**Further Section**

*Nephron 1965;2:367-375*

**Summaries – Résumés**

The action of synthetic angiotensin on renal function in the unanaesthetized rabbit  
In the unanaesthetized rabbit, intravenous infusion of small doses, 0.2 µg/kg/min, of synthetic Val-5-angiotensin octapeptide reduced urine flow and produced small and inconstant changes in excretion of sodium and chloride.  
Intravenous infusion of large doses of angiotensin, 1 µg/kg/min, greatly increased urine flow. During this diuresis, the concentration of sodium and chloride in the urine tended to approximate to that of plasma, irrespective of whether it was initially lower or higher. Inulin clearance did not change in a constant direction, while diodone or PAH clearances always fell during the diuretic phase.  
The effects of synthetic angiotensin were qualitatively similar to those of renin and natural angiotensin.  
The possibility that renin may function as an intrarenal hormone concerned with sodium regulation is discussed.  
Author’s address: Dr. G. W. Pickering, Department of the Regins Professor of Medicine, University of Oxford, Oxford (England).

Effect of mineralocorticoids on tubular reabsorption of sodium ions/Einfluß von Mineralocorticoiden auf die tubuläre Rückgewinnung von Na-Ionen  
Attempts to localize the site of the Na⁺ retaining effect of mineralocorticoids by use of the conventional stop-flow-technique revealed conflicting results. In rats proximal tubular reabsorption of Na⁺ was claimed to diminish shortly after adrenalectomy whereas an impaired distal function could not be observed before 21 days after the removal of the adrenal glands.  
The influence of adrenal steroids on Na⁺ reabsorption in the distal segment of the rat nephron has therefore been investigated, using the modified stop-flow technique of Metaxas.  
In brief, this consists of simultaneous occlusion of the ureter and the vessels of the renal pedicle, thus allowing variation and shortening of the period of occlusion, without ‘smudging’ of the eventual tubulogram due to movement of the trapped urine and the replacement of reabsorbate by new filtrate.  
Occlusion periods of 5, 10, and 20 sec were used in normal Sprague-Dawley rats, and in a second series in which the adrenals had been removed 24 h previously. Reabsorption was calculated as the percentage difference between the ratios of Na⁺ to inulin clearance in the free flow urine and that in the ‘best’ distal fraction.  
Tubular reabsorption of Na⁺ in the distal segment was shown to increase in both groups of animals with prolongation of the period of occlusion, but the percentage reabsorbed during the occlusions was diminished after adrenalectomy.  
It is suggested that the adrenal steroid may increase the rate of sodium reabsorption in the distal segment without affecting the total reabsorptive capacity.
Acidification des urines après ingestion de chlorure de choline
Role de l’oxyde de trimethylamine comme accepteur d’ions H+ dans l’urine
L’ingestion de chlorure de choline determine, chez des sujets sains soumis à un regime constant, un abaissement du pH des urines et une augmentation importante de l’ammoniurie ainsi que de l’acidité titrable, sans modification sensible de l’équilibre acido-basique de l’organisme. Le surplus d’acides excretes correspond à deux milliéquivalents pour trois millimoles de chlorure de choline ingérées.
L’ingestion de chlorure de choline entraîne l’excrétion urinaire de trimethylamine. Dans les conditions expérimentales réalisées, l’oxyde de trimethylamine est un accepteur d’ions H+ qui participe à l’acidité titrable, dans une proportion variable, parfois supérieure à 50%.
L’acidification obtenue par l’ingestion de chlorure de choline, sel parfaitement défini, permet de démontrer le role du cation métabolisable dans l’élaboration d’ions H+. La choline étant un constituant des phospho-amino-lipides qui font partie de l’alimentation normale, les résultats obtenus au cours de cette experimentation suggèrent que ces lipides rendent compte d’une partie des acides formes par le métabolisme.
Adresse des auteurs: Dr. R. Ardaillou, Dr. C. Amiel, Dr. M. F. Pelé et Prof. G. Richet, Hôpital Tenon, 4, rue de la Chine, Paris XXe (France).

Author’s address: Priv. Doz. Dr. G. Senft, Pharmakologisches Institut der Freien Universität Berlin, Thielallee 69-73, Berlin (Germany).

