Heterologous anti-lymphocyte globulin, histo-incompatibility matching and human renal homotransplantation


Twenty consecutive patients received renal homografts from blood relatives, ten to sixteen months previously. All were treated with heterologous antilymphocyte globulin in progressively diminishing quantities for the first four post-operative months and all also received azathioprine, as well as prednisone.

Nineteen or 95% of these patients were alive with good function. In past similar instances, the death rate during comparable intervals was about 30%. The improved results seem attributable to an efficient prevention or treatment of early rejection without the need for such high doses of azathioprine or prednisone, as was necessary prior to the use of globulin therapy. Infectious complications were reduced.

The nineteen surviving patients were followed up for six to ten months after their last globulin injection. Delayed rejection occurred in only two patients. In both, this was controlled with minor increases in the maintenance level of steroids. Two other patients, who were treated with globulin for the first time five and eleven months after transplantation, subsequently had stable renal function for more than one year, while receiving much smaller doses of prednisone than had previously been possible.

In the nineteen surviving patients of the original consecutive series, as well as in nineteen similarly treated recipients who were subsequently provided with consanguineous homografts, there was a spectrum of antigenic matches between the recipients and their donors. Until now, survival had been equivalent in patients with good, intermediate or poor matches. However, the patients with the most compatible donors generally had the best renal function and required the smallest doses of prednisone. These results indicate that a considerable degree of histo-incompatibility can be consistently over-ridden in intrafamilial transplantation by the combination of these agents, but at an increased cost.

Author’s address: Thomas E. Starzl, M.D., Department of Surgery, University of Colorado School of Medicine, Veterans Administration Hospital, Denver, Col. (USA).

Heparin in delayed transplant function


An increase in renal function was noted in five patients who were systemically heparinized, at a time when kidney function was poor after cadaveric renal homo-transplantation. This increase in urine output occurred within 48 h in all but one of the patients. In this individual, the heparin dosage used was the lowest of the group.

None of the patients were thought to be rejecting at the time when heparin therapy was started and the indication for anticoagulation therapy was usually that of a clotted arteriovenous shunt.
In the two patients in whom biopsy reports were available, it was impossible to state that the changes present were specifically those of rejection. It is suggested, however, because of the salutary effect on renal function, that the heparin may have been partially responsible by dispersing platelet aggregates in glomerular capillaries which occur with homograft rejection. Author’s address: Robert McMillan, M.B., Department of Surgery, University of Cambridge, Addenbrooke’s Hospital, Cambridge (England).
Urine fibrinogen fragments in human renal allografts
Nineteen patients excreted fibrinogen fragment D and E in their urine at specific times after renal transplantation. Sixteen patients studied within two weeks of surgery all excreted the fragments. These fragments were absent in 62 specimens from 15 patients who clinically did not show rejection, more than two weeks after transplantation. In four reversible, and three irreversible rejections, the fragments reappeared. They disappeared after intensified immunosuppressive therapy in the reversible and persisted in the irreversible rejections. One allograft from a patient with severe recurrent glomerulonephritis and five patients with other renal diseases, also excreted these fragments.
The fragments may represent fibrinolytic products derived from intra-renal microthrombi induced by the transplantation procedure or local antigen-antibody reactions. Interaction of clotting factors and plasmin with the complement system and vasoactive peptides may contribute to the mechanism of tissue injury.
Author’s address: W.E. Braun, M.D., Division of Research, The Cleveland Clinic, Cleveland, Ohio 44106 (USA).

