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Cadaveric renal transplantation

This report documents the experience at the University of Melbourne with cadaveric transplantation since 1965. Twenty-six grafts were performed in 24 patients. All individuals were prepared with hemodialysis utilizing the Kiil kidney or by repeated peritoneal dialysis. Donors and recipients were matched only in respect of major blood groups. The immunosuppressive regimen used from the time of grafting included: (1) Azathioprine, 3mg/kg daily, this being reduced when renal function was poor; (2) Prednisolone, 100 mg daily for the first week, reduced to 60 mg daily over the next week and then to approximately 20 mg/day at three months and to approximately 10 mg daily at six months; (3) Local radiation of the graft during the first week. Episodes of rejection were treated with: (1) Increase of prednisolone to 300 mg on the first day, 200 on the second day, and 100 on the third day, and thereafter rapid reduction to a slightly higher level than that at which rejection occurred; (2) Irradiation to the transplant; (3) Actinomycin C in a dose of 200 µg intravenously daily for 1 to 3 days. In all but two of the 26 transplants urinary flow began immediately. Twenty out of 24 patients who received a cadaveric renal transplant over the two years included in this study have had satisfactory renal function in the grafted kidney. None of the 20 living patients received more than the 1 graft. Stable renal function has been maintained in five of seven patients who received the graft over a year ago, and in 11 of 14 patients who received the graft over six months ago. It is felt by the authors that this experience would indicate that cadaveric renal transplantation offers a more practical solution to the treatment of chronic renal failure than recurrent hemodialysis.

Author’s address: Dr. Priscilla Kincaid-Smith, University of Melbourne, Royal Melbourne Hospital, Melbourne (Australia).

Chronic hemodialysis in ‘unselected’ patients

Patients were selected on a ‘first come, first served’ basis for a municipally supported chronic hemodialysis program. Liberal criteria governing patient selection were established. Only eight of thirty-four candidates were rejected. Twenty-six patients, five of whom had been rejected from chronic dialysis programs elsewhere, were dialyzed 2423 times for periods ranging from two weeks to twenty-one months, or a total of 267 patient months. Eight patients expired from two weeks to sixteen months following the inception of dialysis. Ten patients returned to work, school, or housekeeping. The mean IQ in twenty-five patients tested was 92. The survival time for arterial and venous cannulae was 4.8 and 4.5 months respectively. Hypertension, initially present in all, was reversed in each instance, although four patients required bilateral nephrectomy. It is concluded that hemo-
dialysis may be successful employed in a municipal hospital and that some patients who superficially appear to be poor candidates may be completely rehabilitated when presented with the opportunity.

Author’s address: Dr. Eugene Schupak, City Hospital at Elmhurst, New York, N.Y. (USA).

Changes in glucose and insulin metabolism induced by dialysis in patients with chronic uremia


The effect of repeated hemodialysis on glucose metabolism was studied in 10 patients with severe uremia. Carbohydrate metabolism was evaluated with determinations of blood glucose and immunoreactive insulin during the first dialysis and again in a subsequent one. Dialysis was performed using 1500 mg/100 ml of glucose in the dialysate in both study periods. Improvement in carbohydrate metabolism was demonstrated in the second period by a lower mean glucose level during dialysis and by more rapid disappearance rates of glucose immediately post-dialysis. This improvement in carbohydrate metabolism was associated with an increase in both mean and maximum insulin levels in 8 of the 10 patients. This increase in serum insulin in response to hyperglycemic stimulation during the second study suggests the removal of a substance by dialysis that either inhibits insulin release or increases insulin degradation.

Author’s address: Dr. Allen C. Alfrey, Department of Medicine, University of Colorado, School of Medicine, Denver, Col. (USA).

Amino acid loss in peritoneal dialysis


The type and amount of amino acids present in the dialysate of 8 peritoneal dialyses performed in seven patients are reported. 4.9 g of amino acids were found per 27.25 l exchanged. Twenty amino acids were individually identified, and the amount of each was quantitated. All the essential amino acids measurable by this technique were present. The amino acid loss was related to the volume of dialysate exchanged and also to the protein content. The authors feel that the amount of amino acid and protein loss during dialysis are significant and should be replaced. They recommend from quantitative calculations as to the amount of amino acid and protein lost per dialysis found in this study or reported in the literature that patients receive a high protein intake during dialysis corresponding to five whole eggs. This is preferably given when the dialysis has been terminated or its equivalent by parenteral plasma or amino acid solution.