The effect of high and low concentrations of calcium on the sodium transport of the isolated toad bladder
Sodium transport was measured in the isolated toad bladder by means of the short-circuit current technique and isotopic labelling. At a calcium concentration of 0.2 mM there was a decrease in active sodium transport but the bladder responded in a normal manner to oxytocin. A calcium concentration of 3.6 mM had no effect on the active sodium transport either before or after the addition of oxytocin. It is suggested that the effect of oxytocin on water movement across the toad bladder may involve a different mechanism than its effect on sodium transport.
Authors’ address: Dr. J. Anderson and Dr. R.W.S. Tomlinson, King’s College Hospital Medical School, London (England).

Utilization and transport of substrate by dog kidney in relation to renal function
By Cohen, J.J.
Our objective is to determine the relationship between specific renal substrate uptake and the pathways of substrate metabolism in the kidney, on the one hand, and renal work, on the other hand. In gaseous metabolic studies (1), the R.Q. of the dog kidney was determined in vivo in unilaterally nephrectomized dogs during the infusion of (a) NaCl, (b) α-keto acids, (c) acute alkalosis (Na-lactate) and (d) acute acidosis (HC1 or H2SO4). The mean (± S.E.) RQ’s were : (a) 1.33 ± 0.07
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(n = 17), (b) 1.27 ± 0.08 (n = 19), (c) 1.18 ± 0.08 (n = 34) and (d) 1.14 ± 0.11 (N = 32). There were no significant differences in O2 consumption between any pair of experimental groups;
thus the variations in RQ were due entirely to differences in CO2 production. The excess in renal CO2 production over O2 consumption was interpreted to indicate that the kidney utilizes substrates by coupled anaerobic oxidation-reductions yielding CO2. A relationship between renal anaerobic metabolism as manifested by excess CO2 production and renal excretory function was postulated.

Consistent with a significant rate of anaerobic oxidative decarboxylation in the kidney is the observation that the major endogenous renal substrates are non-esterified fatty acids (NEFA); the complete oxidation of NEFA should result in an RQ of approximately 0.7, but anaerobic oxidative decarboxylation of NEFA can result in an RQ approximating unity. In further studies, it was observed that infusion of α-ketoglutarate (α-KG) markedly depressed renal uptake of NEFA in vivo with no change in renal oxygen consumption rate. Further, the renal uptake of α-KG was so great that the simultaneous renal O2 consumption could not completely oxidize these amounts of α-KG to CO2 and H2O. It was concluded that exogenous α-KG was displacing NEFA as a major substrate of renal metabolism (3). We have therefore studied the pathways by which α-KG is taken up and dissimilated by the dog kidney using α-KG as a model for renal substrate metabolism.

The simultaneous net renal transport (Tα-KG) and renal utilization (Qα-KG) of infused α-KG have been studied by renal clearance, stop-flow and metabolic techniques in anesthetized (pentobarbital) dogs (2). The kidney was observed to be a major and specific site of α-KG dissimilation in the dog. The mechanisms for reabsorptive transport and transport to a site of metabolism have been shown to be independent of each other (2, 3). Probenecid reduces Qα-KG while not affecting TVα-KG; alkalosis causes parallel decreases in both Tα-KG and Qα-KG, but of differing magnitude in each.

In studies of the separate effects of alkalosis and of changes in blood [lactate] on Tm-PAH, it was found that blood [lactate] and not blood pH determines the magnitude of Tm-PAH. Tm-PAH is not related to rate of net utilization of lactate by kidney (4).

Current studies are directed to the determination of the basis for the specificity of α-KG uptake (6) and the relationships between anaerobic utilization of α-KG and transport mechanisms in vitro (5).