Twenty-four hour storage of kidneys
Canine kidneys were preserved for twenty-four hours by one of four methods in an attempt to define a suitable technique for application to human cadaveric kidneys. Hypothermia was common to all methods, being used alone, supplemented with hyperbaric oxygen or combined with continuous perfusion with 50% blood at 30 mm Hg pressure in an environment of 1 or 3 atm of oxygen. After storage, the kidneys were reimplanted into the pelvis of the donor animal and contralateral nephrectomy was performed three weeks later. Consistently successful preservation was achieved by simple hypothermia. Hyperbaric oxygen conferred significant benefits as judged histologically and biochemically. Continuous perfusion was, on the other hand, associated with vascular damage and poor subsequent function. In the successful experiments, long-term survival was obtained irrespective of the storage method used.
Author’s address: W.F. Hendry, M.B., Department of Urology, Royal Infirmary, Glasgow (Scotland).

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Hemodialysis for methyprylon (noludar) poisoning
A case of methyprylon (noludar) poisoning treated with extracorporeal hemodialysis is reported. The patient showed dramatic clinical improvement with concomitant lowering of serum methyprylon levels from 4 to 0.4 mg/100 ml, during a nine-hour period of hemodialysis. Only negligible quantities of methyprylon were recovered from the bath.
In vitro dialysis of methyprylon revealed this drug to be readily dialysible with a coil clearance of 42 ml/min; about equal to that of the short-acting barbiturates. Less than 10% of the injected dose of methyprylon was recovered in the dialysate. It is, therefore, concluded that endogenous metabolism accounts for the rapid decrease in serum levels of methyprylon. Dialysis of toxic metabolites of the drug may possibly explain the dramatic clinical improvement seen with the reported cases of hemodialysis after intoxication. The value of hemodialysis in methyprylon intoxication remains to be proved in view of the small total amount recoverable in the dialysate.

Author’s address: Melvin Yudis, M.D., Department of Medicine, Hahnemann Medical College, Philadelphia, Pa. (USA).

Insulin-glucose relationships in uremia


Seven chronic uremic male patients were studied with multiple determinations of blood glucose and immunoreactive insulin (IRI) following oral glucose loading (OGTT) and intravenous tolbutamide (IVTTT) before and after intensive hemodialysis. The OGTT was improved after dialysis, strikingly apparent during the early part of the test (< 120 min). No significant differences were found in IRI comparing pre and post OGTT; comparing glucose and IRI in OGTT with a matched group of controls, multiple differences were found in glucose levels between the pre and normal groups. Significantly higher postdialysis glucose values were only apparent in the late samples (> 90 min). The higher IRI levels in uremics when compared to normals also diminished postdialysis. The IRI-blood glucose relationship (slope of linear regression of IRI upon glucose) was not different comparing normals and uremics predialysis. There was, however, a significantly greater IRI-glucose relationship in the postdialysis group than in controls. The IVTTT in the pregroup showed higher glucose and IRI levels when compared to normals. These differences disappeared postdialysis. It is concluded that the defect in glucose utilization in uremia is different from diabetes mellitus in which a diminished IRI-glucose relationship exists. Also the uremic can respond to tolbutamide. A peripheral insensitivity to endogenous insulin would seem to be of prime importance which is partially compensated for, after dialysis, by a relatively greater insulin release.

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Natural history of uremic polyneuropathy and effect of dialysis


Nerve-conduction-velocity determinations were performed serially on: (1) patients with chronic renal failure (serum creatinine greater than 2.4 mg/100 ml)– 14 patients; (2) 20 patients receiving long-term intermittent dialysis, and (3) 18 dialysis patients were also studied with motor nerve and sensory nerve conduction velocities determined within 2 h of the start and again 2 h after the end of a single dialysis session. It was found that a rising serum creatinine was associated with a decline in motor nerve conduction velocity in the patients with chronic renal failure not treated with dialysis. In contrast, all patients treated by intermittent dialysis for more than a year showed improvement in peripheral nerve function. A single dialysis session had no major effect on motor or sensory nerve conduction under the conditions of this study.
The authors recommend that dialysis be instituted early in patients with chronic renal insufficiency in whom clinical signs of neuropathy develop. They also point out that for those patients maintained on dialysis, clinical or electro-physiologic evidence of worsening peripheral nerve function may be an indication of inadequate dialysis.