Author’s address: Dr. G. M. Berlyne, Department of Medicine, Royal Infirmary, Manchester 13 (England).

Extracellular volume in patients with chronic renal disease treated for hypertension by sodium restriction


Extracellular volume and exchangeable sodium were measured using radioactive isotopes of bromine and sodium in controls (10), patients with chronic renal insufficiency (8) and in patients (6) being maintained by periodic dialysis once or twice a week. Lean body mass was calculated by a formula which incorporates body weight, height, and skin fold thickness. When the data were referred in the control group to lean body mass, there was a very close correlation and a small range for the normal values. In patients with chronic renal failure and those being maintained with the artificial kidney, it was found that hypertension was usually related to elevated values. When blood pressure control was ‘adequate’
the values for extracellular volume and exchangeable sodium were normal or slightly increased but were not decreased. It should be pointed out that the patients with chronic renal insufficiency were being maintained on a 0.5-2 g sodium diet. The implications of these findings to the management of the patient on chronic hemodialysis are considered. It is felt that blood pressure can usually be controlled if adequate sodium restriction is maintained between dialyses.

Author’s address: Dr. B. H. Scribner, Department of Medicine, University of Washington, School of Medicine, Seattle, Wash. (USA).

Peritoneal dialysis and hemodialysis of tritiated digoxin
Fourteen patients were studied while undergoing peritoneal dialysis and nine patients during hemodialysis with the twin-coil artificial kidney as to the clearance of tritiated digoxin. The peritoneal clearance rate of tritiated digoxin was found to average 8 ml/min. Utilizing the artificial kidney, the dialysance averaged 10 ml/min and in two in vitro experiments (artificial kidney) 15 ml/min. The in vitro studies also showed a comparable movement of tritiated digoxin across the dialyzing membrane whether the vehicle was serum or saline indicating that protein binding does not contribute to the limited dialysance of digoxin. These experiments indicate that the amount of digoxin removed by dialysis whether peritoneal or blood is sufficiently small that it may be ignored in choosing the digoxin dosage in the patient undergoing dialysis.

Author’s address: Dr. George L. Ackerman, Department of Medicine, University of Arkansas Medical Center, Little Rock, Arkansas 72201 (USA).

Utilisation of ammonia nitrogen for protein synthesis in man, and the effect of protein restriction and uraemia
The effect of dietary protein restriction on the incorporation of \(^{15}\)N-ammonia into body protein was studied in 8 experiments on four healthy individuals and two uremic patients. In the healthy individuals, the more severe the protein restriction, the greater the incorporation of the isotope into the plasma-albumin pool, and the smaller the recovery of the \(^{15}\)N in urine and feces. The stable uremic patients who had been protein restricted for nine months incorporated between three and five times as much ammonia nitrogen into the plasma-albumin as did two healthy individuals after three weeks on a 20 g protein intake, with a total calculated incorporation of 700 and 975 mg of ammonia nitrogen in 24 h, equivalent to about 4.5 and 6.0 g of protein respectively. Evidence is cited that ammonia is the form in which man reincorporates urea nitrogen into protein, and that this ammonia is derived from urea by bacterial breakdown in the intestine. It is suggested that the ability of uremic patients to reutilize their urea nitrogen in protein synthesis could be exploited by providing them with an artificial diet containing keto-acid analogues of the essential amino acids, but no other nitrogen except for lysine and threonine, which may not be formed in sufficient amount in the body from their keto-acid analogues.

Author’s address: Dr. Peter Richards, St. Mary’s Hospital Medical School, London W. 2 (England).

Pore equivalent radii of isolated basement membranes from the rat kidney cortex after aminonucleoside induced nephrosis
Experiments on isolated basement membranes from the cortex of the rat kidney indicated that the pore equivalent radii in the basement membranes are not equal. The borderline molecular weight for the penetration of a molecule into the normal basement membrane was found to be between 80,000 and 90,000. This indicates a maximal pore equivalent radius of 42-45 Å. The mean pore equivalent radius is $29 \pm 10$ Å (1).

