Diagnosis import of virus-like particles in the glomerular endothelium of patients with systemic lupus erythematosus


Examination of existing files of electron photomicrographs of renal biopsies showed virus-like intracellular inclusions in glomerular endothelial cytoplasm from 29 of 30 patients with an unequivocal diagnosis of systemic lupus erythematosus (LE) and in none of a group of 37 with a variety of non-lupus renal lesions. The virus-like particles were found in the glomerular endothelium of two patients with discoid lupus and histologically normal appearing glomeruli. In both these patients systemic lupus, including nephritis, subsequently developed. The particles were found also in 4 of 6 cases of suspected but not proved systemic lupus. Renal-biopsy material from 2 patients who had positive LE-cell preparations while receiving hydralazine did not contain the virus-like particles. This study does not establish the nature or etiologic import of these particles but indicates that their presence is diagnostically helpful in systemic lupus regardless of the extent of histologic or functional involvement of the kidney.

Author’s address: Dr. L.E. Earley, Cardiovascular Research Institute, University of California, School of Medicine, Third and Parnassus, San Francisco, CA 94122 (USA)

Pathology of the nephrotic syndrome in children: A report for the international study of kidney disease in children


The renal biopsy findings in 127 previously untreated children with the nephrotic syndrome of recent origin are reported. ‘Minimal changes’ were observed in 98 (77%) patients, and most responded to corticosteroid therapy. In addition to the well known forms of chronic glomerulonephritis, two distinct but less well recognized conditions are described. In one, focal sclerosing lesions involve the glomeruli to an increasing extent, and may ultimately lead to renal failure; in its early stage the condition may be difficult or even impossible to distinguish from ‘minimal changes’. Most cases are steroid-resistant. In the other condition there is mild mesangial thickening and proliferation similar to that observed in resolving post-streptococcal nephritis. Although some cases may be steroid-resistant and the clinical course protracted, the prognosis is generally favorable.

Author’s address: Dr. J. Churg, Mount Sinai School of Medicine, City University of New York, New York, N. Y. (USA)

The role of fibrinogen in renal disease: III. Fibrinolytic and anticoagulant treatment of nephrotoxic serum nephritis in mice


Nephrotic serum nephritis was induced in mice by rabbit antiserum. The natural history of the lesion was observed for periods up to 30 days. Basement membrane
thickening occurred with only minimal endothelial cell proliferation. Glomerular obsolescence with capsular proliferation was found at 30 days. Immunofluore-scent studies showed deposition of rabbit y-globulin, mouse y-globulin and mouse complement along the basement membranes, while mouse fibrinogen or fibrin was deposited more diffusely within endothelial and mesangial cells as well as along the basement membranes. Fibrinolytic therapy with urokinase decreased the fibrinogen or fibrin in glomeruli but did not lessen proteinuria or progressive thickening of the glomerular basement membranes. Heparin neither reduced fibrinogen or fibrin deposition nor improved the histological appearance. It was concluded that while fibrinogen or fibrin deposition plays an important role in the endothelial cell proliferation and crescent formation characteristic of proliferative types of glomerulonephritis, as shown in other studies, it is not a primary mediator in the pathogenesis of the membranous lesions of nephrotoxic serum nephritis in the mouse.

Author’s address: Dr. J.D. Briggs, Royal Infirmary, Glasgow C4 (Scotland)

Long-term follow-up of renal function and histology after acute tubular necrosis
Renal function and histology were evaluated in 30 patients surviving acute tubular necrosis who were followed from 2 to 15 years. Clinical recovery was complete in all patients. Endogenous creatinine clearance was abnormal in 37%, whereas, 47% failed to concentrate their urine to an osmotic urine to plasma ratio of 3.0. Two patients have an unexplained progressive deterioration in glomerular filtration rate. Ischemic acute tubular necrosis was followed by an abnormal creatinine clearance in 44% compared with 25% of those with a toxic cause. Toxic acute tubular necrosis was followed by a concentrating defect in 58% compared with 39% of the ischemic group. Phenolsulfonphthalein, intravenous pyelogram, maximal acid excretion, urinalysis and urine cultures were abnormal in fewer patients. Renal histological changes were minimal and nonspecific. Patients recovering from acute tubular necrosis are clinically normal and most have normal renal histology. Renal function will approach but not always achieve normal levels in the majority. Progressive deterioration of renal function may occasionally occur.

