentrations and arterial pressure. Results are shown as changes about the mean control values, represented as 0. The hatched areas indicated ±SEM about the mean values of data from control studies. Results were calculated at 2 min 40 s intervals. Vertical bars on results from ouabain-treated arteries are ±SEM. A dose-responsive rise in perfusate K^+ concentration occurred. Both doses contracted the arteries, the higher dose causing a two-phase contraction.

Only change induced was a small but significant rise in perfusate K^+, confirmed by modified χ^2-test (P < 0.001).

With valine^5^-angiotensin II at 10^-7 mol/l (Table 2) perfusate K^+ rose in eight of the 11 studies, sometimes considerably (to +0.16 mmol/l) in the period after angiotensin II, but in the other three studies it fell. Mean K^+ concentration nevertheless rose significantly, but not significantly more than with 10^-11 mol of angiotensin II/l. Perfusate Na^+ did not change significantly. Pressor responses occurred only in the three studies in which perfusate K^+ decreased.

With valine^5^-angiotensin II at 10^-5 mol/l (Fig. 4, Table 2) the falls in perfusate K^+ and Na^+ seen were confirmed by modified χ^2-test (P < 0.001 and <0.010 respectively). No significant changes occurred in perfusate Cl^- or inulin concentrations. All arteries contracted.

**Effect of valine^5^-angiotensin II with neurotransmitter blockade.** Nervous blockade alone did not affect perfusate composition or pressure over a 40 min period. The pattern of responses to low and high doses of angiotensin II was the same as that seen in the absence of nervous blockade, and no significant differences could be shown in the mean perfusate K^+ or Na^+ changes or in pressor responses at any of the angiotensin II doses from the results of the preceding section. Again perfusate concentrations followed infusion of angiotensin II.
inulin and Cl\(^-\) concentrations did not change significantly. Modified \(\chi^2\)-tests confirmed the perfusate Na\(^+\) and K\(^+\) changes (\(P < 0.001\)-<0.001), except for the rise in perfusate K\(^+\) concentration with 10\(^{-11}\) mol of angiotensin II/l, which just failed to reach the 0.05 level of probability.

**Effect of isoleucine\(^5\)-angiotensin II: sequential dose studies.** Neither form of angiotensin II significantly affected perfusate inulin, Na\(^+\) or Cl\(^-\) concentrations in these studies, although perfusate Na\(^+\) concentration did decline in the final 15 min. However, both forms of angiotensin II raised perfusate K\(^+\) concentration by a small amount in a similar pattern over the period of their infusion (Fig. 5). Mean changes in K\(^+\) concentrations during the actual 30 min of infusion of angiotensin II were +0.017 ± 0.002 and +0.020 ± 0.002 mmol/l for valine\(^5\) and isoleucine\(^5\)-angiotensin II respectively, not significantly different from each other, but each significantly (\(P < 0.001\)) elevated above mean control value (+0.001 ± 0.002 mmol/l) with modified \(\chi^2\)-test confirmation (both \(P < 0.001\)). After 10\(^{-4}\) mol of angiotensin II/l, perfusate K\(^+\) fell promptly (Fig. 5). The pressor responses were not significantly different for the two forms of angiotensin II.

**Passive stretch (Table 2).** The only change induced in perfusate composition was a small fall in Na\(^+\) concentration, a finding confirmed by modified \(\chi^2\)-test (\(P < 0.020\)).

**Discussion**

These studies revealed that brief exposure to a low 'physiological' dose (10\(^{-11}\) mol/l) of angiotensin II induced a rise in K\(^+\) concentration in fluid perfusing isolated pig carotid arteries. This effect was still seen with a dose of 10\(^{-7}\) mol/l. Very large doses of angiotensin II (10\(^{-5}\) mol/l) decreased perfusate K\(^+\) and Na\(^+\) concentrations and regularly contracted the arteries. Per fusate inulin and Cl\(^-\) concentrations did not change at any angiotensin II dose, the constancy of the former suggesting that angiotensin did not induce water shifts. Neurotransmitters did not mediate the effects of angiotensin II, but the hydrostatic pressure increase at doses of angiotensin II causing contraction may have contributed to the fall in perfusate Na\(^+\) concentration, as passive stretch also had this effect. Isoleucine\(^5\) and valine\(^5\)-angiotensin II did not differ in their effects on perfusate or pressure.