The partition coefficients of Urea-$^{14}$C, Methylglucose-$^{14}$C, Inulin-$^{14}$C, Poly-vinylpyrrolidon-$^{131}$I, Serum albumin-$^{131}$I and y-Globulin-$^{131}$I were evaluated on isolated basement membranes, derived from rats with aminonucleoside nephrosis. The following observations could be made:

The partition coefficient decreases as the molecular weight of the substances increases. The borderline molecular weight for penetration into the nephrotic basement membranes is around 190,000. This corresponds to a maximal pore equivalent radius of 65 Å.

Different partition coefficients for the investigated substances can be explained, on the basis of a normal distribution of the pore equivalent radii. The mean pore equivalent radius of the nephrotic basement membrane is $36 \pm 16$ Å.

The results indicate that the pore equivalent radii of the nephrotic basement membranes are larger than those of the normal ones. It is suggested that the proteinuria of the nephrotic syndrome results from this increase in pore diameter of the nephrotic basement membranes.

Reference

The nephrotic syndrome in systemic lupus erythematosus
18 patients (17%) with severe nephrotic syndrome are described among 108 cases of systemic lupus erythematosus. All 18 were women, 12 were less than 30 years old.

The nephrotic syndrome developed at different stages of systemic lupus erythematosus; in 5 cases it was the presenting feature. Eight patients died from renal failure, 7 of them within 6 to 12 months from the onset of renal manifestations. The course of the disease in 4 patients with so-called ‘pseudonephrotic syndrome’ with a normal serum cholesterol level was not more severe than in the other patients.

Steroid therapy did not seem to be of great influence on the disease, this possibly was due partly to the late onset of steroid therapy or previous inadequate treatment. In some patients treatment with antimalarial drugs was very useful.

Authors’s address: Dr. V. V. Sura and Dr. I.E. Tareyeva, Institute of Internal Medicine, 10 Petrovskiy str., Moscow (USSR).

Influence of dietary sodium on stimuli causing renin release
Dietary sodium importantly influences release of renin stimulated by aortic constriction or infusion of norepinephrine. Dogs maintained on a low-sodium diet released renin more readily and in larger quantities in response to either stimulus than dogs on a standard kennel diet. In contrast with the correlation between renin release and dietary sodium, there was none between release of renin and the hemodynamic effects produced by norepinephrine. In dogs fed a regular
diet, intravenous infusions of sodium nitroprusside caused release of renin when the initial rate of urinary sodium excretion was low and, conversely, failed to stimulate renin release when the initial rate of sodium excretion was high. In addition to the possibility that release of renin depends on the rate of tubular sodium re-absorption, it is proposed that sodium may act by conditioning sensitivity of response of the renin releasing mechanism to change in transmural pressure at or near the afferent arteriole.

Authors’ address: Dr. R.D. Bunag, Dr. I.H. Page and Dr. J. W. McCubbin, Research Division, Cleveland Clinic Foundation, Cleveland, Ohio (USA).

A summary of observations on the effects of renal artery infusion of NaCl on renin release
By Rostorfer, H.H.

Renin was released by the kidney of the anesthetized dog in response to renal artery (Fig. 1 A) and i.v. infusion of catecholamine (Fig. 1C), but the marked response to the latter occurred only during the recovery from a 15 to 30 min i.v. noradrenaline infusion. Response to renal artery infusion begins during the second minute of infusion. Catecholamines do not appear to specifically excite a release of renin, but initiate a change in renal function which promotes the release. The response was diminished by the infusion of 1.3 mEq NaCl/min into the renal artery during renal artery infusion of noradrenaline, (Fig. 1B) or following i.v. catecholamine (Fig. 1D) in comparison to the responses when hypertonic saline was not infused (Fig. 1C). Renin release response to controlled clamping of the suprarenal aorta (Fig. 1E) was markedly reduced by the renal artery infusion of 2.6 mEq NaCl/min only if the salt infusion was initiated at least two minutes before clamping (Fig. 1F). Depression of renin release occurred in response to renal artery infusion of NaCl only when the rate of sodium excretion was markedly elevated. These results indicate sodium chloride may play a role in the control of renin secretion, perhaps at a tubular site rather than from the vascular lumen.

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10% RENAL ARTERY NORADRENALINE

Norad

NaCl + Norad

25

20

15

10

<

Di

25-20
Fig. 1. Plasma renin values expressed as ng angiotensin formed during incubation of treated plasma at 37°. Broken lines ( ) represent renal vein plasma renin (RV) and solid lines represent arterial plasma renin (FA).