Author’s address: Dr. R.H. Jebsen, Department of Physical Medicine and Rehabilitation, University Hospital, Seattle, Wash. 98105 (USA).

Uraemic bleeding: A reversible platelet defect corrected by dialysis

Platelet numbers and function were studied in 17 severely uremic patients with both acute and chronic renal failure before, and again after treatment by dialysis. Peritoneal dialysis was used on 11 occasions, and the artificial kidney on nine. The platelet abnormality was improved by dialysis in 19 of 20 treatments, and the improvement was noted as early as the first postdialysis day. Of the 65 tests which were abnormal before dialysis, 38 were restored to normal when retested one to six days later, and there was considerable improvement in 14 others. Only 13 tests failed to show improvement. The beneficial effect of dialysis was apparent in all parameters measured, particularly in respect to platelet numbers, platelet adhesiveness, prothrombin consumption, and clot retraction. The tests most sensitive to the platelet disorder in predialysis patients and least responsive to dialysis, were the bleeding time with venous stasis and platelet aggregation. The qualitative platelet defect, as measured by platelet aggregation, factor-3 availability, and clot retraction could not be reproduced by the in vitro addition of the urea, dextrose, mannitol, creatinine, urate, phosphate, potassium, or magnesium or by changes of pH or osmolality, within the range that might be encountered in the severely uremic patient, nor could it be corrected by dialysis in vitro or mixing with normal blood platelet poor plasma. It is concluded that thrombocytopenia and the qualitative platelet defect in uremic patients is caused by retention in the body fluid of a dialyzable substance and that this defect is considerably improved by dialysis, but fully corrected only by successful renal transplantation.

Author’s address: Dr. J.H. Stewart, Kanematsu Memorial Institute, Sydney Hospital, Sydney (Australia).

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The Twin Minicoil artificial kidney

Five chronic patients have been treated with a Twin Minicoil artificial kidney, three patients for approximately two years, one for one and a half years and one for three months. Three of these patients are now on home dialysis, for nine and three months and one month respectively. The patients are dialysed for 14 h twice weekly with cellophane coils or 12 h twice weekly with cuprophane coils. The clinical results are good and only one patient is not fully rehabilitated. The Twin Minicoil is entirely disposable, has a surface area of 0.9 m2 and a priming volume of 450-500 ml, tubing included. With a pump a blood flow of 150-175 ml/min is obtained. The coil is sealed in a polyvinylchloride envelope and the dialysate is sucked through at a rate of 500 ml/min at a negative pressure of 50-70 mm Hg. With cuprophane tubing the clearance of the Minicoil is similar to the clearance of a two layer Kill dialyser. No priming with blood is needed. The Twin Minicoil is considered ideal for home dialysis.

Author’s address: Dr. K.M. Simpson, City General Hospital, Newcastle Road, Stoke-on-Trent, Staffs. (England).
Problèmes d’anesthésie, lors de la transplantation rénale / Anaesthesie-probleme bei klinischer Nierentransplantation


Sur un total de 16 patients ayant subi une transplantation rénale l’auteur a observe dans cinq cas des manifestations neurologiques graves dans les suites immediates de l’intervention. Ces malades ont presente une apnee suivie de convulsions et de coma necessitant l’usage d’un respirateur artificiel. Ces symptomes ont persiste pendant une duree variant de 32 h a plusieurs jours. L’auteur retient deux causes possibles: l’edeme cerebral ou l’accumulation de produits anesthesiants et curari-sants consequente a l’insuffisance renales.

P.S. Nous avons eu connaissance d’accidents similaires, non publies, survenus dans un autre centre. La limitation de ces accidents a certains centres semble con-firmer qu’ils sont dus a la nature ou a la dose des produits utilises en cours d’anesthesie (N.D.L.R.).