Author’s address: Dr. Donald T. Lewers, Renal and Electrolyte Division, Georgetown University Hospital, Washington, DC (USA)

Immediate and long-term prognosis in acute renal failure
The rate and extent of return of renal function and its maintenance after initial improvement and factors influencing renal recovery were studied in 186 patients with acute renal failure. Renal function was evaluated by standard clearance techniques (C\textsubscript{iin}, C\textsubscript{PAH} = \text{aminohippurate}) in 40 of 87 survivors. The interval between the episode of acute renal failure and follow-up averaged 45.0 months. Of 36 patients studied more than 3 months after recovery, 22 (61%) had ‘incomplete’ renal functional recovery, or Cin\textsubscript{ut}/\text{Cin}, and C\text{PAH} values more than 1 SD below expected values. Patients with impaired clearances were older at the onset of acute renal failure and had a longer period of oliguria than patients who had ‘complete’ recovery. Failure to regain expected clearance values was apparent in the third decade, and patients 40 years of age or older attained at most 75% of normal values. Serial observations in some suggested a decline in renal function after initial improvement.

Author’s address: Dr. Jack W. Hall, Division of Nephrology, Mayo Clinic and Mayo Foundation, Rochester, Minn. (USA)
Renin and acute renal failure: studies in man
Plasma renin concentration was increased, usually appreciably in 22 out of 25 patients with acute renal failure, the average value being 226 U/L (mean for normal subjects 8.2 U/L). The highest renin values were found in the first 10 days of the disease; lower and sometimes normal values were found subsequently. Unequivocal acute tubular necrosis was present in only 2 of the 8 cases examined post mortem. These findings are compatible with the proposal that an excess of renin and angiotensin may act within the kidney to produce renal failure (acute).
Author’s address: Dr. J.J. Brown, Blood Pressure Unit, Western Infirmary, Glasgow W 1 (Scotland)

Bone fluoride in patients with uremia maintained by chronic haemodialysis
Bone specimens from 42 patients with end-stage renal disease and from 9 patients with renal or bone disease were analyzed for the content of fluoride, calcium and phosphorus. Thirty-one patients were treated with chronic hemodialysis for periods ranging up to 56 months by employing dialysate made up with tap water containing 1 ppm fluoride. Fluoride content of cortical hard bone was increased in the great majority of the patients with kidney disease. There was no significant difference with bone fluoride content between the patients who were dialyzed and those who were not. However, the content of calcium and phosphorus was lower in the patients treated by hemodialysis. There was no correlation between duration of uremia or number of dialyses and bone fluoride content.
Author’s address: Dongsuk Kim, M.D., Department of Medicine, Northwestern University Medical School and V. A. Research Hospital, Chicago, Ill. (USA)

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Summaries – Resumes
Arteriovenous vein graft for chronic hemodialysis: a preliminary report
A new method is described for creating an arteriovenous fistula for use in hemodialysis by venipuncture technique in patients who have proved unsuitable for creation of the usual arteriovenous fistula. A segment of long saphenous vein is inserted as a bridge between an artery at the wrist and a vein below the antecubital skin crease. The 25- to 30-cm vein graft may serve as a site of veinpuncture in patients who have no other suitable veins for hemodialysis. Two such graft arteriovenous fistulas were created in female patients in whom previous attempts to create the standard arteriovenous fistula had failed.
Author’s address: Dr. M. Mozes, Department of Surgery, Tel-Hashomer Government Hospital, Tel Aviv (Israel)

Hyperaluminaemia from aluminium resins in renal failure
The effect of ingestion of aluminium cycle resins and aluminium hydroxide on serum-aluminium levels, determined by neutron activation, colorimetry and atomic absorption spectrophotometry were studied in patients with advanced renal failure. Raised serum-aluminium levels were found in 6 out of 20 patients taking 45 g of aluminium resin or more a day, in 2 out of 6 patients taking 3-6 g of aluminium hydroxide a day, and in 3 out of 6 patients on dialysis who were not taking
oral aluminium salts but were fortuitously exposed to dialysate with a relatively high aluminium content. It is concluded that aluminium resins and salts should be avoided in renal failure until more is known about the possible toxic effects of hyperaluminaemia and more rigid control of aluminium concentration in dialysis fluids is necessary.

Author’s address: Prof. G.M. Berlyne, Central Negev Hospital, Beer-Sheva (Israel)

The haemodynamic response to chronic renal failure as studied in the azot-aemic state


Fifty-nine haemodynamic studies were performed in 21 patients with chronic renal failure, usually on a day following at least 6 h of haemodialysis. A miniature polyethylene tubing was ‘floated’ into the right ventricle under manometric guidance without x-ray control. Indocyanine green was injected into the right ventricle for cardiac output estimations. Cardiac index, stroke volume, total peripheral resistance and mean arterial pressure were all found to be high. The total blood volume measured with $^{125}$I isotope was not significantly expanded. Three patients with acute pulmonary oedema had normal central venous and right atrial pressures, showing that pulmonary capillary permeability is probably the principal factor in the pathogenesis of the ‘uraemic lung’, and that in these circumstances monitoring of central venous pressure is not reliable in warning the physician of impending pulmonary oedema.