Ouabain also increased perfusate K\(^+\) concentration, but in a dose-dependent manner. It did not measurably affect perfusate Na\(^+\), probably because it inhibits Na\(^+\)/K\(^+\) exchange on a 1:1 basis in arteries (Friedman & Friedman, 1974),

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**Table 2. Effect of valine\(^5\)-angiotensin II and passive stretch on composition of pig carotid artery perfusate and pressure**

Mean changes ± SEM for inulin, Na\(^+\), Cl\(^-\) and K\(^+\) concentrations in perfusate from minute 19 to minute 40 of 40 min experiments, i.e. over the period in which an intervention may have had an effect. Also shown are mean changes ± SEM in intra-arterial pressure which occurred during the intervention (angiotensin or passive stretch) between minutes 13 and 21. 'Nerve blocked' refers to adrenergic and cholinergic blockade during experiments. Changes marked with an asterisk were significantly different from mean control results on \(t\)-test, all significant changes lying within the range \(P < 0.010\)-<0.001. Numbers of experiments are shown in parentheses: each experiment was in a different artery except in the passive stretch group (F), in which eight arteries were used for all experiments.
Effect of angiotensin on perfused artery electrolytes

Effect of an angiotensin on perfused artery electrolytes. The same conventions are followed in this Figure as in Fig. 3. This dose of valine-angiotensin II lowered perfusate Na\(^+\) and K\(^+\) concentrations and caused a pressor response.

Fig. 4. Effect of 10\(^{-4}\) mol/l doses of valine-angiotensin II (---, \(n = 10\)) and isoleucine-angiotensin II (----, \(n = 12\)) on perfusate K\(^+\) concentration and arterial pressure. Conventions used in Fig. 3 are followed, except that charts were read at 1 min intervals. Top: the similarity of effects of both forms of angiotensin II on perfusate K\(^+\) concentration is shown. Middle: mean values from the combined data for K\(^+\) (---, \(n = 22\)) with ±SEM shown as vertical bars at 2 min intervals. Bottom: 1 SEM above or below the mean data line for pressure tracings is shown by vertical bars at 1 min intervals. Both forms of angiotensin II raised perfusate K\(^+\) concentration in low doses, but this was followed by a fall to control values after high doses. Similar pressor responses occurred with both forms of angiotensin II.

which would make perfusate Na\(^+\) concentration changes too small to detect. The pressor response to ouabain was expected (Friedman, Nakashima, Palatý & Walters, 1973), but its biphasic nature with the higher dose could not be explained.

The pig carotid artery was used because it required minimal handling and contained a relatively large amount of smooth muscle. Viability was indicated by the reasonable correlation in its warm composition with that of fresh dog carotid arteries (Jones et al., 1964), by the capacity to extrude Na\(^+\) and gain K\(^+\) during warming, the reversibility of that process for K\(^+\) by ouabain, and by pressor responses to vasoactive drugs, responses which for 10\(^{-4}\) mol of angiotensin II/l were undiminished up to 72 h storage (J. K. Healy, A. J. Elliott & I. J. Owczkin, unpublished observations). Other evidence of viability of similarly collected pig carotid arteries has been reported (Herlihy & Murphy, 1973).

It would have been desirable to have had more experiments with complete data, but the com-
plexity of the multiple Auto-analyzer system did not permit recommencement of the 10 h studies if a fault developed in one component. Nevertheless, in group D all data were available, which permitted assessment of directions of electrolyte flux with more confidence than for pooled data. It could be concluded from group D that $10^{-11}$ mol of angiotensin II/l caused net K$^+$ efflux from the arteries and that $10^{-5}$ mol/l caused net K$^+$ and Na$^+$ influx into the arteries, as inulin concentrations were unchanged. Support at least for induction of net K$^+$ efflux by lower doses of angiotensin II was derived also from the sequential dose studies, in which all experimental data were complete.

The accumulated data in Figs. 3 and 4 (group C) help to establish the results of the smaller group D. The precise timing of the rise in perfusate K$^+$ concentration after $10^{-11}$ mol of angiotensin II/l varied by some minutes in the different series. These differences may be within the limits of biological variation. Once established, the rise in perfusate K$^+$ lasted some 20 min.