Adresse de l’auteur: Dr. R. Gattiker, Institut fur Anaesthesiologie der Uni-verta-sitatskliniken, 8000 Zurich (Suisse).

L’anesthesie au cours de l’insuffisance renales aigue


L’anesthesie des malades en insuffisance renales aigue est difficile car il s’agit de sujets prives plus ou moins completement de fonctions excretrices, presentant des troubles biologiques particulierement complexes et severes dont l’etat est souvent a la merci du moindre desequilibre cardiorespiratoire.

La pratique de l’anesthesie chez de tels malades nous a conduit a schematiser notre technique de la sorte. En premier lieu une correction biologique aussi parfaite que possible. La prémédication, administree sous surveillance, comporte une

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association de promethazine et pethidine. L’anesthesie, induite par le thiopental a 1% injecte doucement en evitant l’apnee et en oxygenant le malade, est entre-tenue par l’halothane (0,25 a 0,50%) associe a un melange protoxyde d’azote-oxygen (50%). Une analgesie de complement si elle est necessaire est realisee par des doses fractionnees de pethidine diluee. Une resolution musculaire complete, si elle est indispensable, est obtenue par la succinyl-choline en perfusion dont le debit est regle a la demande; on est alors presque dans l’obligation de contrôler la ventilation, de preference par un respirateur. La mesure continue de la pression veineuse permet de compenser les pertes sanguines en limitant le risque de surcharge. Le rythme cardiaque doit être surveille en permanence par le cardioscope, de façon a depiester precocement un trouble du rythme ou de la conduction.

A ce prix, l’anesthesie permet au chirurgien de tenter le traitement des even-tuelles lesions associees si souvent responsables de la mort au cours des insuffisances renales post operatoires ou post traumatiques, entre autres.


Clinical observations in the so-called idiopathic edema / Klinische Beob-achtungen beim sogenannten idiopathischen Odem


The so-called idiopathic edema represents a rare disturbance in water and salt metabolism, which can be observed in general in females aged 20 to 50. On the basis of two cases the authors
studied the clinical symptomatology and the possible pathogenesis of the idiopathic edema, which is characterized by diffuse, mostly symmetrical swellings, particularly in the lower legs, at the back of the hands and in the face. This edema occurs periodically every 3 to 10 days, appears within a few hours, lasts for 12-48 h and then vanishes starting with polyuria. During the time of extensive water retention blood pressure elevation, pulmonary edema, backache double vision, headache, convulsions due to cerebral edema can be observed. In all patients with idiopathic edema NaCl tolerance is reduced. Psychiatric symptoms did not occur in our cases. Cardiogenic, renal, hepatic, inflammatory, lympho-genic, allergic and thyreogenic causes could be excluded. Though distinctive hormonal imbalance could not be proved, the following features are nevertheless in favor of hormonal etiology of the edema: Preponderance in females, improvement after pregnancy, comparatively low pregnandiol excretion during the second half of the cycle and diminished salt tolerance. The female sex hormones and the angiotensin-aldosteron-system may play some part in the genesis of the idiopathic edema. We did not find any increase in the aldosterone excretion or any changes in the tests which depend on ADH secretion. The injection of 10 mg of progesterone, which has a natriuretic effect and the metabolic end product of which is pregnandiol in urine, given to one of our patients on the 15th, 16th and 17th day of the cycle was followed by loss of edema. During the formation of the edema there was an increase in plasma volume, a decrease of hematocrit, but no change in serum osmolality or serum sodium. This points to isotonic hyperhydration. The most effective therapy is a strict salt restriction and in case of obesity an additional restriction in caloric intake. Authors’ addresses: Dr. H. Brass, Prof. Dr. R. Heintz, I. Medizinische Universitätsklinik, Ludwig-Rehn-Strasse 14, 6 Frankfurt a.M. and Prof. Dr. G. Stark, Universitätsfrauenklinik, 65 Mainz (Germany).