(A) response to renal artery infusion of 3 µg noradrenaline per minute, (B) response to the renal artery infusion of 3 µg noradrenaline/min in 10% NaCl (1.3 mEqNaCl/min) and to 3 µg Noradrenaline, (C) response to the withdrawal of i.v. noradrenaline given at 16 ng/min, (D) response to the withdrawal of i.v. noradrenaline at 16 ng/min when 1.3 mEq NaCl/min was infused into the renal artery, (E) response to controlled suprarenal aortic clamping when 1.3 mEq NaCl was infused into the renal artery after clamping began. (F) response to aortic clamping and the effects the infusion of 2.6 mEq NaCl/min into the renal artery beginning two minutes prior to the onset of clamping.

Author’s address: Dr. Howard H. Rostorfer, Department of Physiology, Indiana University, Mvers Hall, Bloomington ind. 47401 (USA).
Serologic factors in human transplantation

This report is concerned with a retrospective correlation between leukocyte group antigens recognized by the Hu-1 immunogenetic system (considered a human equivalent of the mouse H-2 system) and the fate of 59 renal transplants obtained from related individuals. Serologic ranks of compatibility were correlated with the clinical outcome of such transplants, with particular reference to the long-term survival of renal transplants. In addition, the characterization of heterophile antibody responses associated with human allograft rejection (skin and kidney) were considered.

Unfavorable outcome (renal transplantation) occurred in 55.6% of the incompatible subjects, but in only 15.7% of the compatible recipients. Differences in transplant acceptance as shown by rejection patterns became even greater as time went on as indicated by data on 37 recipients considered 28 months after transplantation. Sixty-three and nine-tenths percents of subjects with transplants obtained from incompatible donors had rejected their grafts or were in the process of rejecting them at this time; this was true for only 8.3% of the compatible subjects. It should also be noted that 30.7% of kidneys obtained from incompatible donors retained satisfactory function at 28 months as compared to 91.7% of those taken from compatible donors.

At the end of 3 years, 7 of 21 incompatible grafts (33%), but only 3 of 38 compatible grafts (8%) had been rejected. There were increases in heterophile hemagglutinin titer in 20 of 22 kidney transplant recipients. The most impressive rises in titer were observed against rat erythrocytes and this system appeared to be the most sensitive monitor of the kidney allograft reaction in that 16 of 22 subjects had high titers (i.e. higher than for sheep or guinea pig red cells). These antibodies were identified as IgG and IgM and were not of the Forssman or Paul-Bunnell type.

The authors are careful to point out that a significant number of long-term survivors (renal allografts) showed satisfactory renal function in the face of definite leukocyte group incompatibilities. In addition, some subjects rejected renal transplants in the absence of any serologic evidence of leukocyte group incompatibility, indicating that the battery of antisera currently used was incapable of detecting all of the antigenic specificities which may condition transplant rejection in man. In spite of these shortcomings, however, the authors conclude that a statistically significant correlation exists between leukocyte group compatibility and the duration and quality of renal allograft survival in man.

Author’s address: Dr. Felix T. Rapaport, Department of Surgery, New York University Medical Center, New York, N. Y. (USA).

Micropuncture evidence indicating the lack of a direct effect of angiotensin on sodium reabsorption in the proximal convolution and loop of Henle in the rat kidney


Micropuncture experiments on the rat kidney were performed to reveal the possible influence of angiotensin upon tubular sodium reabsorption. Half-time reabsorption, as measured by the split droplet method, was constant, (9.4 ± 0.4 s) at glomerular filtration rates ranging from 0.66-1.26 ml/g kidney/min.
Elevating intratubular (25 and 250 × 10^-6 g/l00 ml) or peritubular (0.18 × 10^-6 g/kg/min) angiotensin concentration did not significantly alter the half-time reabsorption of sodium, indicating no direct effect of angiotensin upon transporting capacity of the proximal tubule for sodium.