The differences in timing in the sequential dose studies make comparison with other groups difficult. However, lower angiotensin II doses again caused net K$^+$ efflux. Per fusate Na$^+$ and K$^+$ may not have fallen below control values after high angiotensin II doses because of the effects of earlier doses, or because the studies then ended within 15 min.

Normal plasma angiotensin II concentrations in pigs are not available, but in other species values of $10^{-11}$ mol/l have been reported (McDonald, Louis, Renzin, Boyd & Peart, 1970; Boyd & Peart, 1974). It is therefore possible that the present data have physiological relevance. Although the rise in perfusate K$^+$ concentration after $10^{-11}$ mol of angiotensin II/l seemed small, it was about a quarter of that produced by a huge dose of ouabain, a potent inhibitor of K$^+$ influx. This suggests that the net K$^+$ loss induced by angiotensin II may not be unimportant, especially if it is a widespread effect in arterial smooth muscle.

The cellular mechanism of effect of angiotensin II on K$^+$ movement is difficult to conceive. It could involve effects on Na$^+,K^+$-activated ATPase, but angiotensin II does not affect this enzyme in other tissues (Bonting, Canady & Hawkins, 1964). It could affect K$^+$ movement indirectly by influencing a Na$^+$-Ca$^{2+}$ exchange pump in the artery wall (Bohr, Seidel & Sobieski, 1969) or it could affect the K$^+$ permeability of the smooth muscle cell. Any proposed effect must somehow be reversible with high dosage. An effect of angiotensin II on K$^+$ transfer is nevertheless not unique as it stimulates distal renal tubular K$^+$ secretion (Healy & Elliott, 1976).

The opposite effect of high doses of angiotensin II on K$^+$ movement may have been linked with the contraction that occurred. However, K$^+$ influx is not a regular feature of smooth muscle contraction (Headings & Rondell, 1962), so that the reversal may relate simply to dosage, just as the effects of angiotensin II on electrolyte transport in other tissues may reverse in a dose-dependent fashion (Davies et al., 1970). Increased hydrostatic pressure did not explain the fall in perfusate K$^+$ concentration with pressor doses of angiotensin II, as it did not do this in passive stretch studies. This contrasts with a previous report (Guignard & Friedman, 1970). Differences in species and arteries may account for this.

Unlike K$^+$ (Headings, Rondell & Bohr, 1960), much of the Na$^+$ in artery walls lies extracellularly, both free, and bound in the paracellular matrix by mucopolysaccharides (Jones & Swain, 1972), so that the changes seen in perfusate Na$^+$ concentration with high angiotensin II dosage cannot be directly related to smooth muscle cells or their contraction. The failure of perfusate Cl$^-$ to fall may suggest that Na$^+$ moved into anionic binding sites in the paracellular matrix, a process not in need of a concurrent Cl$^-$ shift. Hydrostatic pressure could also have contributed to this process.

Previous studies have produced conflicting reports. Three technical approaches have been employed: (i) assessment of arterial composition after exposure to angiotensin II; (ii) radioisotope studies; (iii) study of Na$^+$ and K$^+$ content (but not of water) of arterial perfusates, as in the present work. From (i), no agreement has emerged (Friedman & Friedman, 1964; Rorive et al., 1967). From (ii), there are indications that angiotensin II might increase Na$^+$ and K$^+$ efflux from arteries (Türker et al., 1967; Rorive et al., 1967; Jones, 1973), but little information is provided on influx or net flux rates. From (iii) above, in studies of artery perfusate in the past only large doses of angiotensin II were used (lowest dose, by calculation, was $0.5 \times 10^{-6}$ mol/l: Guignard & Friedman, 1971). Possible water shifts were not assessed, and no consistent pattern of behaviour emerged (Jamieson & Friedman, 1961; Friedman & Allardyce, 1962; Guignard & Friedman, 1971).

The significance of Na$^+$ and K$^+$ exchanges between arteries and their contents may lie in (a) a possible role in the contractile process or in regulation of vascular tone, and (b) the potential
role of these exchanges in Na\(^+\) and K\(^+\) homeostasis.

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References