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Dietary methionine and its influence on cystine excretion in cystinuric patients
The intake of methionine containing foods was restricted in one cystinuric patient. L-methionine was administered to three other cystinuric patients in amounts of 1 g daily. Neither experiment influenced the urinary excretion of cystine to an appreciable extent.
Our experiment of L-methionine administration was undertaken in the hope of furnishing this precursor to homocysteine, and thus making an increased amount of homocysteine available for the formation of the more soluble homocysteine -cysteine disulfide. In this manner more cysteine might be diverted from the oxidation to the poorly soluble cystine. The amount of disulfide did indeed increase, as did the excretion of cystathionine and total sulfur. However, the excretion of cystine was not altered materially, neither was the excretion of ornithine, lysine, arginine and other amino acids.
Previous studies which found an increased cystine excretion with high methionine intake and a decrease with methionine restriction, employed methods which in fact measured not only -SS- but also -SH compounds, so that their values comprise not only cystine but also the homocysteine disulfide; the excretion of the latter is indeed dependent on methionine intake. The results of this study suggest that the dietary restriction of methionine is of doubtful merit in the management of cystinuric patients.
Author’s address: Dr. H.H. Zinneman, Clinical Laboratories, Veterans Administration Hospital, Minneapolis, Minn. (USA).
Mortality trends for acute and chronic nephritis and infections of the kidney
Analysis of published mortality data for the United States and England and Wales showed that death-rates from acute and chronic nephritis (as defined by the International Statistical Code) fell between 1950 and 1964 by about 65% but that there was a concomitant rise in the death-rate from infections of the kidney—148% in the USA, 163% in England and Wales. The decrease in the rates for nephritis seemed to be explained in part by competition from cardiovascular disease for the position of underlying cause of death. While the published death-rate for nephritis declined that for cardiovascular disease (CVD) rose and CVD as a percentage of all underlying causes with which chronic nephritis was associated rose from 5.5% in 1940 to 55.5% in 1955. Diabetes mellitus also appeared to be a diagnosis competing for the position of underlying cause, due probably to the increasing recognition of diabetic nephropathy during the 1940-55 period. The interest in urinary tract infection during the past 20 years may have led to its more frequent diagnosis as a cause of death, seemingly at the expense again of chronic nephritis, particularly in young females. However, despite the evidence for a purely arte-factual explanation for the rapid decline in the death rates for the chronic nephritis, the possibility that a true change may have taken place in the natural history of the diseases is not ruled out. It was estimated from mortality data that 5.1 per 100,000 persons aged 15 to 55 in the United States would be eligible for chronic intermittent dialysis per year.

Author’s address: Dr. David M. Kessner, Yale University School of Medicine, New Haven, Conn. (USA).

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Hyperparathyroidism as the cause of hyperaminoaciduria and phosphaturia in human vitamin D deficiency
The effect of Vitamin D deficiency on mineral metabolism and on renal tubular function of 39 human infants was evaluated. Three stages of deficiency were observed: Stage I, hypocalcemia and minimal rickets; Stage II, normocalcemia, hypophosphatemia, hyperaminoaciduria, and moderate rickets; Stage III, hypocalcemia, hypophosphatemia, hyperaminoaciduria, and severe rickets. Hypophosphatemia and hyperaminoaciduria reflected diminished net tubular reabsorption of solute. Tubular dysfunction was rapidly suppressed by induced hypercalcemia and was exaggerated by exogenous parathyroid hormone, despite persisting Vitamin D deficiency. Secondary hyperparathyroidism was proposed as the cause of the renal tubular dysfunction in Vitamin D deficiency.

Studies in the rat (Grose, J. and Scriver, C.R.: Amer. J. Physiol. 214: 3170, Feb. 1968), designed to test the importance of parathyroid hyperactivity in the genesis of tubular dysfunction of Vitamin D deficiency, and embracing procedures precluded in human investigations, confirmed that tubular dysfunction is parathyroid-dependent in vitamin D deficiency.