References


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Is inulin suitable for the estimation of glomerulum filtration rate in warmblooded animals? / 1st
Inulin zur Messung des Glomerulumfiltrates beim Warmblüter geeignet?
An isotonic NaCl solution containing radioactive inulin and the dye Lissamin-Green was infused into single proximal tubules of rat kidneys by means of a micro infusion pump; the rate of
infusion was comparable to the normal rate of filtration through a single glomerulus. The inulin
used was a homogenous fraction, the molecular weight of which was more than 5000, as
determined by means of Sephadex column-chromatography. The excretion of radioactive inulin via
each ureter was individually determined from the start of the infusion. In 7 of 21 per-fusions
less than 1% of the inulin was recovered from the contralateral kidney, i.e. less than 2% had been
transported in the circulation. In technically defective experiments, in which the infused solution
was partly flowing towards the glomerulus this percentage was higher, being even as great as
31.4%. These experiments constitute a direct proof that there is no considerable transtubular
reabsorption of inulin, and measurement of inulin clearance affords a suitable means of
measuring glomerular filtration rate.
Authors’ address: Drs. K. Baumann; H. Oelert; G. Rumrich und Prof. Dr. K.J. Ullrich,
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Renal blood flow measured with Xenon-133 wash-out technique and with an electromagnetic
flowmeter
Measurements of the renal blood flow by use of the wash-out curve of a radioactive inert gas
from the kidney were introduced by Thorburn et al. (1) in animal experiments and by Ladefoged
and Kemp (2) in man. The present paper concerns 30 simultaneous measurements of the renal
cortical blood flow with this technique and the total renal blood flow with an electromagnetic
flowmeter carried out in eight dogs. Xenon-133 was used as the indicator by the wash-out
measurement: The disappearance of 2-5 mC Xenon dissolved in saline from the kidney after a
rapid injection into the renal artery was monitored externally. The disappearance curve was
resolved graphically on semilogarithmic paper in three components. From the half time (T 1/2) of
the fastest component the cortical blood flow (F) was calculated by F = (In 2)/(T 1/2) × λ,
where λ denotes the partition coefficient for Xenon-133 between kidney-tissue and blood. A figur of 0.7
for the λ was used corrected for variations in the hematocrit by
1.69 λct x = 0.7 × Lo5 + 0.013 ×hctx < 3 > -
The renal blood flow was varied to obtain a broader range in the experimental conditions.
A highly significant correlation was found between the two measurements. The slope of the
correlation line was 1.18 and the standard error of the estimate was 0.81 ml/g cortex/min.
The results show that measurements with the Xenon-133 wash-out technique give values for
renal cortical blood flow consistent with the figures of the methods usually employed.

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A.C.: Intrarenal distribution of nutrient blood flow determined with Krypton-85 in the
Authors’ addresses: Dr. J. Ladefoged, Department of Clinical Physiology, Glostrup Hospital, Glostrup, Copenhagen (Denmark) and the Institute of Physiology, University of Göttingen, Göttingen (Germany).

The fate of pseudomonas aeruginosa, proteus mirabilis and escherichia coli in the mouse kidney
Intravenous injection of Pseudomonas aeruginosa, Proteus mirabilis or Escherichia coli was found to produce pyelonephritis in mice. Quantitative studies were made of the inoculated bacilli both in pyelonephritic and in normal kidneys. The growth curves of Ps. aeruginosa and Pr. mirabilis in the kidneys were similar. Pr. mirabilis killed many more mice than the other organisms, possibly because it caused progressive renal failure. E. coli was the least efficient in producing renal abscesses and its viable count in the kidneys was comparable with the counts of the other organisms only during the first week after infection. There was, however, considerable persistence of viable E. coli bacilli in the kidneys.
Kidneys that escaped the development of lesions visible to the naked eye appeared nevertheless to support some bacterial multiplication and viable bacteria persisted in them for some weeks.
Author’s address: Dr. R. H. Gorrill, Department of Bacteriology, Guy’s Hospital Medical School, London Bridge S.E. 1 (England).

Serological grouping of urinary Escherichia coli
Five hundred and thirty-four strains of E. coli from urine were serologically grouped using 12 ‘O’ antisera. 316 were from urines with bacterial counts of more than 100,000; 86 between 10,000 and 100,000, and 132 below 10,000 organisms per ml urine. 56.6% of all strains, 65.7% of those strains isolated from symptomatic infections, were typable. The reproducibility of using one colony from a diagnostic plate was good, 325 of 350 colonies from 70 specimens showed complete agreement, 25 of the colonies were rough and untypable.
Statistically there was no significant difference in the number of typable strains from the high and low bacterial counts; in the frequency of typable strains in primary symptomatic infection and in infection associated with urinary tract abnormalities; or in the frequency of specific groups in the high and low bacterial groups or in the sexes.
Author’s address: Dr. J. McGeachie, University Department of Bacteriology, Glasgow Royal Infirmary, Glasgow C. (Scotland).