Sodium reabsorption in Henle’s loop was studied by means of perfusing single loops with isotonic saline. From the increase in inulin concentration in the perfusate and from the sodium concentration in the early distal segment, sodium reabsorption along Henle’s loop was calculated. The relationship between perfusion rate and sodium reabsorption was found to be the same in the control experiments and during the perfusion with saline containing angiotensin at concentrations of 0.5 and 5.0 × 10^-6 g/l00 ml. These results, together with the findings that urine volume and sodium excretion in the anaesthetized rat remain unchanged during the i.v. infusion of angiotensin, indicate that angiotensin has no direct effect upon tubular transporting capacity for sodium.

Author’s address: Dr. M. Horsier, Physiologisches Institut der Universität, Pettenkoferstraße 12, München 15 (Germany).

Indirect action of angiotensin infusion to inhibit renal tubular sodium reabsorption in dogs

In conscious dogs during water diuresis intravenous infusion of lower doses of angiotensin (< 4 µg/min) caused depression of glomerular filtration rate and renal plasma flow and sodium and water retention. The effects of angiotensin on renal hemodynamics were blunted by pentobarbital anesthesia, by administration of a hypertonic urea-saline infusion, and in dogs with ascites produced by caval occlusion. With these experimental modifications, and also whenever large doses (8-50 µg/min) were employed, intravenous angiotensin induced natriuresis and diuresis with characteristics (CNa/Cosm, % or/T%o) indicative of inhibition of renal tubular sodium reabsorption. However, direct renal artery infusion of angiotensin under similar conditions did not produce a similar natriuresis. Therefore the data suggest that angiotensin does not inhibit tubular sodium transport directly, but rather as a consequence of its effects on the systemic and renal circulation. The final natriuresis may result from an induced change in intrarenal hemodynamics or from other extrarenal factors to which tubular sodium transport processes are responsive.

Author’s address: Dr. P.J. Cannon, Department of Medicine, Columbia University, New York, N.Y. (USA).

Effect of angiotensin infusion on urine concentration in man injected with A.D.H.

Diuresis was produced by infusion of glucose, sterofundin, sterofundin plus urea, or by hydrochlorothiazide in six normal volunteers and one patient with diabetes insipidus centralis. Having established an urine concentration maximal under these conditions by infusion of 30 µU/kg/min ADH (651-812 mOsm/kg/%O, DI 615 mOsm/kg/%O), additional 0.01 µg/kg/min angiotensin were infused.

Angiotensin infusion increases urine concentration distinctly above the values obtained by ADH-infusion alone (up to 774-1000 mOsm/kg/%O, DI 650 mOsm/322

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kg/lO). An increase of the interstitial osmotic concentration within the inner medulla is suggested to be responsible for this. It is concluded, that in order to obtain maximal urine concentration ADH has to be effective together with an ADH-independent change of intrarenal hemodynamics. 

In the present experimental conditions, angiotensin increases the urine concentration, and decreases urine volume, Cosin, and the urine sodium concentration. C O becomes less negative. Urinary concentrations of potassium, ammonium, urea, inuline, and PAH, however, increase. These effects of angiotensin are explained by alteration of the intrarenal hemodynamics and increased distal sodium and water reabsorption. The same changes in solute concentrations in unilateral renal artery stenosis develop in relation to the opposite kidney. It is suggested, that these concentration differences seen in the Howard test could be explained by an intrarenal angiotensin effect within the kidney with artery stenosis. Author’s address: Dr. Rolf Schroder, II. Med. Klinik und Poliklinik der Freien Universität Berlin, 1 Berlin 29, Spandauerdamm 130 (Germany).

Neural stimulation of release of renin
By Bunag, R.D.; Page, I.H. and McCubbin, J. W.: Circ. Res. 19: 851-858 (1966). Increased vasomotor discharge induced by bleeding caused renal release of renin in anesthetized dogs whether or not there was measurable change in either arterial pressure or total renal blood flow. Release of renin was prevented by ganglion blockade or local anaesthesia of the renal nerves. Hemorrhage-induced release of renin occurred more consistently in dogs fed a low-sodium diet than in those fed a standard kennel diet. Stimulation of sympathetic vasomotor discharge by occlusion of the common carotid arteries, while renal perfusion pressure was kept constant, also caused release of renin, as did infusions of norepinephrine, tyramine, or DMPP. Isoproterenol, angiotensin, vasopressin, serotonin, or acetylcholine infused into the renal artery did not cause release of renin. It is concluded that neural stimuli are capable of causing release of renin in the absence of gross change in renal perfusion pressure or flow. Authors’ address: Dr. R. D. Bunag, Dr. I.H. Page, and Dr. J. W. McCubbin, Research Division, Cleveland Clinic Foundation, Cleveland, Ohio (USA).