Author’s address: Dr. D. Fraser, DeBelle Laboratory for Biochemical Genetics, McGill University, Montreal Children’s Hospital Research Institute, Montreal (Canada).

Albumin metabolism in the nephrotic syndrome in adults
1. Thirty adult nephrotic patients with normal or only slightly elevated serum creatinine were investigated with radioiodinated albumin.
In nineteen cases an increased fractional catabolism of albumin (percentage of intravascular mass/day) was demonstrated. In the same nineteen patients the absolute amount of albumin degraded was normal or subnormal. The rate of synthesis of albumin was increased in eleven of thirty patients and decreased in none. The average percentage of total albumin mass located intravascularly, was greater than normal. As yet there is no explanation for the elevated fractional catabolism, but the present results are compatible with the hypothesis that albumin degradation in the kidney is increased in nephrosis. 

Author’s address: Dr. H. Jensen, Medical Department P, Rigshospitalet, Copenhagen 0 (Denmark).

Renal hemodynamics and albumin clearance in nephrotic syndrom in relation to different intake of protein and water / Nierenhämodynamik und Albuminclearance bei nephrotischem Syndrom in Abhängigkeit von unter-schiedlicher Nahrungseiwiss- und Wasserzufuhr


To study the influence of high protein diet on the clearances of inulin, PAH and albumin, 7 patients with nephrotic syndrome were placed on low (30 g/day) and high protein diets (120 g/day) for a 10-day periods. Clearances were performed at the end of each 10-day period. High protein diet induced a reduction in GFR and clearance of PAH by approximately 30%. The excretion of albumin increased by approximately 100%. These alterations were attributed to functional changes, actually analysed by the authors.

Author’s address: Dr. R. Kluthe, Med. Universitäts-Poliklinik, Bettenabteilung, Wonnhalde 1-5, 78 Freiburg i.Br. (Germany).

Influence of the glomerular filtration rate on the maximum tubular reabsorption of glucose in infants / Einfluß der glomerulären Filtrationsrate auf die tubuläre Glukosereabsorption bei Kindern


Glomerular filtration rate (GFR) and maximum tubular reabsorption of glucose (%g) were determined in 10 infants and children aged 14 days to 6½ years. In agreement with experiments performed on animals by other authors we found a linear correlation between GFR and %g.

Changes in the GFR result in a proportional alteration of TmG. The cause for this correlation is unknown. Experiments using the microperfusion method on single rat nephrons indicate, that this correlation can be attributed to a change in the internal diameter of the proximal tubule. The ratio GFR/TmG expressing the glomerular-tubular balance—is higher than in adults and dependent on the age of the infant: the younger the child, the higher is the ratio. During the first month of life the size of the proximal tubule is relatively short in comparison with the glomerulus. We suppose that this is the cause for age dependence of the ratio.

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The relation between secretion of urate and / >-aminohippurate in the rabbit kidney


The effect of various substances on the renal excretion of urate in rabbits anaesthetized with pentobarbital was investigated. In the control periods, urate clearance exceeded inulin clearance, indicating net tubular secretion of urate. During infusion of increasing amounts of PAH or Diodrast urate excretion was reduced in proportion to the secretory rate of these substances, and at maximal secretion rates of PAH or Diodrast urate clearance was a little smaller than inulin
clearance. Stop-flow experiments showed that tubular secretion of urate was almost abolished at maximal values for secretion of PAH or Diodrast. On the other hand, PAH secretion was only partially inhibited during infusion of urate. 2,4-dinitrophenol, fumarate, succinate, salicylate, and probenecid depressed the excretion of both urate and PAH, but the tubular secretion of urate was more affected than that of PAH. It is concluded that urate and PAH are secreted by a common transport system in the rabbit kidney, but that the affinity of the transport system for urate is smaller than for PAH.

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