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The nephropathy of experimental magnesium deficiency: An electron microscopic study
Dietary magnesium deficiency was experimentally produced in rats for 3 and 13 days and then muscle, kidney, and plasma were analyzed for their magnesium and calcium contents and the kidneys were examined by the light and electron microscopes. Progressive depletion of the magnesium content of the skeletal muscles and a fall in plasma magnesium were noted while the only highly significant result in the calcium estimations was a marked increase of calcium in the kidneys.
Electron microscopy has shown that the lesion of magnesium depletion is localized to the proximal tubules, beginning in the pars recta and extending to the pars convoluta. The lesion consists of dilatation of the tubule, initial swelling and vacuolization of the cells, followed by the gradual disappearance of the microvilli, the formation of cytoplasmic granules of varying density and finally the extreme flattening out of the cells lining the very dilated tubules (Fig. 1). The mitochondria and the basement membranes remain intact.

It seems possible that in magnesium deficiency the proximal tubule cells which normally reabsorb Ca++ and Mg++ by a common transport mechanism, reabsorb an excess of Ca++ from the glomerular filtrate which is deficient in Mg++. The excess of absorbed calcium ions is largely deposited locally in these cells appearing as the dense granules. This would explain the high calcium content in the kidneys and the nephrocalcinosis in late stages. Some obscure instances of nephrocalcinosis in humans might thus be the result of an episode of magnesium deficiency.

Since pure dietary depletion of potassium was found to produce no lesions in the proximal tubules when the kidneys were examined by the electron microscope (1), while in the reported human cases of what has been termed ‘chronic depletion of potassium’ the kidneys frequently showed lesions in the proximal tubules, it is suggested that these lesions are most likely due to an associated depletion of magnesium that has been missed.

Reference

Author’s address: Dr. M.S. Sabour, Department of Medicine, Ain-Shams University, Abbasieh, Cairo (Egypt).
Reactions of kidney cells during autolysis: Light microscopic observations
The processes of cell death and necrosis have been studied by light microscopy in different types of kidney cells kept in vitro at 37 °C over a 24-h period. Osmium fixation and plastic embedding give significantly better results than fixation in Helly’s or Technicon solution and paraffin embedding, which produce striking shrinkage of cells as well as accelerating karyorrhexis in distal tubules.
Most cell types show pyknotic necrosis characterized by shrinkage and increased basophilia of the nuclei. Margination of chromatin at the nuclear envelope occurred in all types of cells undergoing pyknosis and may ultimately prove to be a constant precursor of pyknosis. In spite of these basic similarities there was considerable variation in the different cell types in the rate and extent of nuclear and cytoplasmic changes.
In glomeruli cytoplasmic swelling, prominent in mesangial cells and less marked in endothelial cells, appeared early and closed glomerular capillary lumens.
In proximal convoluted tubules swelling of the apices occurs within a few minutes and fills the normally open tubular lumens. There is considerable activity in the larger cytoplasmic organdies over the first four hours.
In distal convoluted tubules the nuclei became pyknotic before nuclear fragmentation occurred. In collecting tubules few changes were noted until after eight hours.
Primary karyolysis occurred in some cells of the outer proximal tubules, probably due to contact with normal saline or its vapor. This light microscopic study forms a basis for evaluating early changes of disease in renal biopsy or autopsy tissue.
Author’s address: Dr. H. Latta, Department of Pathology, University of California School of Medicine, Los Angeles, Calif. (USA).
Changes in renal glomeruli during autolysis: Electron microscopic observations
Electron microscopic changes in rat glomeruli have been described during autolysis in vitro. Bowman’s space becomes filled with swollen epithelial cytoplasm after one hour. Herniation or reflux of proximal tubule epithelium into Bowman’s space may be seen at the start. In the glomerular epithelial cytoplasm the endoplasmic reticulum and mitochondria swell with time, and myelin figures and microvilli develop. No change in other cytoplasmic bodies is apparent within the first eight hours. Pyknosis in endothelial and mesangial nuclei proceeds more rapidly than in epithelial nuclei. In the process of pyknosis there is margination of chromatin at the nuclear envelope and loss of chromatin granules from the nucleoplasm. Mesangial cells show more rapid and more marked swelling than endothelial cells. Swollen mesangial processes project into overlying endothelial cells and into capillary lumens. This mesangial swelling combines with the swelling of endothelial and other glomerular and tubular cells to obliterate capillary lumens.
Author’s address: Dr. H. Latta, Department of Pathology, University of California School of Medicine, Los Angeles, Calif. (USA).
Changes in renal cortical tubules during autolysis: Electron microscopic observations
The processes of cell death have been studied electron microscopically in proximal, distal, and collecting tubules of the rat renal cortex during autolysis in vitro. Striking features of autolysis
involve dynamic changes in various membrane systems taking place for several hours and the persistence of these membranes until the late stages of autolysis. Nuclear changes develop after cytoplasmic changes become marked.