Effect of alterations in plasma osmolality on renal blood flow autoregulation
By Navar, L. G.; Guyton, A.C. and Langston, J.B.: Amer. J. Physiol. 211: 1387-1392 (1966). Experiments were conducted on anesthetized dogs to investigate the acute effects on renal blood flow and renal autoregulation caused by intravenous infusions of hypertonic solutions of sodium chloride, mannitol, glucose, and urea. An electromagnetic flowmeter was used for the measurement of left renal blood flow. Renal perfusion pressure, measured directly from the renal artery, was altered with a plastic clamp placed on the renal artery distal to the flow probe. Control pressure-flow relationships demonstrated typical autoregulation, and the control renal blood flow recovery patterns obtained following a 1 min occlusion of the renal artery exhibited a large initial overshoot and subsequent oscillation in the process of returning to the preocclusion level. Increases in plasma osmolality of less than 20% following infusions of osmotically active agents such as NaCl, mannitol, or glucose caused elevation of the autoregulatory plateau, though with somewhat less perfect regulation; but the oscillatory behavior in the recovery pattern was maintained or slightly accentuated. Greater increases in plasma osmolality were associated with progressive increases in the steady-state blood flows up to as much as 100% above control values. Under these
circumstances, the pressure-flow curves became passive in appearance, and the oscillatory behavior of the recovery patterns was largely abolished.

Author’s address: Dr. L. Gabriel Navar, Instructor in Physiology, Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, Miss. 39216 (USA).

Magnesium depletion in normal man
Two normal subjects were depleted of magnesium for 39 and 49 days, respectively, by means of a diet low in magnesium (1-2.5 mmoles), high in calcium (30-50 mmoles), and normal in protein and caloric content. Intravenous infusions of sodium and potassium sulfate were given frequently in order to augment renal magnesium loss. However, the principle magnesium loss occurred via fecal excretion, which exceeded intake, evidently as a result of the high calcium intake. Both calcium and magnesium clearance fell markedly, especially when expressed in relation to sodium clearance. Magnesium repletion increased the clearance of magnesium more than that of calcium. Cumulative negative magnesium balance amounted to 92 and 86 mmoles, respectively, or 8 to 10% of body magnesium. Calcium balance was zero. No increase in magnesium loss followed the ingestion of 10 ounces of whiskey daily. Plasma calcium remained normal, but plasma and erythrocyte magnesium fell moderately. Muscle magnesium remained normal; consequently, the source of the lost magnesium must have been bone. No untoward effects occurred.

Author’s address: Dr. M. J. Dunn, Department of Metabolism, Walter Reed Army, Institute of Research, Washington, D.C. 20012 (USA).

Micropuncture study of inulin reabsorption in Necturus kidney
To test whether inulin is reabsorbed by the kidney tubules of the salamander Necturus maculosus, solutions containing inulin-carboxyl-14C were infused slowly into single proximal tubules. Experiments were done on normal blood-perfused kidneys and on kidneys perfused with Ringer solutions. The quantity of inulin reabsorbed was estimated from the amount of inulin appearing in plasma or in perfusion fluid which had passed through the kidneys. Insignificant quantities of inulin were reabsorbed. Hence, inulin is a suitable substance for measuring glomerular filtration rate in this amphibian species.

Author’s address: Dr. G. A. Tanner, Department of Physiology, Cornell University Medical College, New York, N. Y. (USA).

Effect of metabolic inhibitors on the response of the toad bladder to vaso-pressin
This study was designed to explore the relationship between metabolism and the response to hormone. Iodoacetic acid (IAA), 10^-4 M, dinitrophenol (DNP), 324

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10^-3 M, anaerobiosis (Na), azide, 10^-3 M, and fluoroacetate (FAc), 10^-2 M, caused a fall in short-circuit current (SCC) and the SCC response to vasopressin. With the exception of FAc, each agent inhibited the permeability response to vasopressin as estimated by the flow of 32O along an osmotic gradient across the bladder. IAA, azide, and DNP inhibited the permeability response in a Ringer’s solution in which all sodium was replaced by choline. In general, the effect of inhibitors on the permeability response to cyclic 3',5' AMP resembled the effect on the response to vasopressin. The data are interpreted as demonstrating a metabolic dependence of the SCC and permeability response of the toad bladder to vasopressin.
Die Bedeutung des Anions für den renal tubulären Transport von Na+ und die Transporte von Glucose und PAH / Role of Anions in the transport of sodium and glucose and PAH in the renal tubule


In the isolated artificially perfused kidney of Rana ridibunda at NaCl-concentrations in the glomerular filtrate from 20.0-76.5 mM/l the rate of net-Na+-transport depends linearly on the filtered Na+-load.