Author’s address: Dr. J.W. Mostert, Department of Anesthesia, Regional New York Kidney Center, Buffalo, N. Y. (USA)

Hyperparathyroidism in chronic renal failure: assessment of autonomy by plasma-parathyroid-hormone response to alterations in calcium


Increased concentrations of immuno-assayable parathyroid hormone were found in the blood in 80% of patients with chronic renal failure. Responses in circulating hormone concentration to alterations in plasma-calcium were studied in 6 patients. In 4, acute elevations in calcium were associated with reciprocal falls in the circulating concentration of parathyroid hormone; and similar responses were demonstrated in secondary hyperparathyroidism associated with hypocalcaemia due to causes such as malabsorption. In two patients with renal failure, elevation of calcium had no effect on hormone concentration and a similar lack of response was demonstrated in primary hyperparathyroidism due to parathyroid adenoma. Investigation of whether or not acute alterations in calcium cause reciprocal alterations in circulating parathyroid hormone concentration may enable autonomy of the parathyroid glands to be recognised in patients with chronic renal failure.

Author’s address: Dr. R.M. Buckle, Department of Endocrinology, General Hospital, Southampton (England)

Prolongation of canine renal homograft survival by post-transplantation treatment with antithymocyte serum


A relatively nontoxic antiserum raised in rabbits by the injection of neonatal puppy thymocytes was shown to significantly prolong canine renal homograft survival when given only after transplantation without any preoperative immuno-suppressive therapy. A single injection of 6.5 ml/kg of this antiserum up to 24 h after transplantation, produced prolonged survival in some animals; and if weekly injections of 1 or 2 ml/kg were given after the initial dose, then
prolongation of survival was regularly obtained. The addition of small doses of azathioprine to serum treatment appeared to lengthen survival further. Pretreatment of the host animals with no treatment after transplantation also produced significant immuno-suppression.

Author’s address: Dr. E.J. Hinchey, Department of Physiology, McGill University and Montreal General Hospital, Montreal (Canada)

Summaries – Resumes

Kidney transplantation for rapidly progressive glomerulonephritis

Two patients oliguric from rapidly progressive glomerulonephritis received successful kidney grafts from cadaver donors. Each had poststreptococcal immune-complex nephritis. They both tolerated periodic haemodialysis and bilateral nephrectomy well. One patient, despite stable renal function, had persistent proteinuria since transplantation. Examination of a biopsy specimen, taken 2 years after grafting, showed electron-dense deposits consistent with recurrent immune-complex disease, but no proliferative glomerulonephritis. It is concluded that patients with renal failure from poststreptococcal rapidly progressive glomerulonephritis can be treated successfully by haemodialysis and transplantation.

Author’s address: Dr. J.A. Richardson, Dialysis Center, US Public Health Service Hospital, San Francisco, Calif. (USA)

Cure of dysgerminoma with widespread metastases appearing after renal transplantation

It has been recently noted that 13 cancers had appeared in approximately 2,000 recipients of renal transplant. This figure (5/1,000 under the age of 40) greatly exceeds the risk in the population (8.2/100,000). This increased incidence constitutes evidence that the immune surveilance mechanism against malignant mutations is impaired by immunosuppressive drugs. Almost all patients died suggesting a more rapid course of the malignant process of such cases. This report documents a patient with malignant dysgerminoma with wide-spread metastases appearing two years after transplantation. The tumor was obliterated by intensive therapy (radiotherapy) despite the fact that immunosuppressive drugs were maintained throughout. The patient expired 51 months after transplantation (16 months after discovery of the tumor) and no evidence of cancer was found at the time of death.

Author’s address: Dr. R.L. Simmons, Box 185, Mayo, University of Minnesota Hospital, Minneapolis, MN 55455 (USA)

Selection of allograft recipients by leucocyte and kidney cell phenotyping

A system is described for recipient selection by typing cadaver donor leukocytes and kidney cells. HL-A factors were detected on kidney cells and not on leukocytes of the same individual by both the fluorochromasias and 51Cr cytotoxicity techniques. HL-A 7 and 8 were the antigens most frequently represented on kidney cells and not leukocytes. Several patients who rejected their grafts, developed antibodies against only the donor’s kidney cells. Twelve of the 34 grafts had one or more additional antigen mismatches for kidney cells than for leukocytes, making the match grade worse in 44% of the patients. It is suggested that matching
recipients for HL-A factors on both leukocytes and kidney cells will improve the long-term results of cadaver transplantation.