In the proximal convoluted tubules, rapid swelling of the cytoplasm is followed by the development of myelin-like figures of concentric plasma membranes, swelling and fragmentation of mitochondria, vesiculation and swelling of the endoplasmic and Golgi membranes, and loss of the microvilli of the brush border. The outer mitochondrial membranes appear less reactive than the membranes of cristae. A variety of cytoplasmic bodies is present in the normal cell and during autolysis many large bodies with membranes and light flocculent contents develop. Margination of chromatin granules is a constant early stage in the development of pyknosis.

In the distal convoluted tubules the plasma membranes retain their triple-layered structure until the entire membrane disintegrates. The mitochondrial cristae develop vesicles which are larger and appear more rapidly than those in the proximal tubule mitochondria. Shrinkage of pyknotic chromatin away from the nuclear envelope suggests that the latter is a passive participant in the nuclear changes. Karyorrhexis may follow pyknosis in these nuclei without any other apparent change in the cells.

In the collecting tubules, most changes develop quite slowly although most cytoplasmic bodies disappear within the first hour.

Author’s address: Dr. H. Latta, Department of Pathology, University of California School of Medicine, Los Angeles, Calif. (USA).

The renal excretion of hydrogen ions in infants and children

The renal ability to excrete hydrogen ions was assessed in 12 normal, artificially fed infants aged 2-11 ⅛ months and 14 children aged 1 year 1 month to 16 years on ordinary diets, and in most cases on the third day of continuous ammonium chloride administration (115-166 mEq/day/1.73 sq.m.). The total hydrogen ions excreted in urine, i.e. titratable acidity plus ammonium ions minus bicarbonate— were determined on day-time urine collections of average duration of 6 h, and they were found to have reached adult levels in both age groups. Capillary plasma carbon dioxide content was also estimated in the middle of urine collection periods.

The mean value of the hydrogen ion clearance index, calculated as the product of the hydrogen ions excreted in urine (mEq/min/1.73 sq.m.) and the plasma carbon dioxide content (mEq/l), on the third day of ammonium chloride administration, was 1.61 for the infants and 1.69 for the children, and ranged from 1.20 to 3.44 and 1.25 to 2.30 respectively. They are the same as adult levels.

It is considered that these values are suitable to use as a standard that can be applied in assessing whether acidosis is, or is not, primarily of renal origin in children from the age of about 3 months, as well as in detecting latent cases of renal acidosis.

Author’s address: Dr. B. Levin, Queen Elizabeth Hospital for Children, Hackney Road, London, E. 2 (England).

Zur Frage einer Beteiligung von Nichtelektrolyten (Harnstoff, Kreatinin) am Vorgang der Harnkonzentrierung beim Menschen
On the contribution of nonelectrolytes (urea, creatinine) to the urinary concentrating process in man


In persons, thirsting for over 18 h with low protein intake and with or without disturbance of renal function, the different parameters limiting urine concentration under maximum ADH-influence have been investigated during acute urea-or creatinine loading.

In all examined subjects the maximum urine osmolality, determined during oliguria, increases within one hour after simultaneous oral and intravenous loading with urea. At the same time urine volume (V), osmolal clearance (COSm), back-diffusion of free water (T°O) and U/POSm increase slightly. The inverse relationship between U/P osm and C_vOSm is no longer demonstrable at urine volumes of 1 ml/min/1.73 m2 and values of COSm of 2 ml/min/1.73 m2. During hydropenia and oliguria an increase of serum creatinine concentration from an average value of 0.88 up to a maximum value of 10.8 mg/l00 ml causes a falling tendency of maximum urine osmolality and U/Posm.

In hydropenic and oliguric subjects under creatinine loading the contribution of potassium with (a monovalent anion) to maximum urine osmolality decrease to the same extent as that of creatinine increases.

Data, bearing on the behaviour of Tm°O (measured during infusion of hypertonic mannitol solution) under i.v. creatinine loading are being presented.

It is concluded that acute urea loading during oliguria increases the ‘osmotic ceiling’ (Smith, 1956) and that creatinine does not take part neither in healthy subjects nor in patients with kidney disease (without retention) in the build up of a hypertonic medullary interstitium. The partial permeability towards creatine which is often observed in functional disturbances of the kidney must be attributed to segments of the nephron other than the collecting ducts.

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