Upon substitution of NaCl by Na₂SC > 4 an apparent Tm for Na⁺ can be observed. This is interpreted as a consequence of the relative impermeability of the tubular cells to SO₄⁻. Using sodium salts with anions of different size one can thus vary Na⁺-transport at constant Na⁺-concentration. This experimental opportunity stimulates the following two questions: (1) Do the anions – apart from the role played by their physical size – influence the Na⁺-transport mechanism? (2) Which of the two, Na⁺-concentration or rate of Na⁺-transport, is the decisive parameter for the known Na⁺-dependence of tubular glucose- and PAH-transport?

Therefore, kidneys were perfused with solutions containing 20.0-76.5 mM/l NaCl (MW 58.45), Na-benzenesulfonate (MW 180.16) and Na-cyclohexanesulf-amate (MW 201.23). The amounts of reabsorbed Na⁺, glucose, and PAH were measured. With increasing size of the anion the amount of reabsorbed Na⁺ decreases. The more sodium is reabsorbed the more glucose is reabsorbed or PAH is secreted and vice versa.

The results give an indication of the importance of the anion-partner of sodium in the process of Na⁺-transport. They show, furthermore, that the rates of glucose- and PAH-transport depend on the rate of Na⁺-transport and not on the extracellular Na⁺-concentration.

Author’s address: Prof. Dr. med. G. Vogel, Biologisches Institut Dr. Madaus, Ostmerheimerstraße 198, 5 Köln-Merheim (Germany).

Relation between potassium balance and aldosterone secretion in normal subjects and in patients with hypertensive or renal tubular disease


Metabolic balance studies with measurement of aldosterone secretion/excretion were carried out in 23 normal volunteers and 23 patients to examine the role of potassium loading and potassium depletion on the production of aldosterone. In normal subjects on normal sodium intake (100 mEq/day), potassium loading (120 mEq/day) produced modest increments in aldosterone secretion (+107 µg per day). When comparable studies were conducted on normal subjects during sodium deprivation, a marked increase in aldosterone secretion (+ 841 µg/day) was noted. Potassium depletion by dietary deprivation in normal subjects was associated with a fall in aldosterone secretion when dietary sodium intake was maintained at normal levels, and a modest but subnormal rise in aldosterone secretion when dietary sodium intake was restricted. When potassium depletion was induced in normal subjects by diuretics a greater rise in aldosterone secretion was seen.

In patients with primary (essential) hypertension potassium loading caused qualitatively similar changes in aldosterone secretion as occurred in the normal subjects. Patients with hypertension...
secondary to renal arterial stenosis had greater than normal rises in aldosterone secretion on potassium loading, as did patients with advanced and malignant hypertension and as did three patients with primary aldosteronism due to aldosterone-secreting adenomas. Potassium loading during salt restriction in a patient with renal tubular acidosis and in another patient with sodium losing nephropathy was associated with dramatic rises in aldosterone secretion to 2,618 and 6,500 µg/day, respectively.

The increment produced by potassium loading in aldosterone secretion during periods of sodium restriction were equal to or greater than known data for angio-tensin stimulation. A relationship was found between pre-existing levels of aldosterone secretion and rises in aldosterone secretion during potassium loading. The higher the pre-existing rate of aldosterone secretion, the greater the rise in aldosterone secretion observed during potassium loading.

The changes in aldosterone production did not closely correlate with changes in plasma potassium concentrations suggesting that adrenal uptake of potassium may be more important than absolute blood levels as an initiating signal to increase aldosterone secretion.

The effect of aldosterone on sodium and potassium distribution in man


Total exchangeable sodium, potassium and bromide space were measured by a triple isotope technique, and antipyrine space, body weight, plasma electrolyte concentrations and urine electrolyte excretion were determined before and after intramuscular injection of 0.5 mg aldosterone 6 h for 6-8 days in nine convalescent men.