Author’s address: Dr. S.L. Kountz, Department of Surgery, University of California School of Medicine, San Francisco, Calif. (USA)

Hypercalcemia after renal transplantation

Hypercalcemia and hypophosphatemia after renal transplantation are described. Serum and urine calcium, phosphorus, creatinine and serum levels of parathyroid hormone (PTH) were followed in 34 patients who received transplants. Hypophosphatemia occurred in nearly all those with successful transplants and correlated with the administration of oral hydroxide antacids. Clinical effects of phosphorus depletion included weakness, intention tremor, bone pain, pseudofractures and hypercalcemia. Treatment with oral phosphate reversed the abnormalities. The administration of aluminum phosphate gel did not induce hypophosphatemia. Hypercalcemia of 12 to 15 mg% necessitated subtotal parathyroidectomy in 5 patients, two of whom had oliguria and one polyuria due to hypercalcemia.

Author’s address: Dr. G.H. Schwartz, Cornell University Medical College, 1300 York Avenue, New York, NY 10021 (USA)

Hypermagnesemia after renal homotransplantation

The clinical and biochemical features of 3 patients who developed magnesium intoxication after renal homotransplantation are described. All patients were receiving magnesium-containing antacids at a time when renal function was reduced. When renal function was adequate, magnesium supplementation in the form of antacids resulted in an eight-fold increase in urinary magnesium and only a modest rise in serum levels. However, during transplant rejection urinary magnesium rapidly falls, and hypermagnesemia may develop. Hemodialysis is the most effective method of treating this complication in the transplant patient. Magnesium intoxication represents an additional hazard of high dose antacid therapy in the post-transplant period. The serum magnesium concentration should be routinely monitored in transplant recipients with reduced renal function receiving magnesium-containing antacid. At times of severely compromised renal function these antacids should be avoided.

Author’s address: Dr. A.C. Alfrey, Department of Internal Medicine, University of Colorado Medical Center, Denver, Colo. (USA)

Urinary fibrin/fibrinogen degradation products after renal homotransplantation

Using a tanned red-blood-cell haemagglutination-inhibition immunoassay (T.R.C.H.I.I.), urinary fibrin/fibrinogen degradation products (F.D.P.) were studied daily in thirty-four recipients of renal allografts for varying periods of time. All episodes of clinical rejection coincided with a profoundly abnormal elevation of F.D.P. excretion. However, there were other elevations which are considered to represent occult spontaneously reversible rejection. Administration of antilymphocyte serum was also associated with grossly abnormal increased F.D.P. excretion. Successful improvement in renal function after rejection crises,
subsequent to increased immunosuppression and/or the introduction of anticoagulants seemed to be related to a reduction in urinary F.D.P. content.

Author’s address: Dr. A.R. Clarkson, South-East Scotland Regional Blood Transfusion Centre and Medical Renal Unit, Edinburgh (Scotland)

Long-term integrity of renal function in cadaver allografts


In general, renal transplant recipients of cadaver kidneys fare less well than recipients of living related donor kidneys in regard to incidence of rejection episodes and stability of renal function. Specific renal function measurements of four cadaver recipients surviving a mean of 29 months without experiencing rejection are compared with those of seven well-matched living related donor recipients who have maintained optimal stability of renal function a minimum of one year following transplant. Renal function of the cadaver group compared favorably and in certain instances exceeded that of the living donor group. These data indicate that even without histocompatibility testing, transplantation of cadaver kidneys can occasionally result in a sustained preservation of renal function which closely parallels that seen in well-matched recipients. Excluding chance histocompatibility, the factors related to such therapeutic success are unknown.

Author’s address: D. Shelp, M.D., 1300 University Avenue, Madison, WI 53706 (USA)

Renal homotransplantation in children


Renal homotransplantation has been performed in 19 children with terminal, irreversible, renal disease. Techniques used in adults for preoperative and operative management have been successfully modified. There have been no technical problems related to uraterovesical and vascular anastomoses. Rejection episodes were mild and when recognized and appropriately treated early were easily reversed. Normal growth patterns of children are altered by the presence of renal disease and during periods of heavy steroid administration. However, favorable growth curves have been noted in all children under 15 years of age in long-term follow up. The overall recipient and transplant survival was 94.7%. The general overall results with renal homotransplantation in children and particularly the low incidence of late problems have been encouraging.

Author’s address: L.L. Gonzalez, M.D., Department of Surgery, University of Cincinnati College of Medicine, Cincinnati, OH 45219 (USA)