After the treatment with aldosterone there were mean increases in body weight of 2.5 kg, 2.5 l in total body water, and 3.0 l in extracellular fluid volume; a slight decrease in intracellular fluid volume was not significant. The mean total exchangeable sodium increased by 463 mEq and the mean cumulative urinary excretion of sodium decreased by 444 mEq. The sodium was retained in the extracellular fluid without significant change in exchangeable intracellular sodium. Mean total exchangeable potassium was reduced by 207 mEq while mean cumulative urinary potassium excretion increased by 88 mEq. The potassium loss was entirely intracellular.

The main source of error arose from isotope counting. The coefficient of variation of the sample count minus the background exceeded ± 3% in 18 out of 150 samples: these results were discarded. Sixteen of the inaccurate counts were due to low concentrations of sodium or potassium in the specimens.

Authors’ address: Dr. J. R. Cox, Dr. M. M. Platts, Dr. M. E. Horn, Dr. R. Adams and Dr. H. E. Miller, Departments of Medicine and Medical Physics, University of Sheffield, Sheffield (England).

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Effects of cyanide, amytal, and DNP on renal sodium absorption


The effects of cyanide, amytal, and 2,4-dinitrophenol (DNP) on sodium chloride and water absorption were studied in the proximal tubule of the intact rat kidney with the Gertz and Ullrich micropuncture method. Cyanide and amytal markedly decreased absorption suggesting that the electron transport system is essential for absorption at a normal rate, and that succinoxidase activity alone is incapable of maintaining this normal rate. Although DNP was less inhibitory
than cyanide or amytal, the data indicate that the normal rate of absorption of sodium chloride and water is dependent, at least in part, upon the synthesis of ATP (Fig. 1). The control data when expressed as the ratio of the perfusate remaining at a specific time to the initial volume can be described mathematically as \( R(t) = e^{-\beta t} \), where \( R(t) \) is the per cent of initial perfusate remaining at time \( t \), \( t \) is time in seconds, and \( \beta \) is a least squares estimate of absorption rate.

This work was performed in part under the auspices of the U.S. Atomic Energy Commission.

Fig. 1. Effects of sodium cyanide, sodium amytal, and DNP on sodium chloride and water absorption in the proximal tubule of the rat kidney. Each point represents the mean of seven observations.

Author’s address: Dr. R.J. Chertok, Bio-Medical Division, Lawrence Radiation Laboratory, University of California, Livermore, Calif. (USA).

Effect of temperature and medium K on Na and K fluxes in separated renal tubules


The effects of temperature and medium K concentration on the concentrations and fluxes of Na and K in suspensions of separated rabbit renal tubules have been investigated. The major findings are as follows: Decrease in the temperature of the bathing medium did not result in diminution of the concentration gradients for Na and K between tissue and medium or in swelling of the tissue. However, a large decrease in Na and K flux was observed, suggesting similar temperature coefficients for both active transport and passive permeability over the range of temperatures examined (15-37°C). Removal of K from the bathing solution reduced active Na efflux. At least two tissue K compartments were present, probably representing the heterogeneity of the tubule population in the suspension rather than multiple compartments within individual cells. At least two tissue Na compartments were also observed, but no consistent relationship was found between the size or exchange rates of the individual Na and K compartments.

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Book Review – Livre Nouveau

LDH Isoënzymen bij nieraanandoeiningen. Experimentele en klinische studies


Dans cette monographie, rédigée en Néerlandais et comportant un résumé en langue Française et Anglaise, l’auteur étudie de façon systématique dans les circonstances normales et pathologiques, la répartition des divers isoenzymes de la dehydrogenase lactique dans le rein, le sérum et les urines du rat, du chien et de l’homme. La signification pratique des résultats obtenus semble limitée, sauf en ce qui concerne les insuffisances rénales aiguës. Par contre, dans la transplantation rénale l’auteur n’a pu confirmer les travaux qui attribuaient une importance aux modifications des isoenzymes de la LDH dans le diagnostic de la crise du transplant.

Le livre, qui comporte plus de 300 références, intéressera avant tout ceux qui s’occupent d’enzymologie rénale.

P. Michielsen, LEO ven