Survival data for patients undergoing chronic intermittent hemodialysis
Survival data have been compiled on 302 patients undergoing chronic intermittent hemodialysis in 14 centers. This represents approximately one third of the total dialysis population in the United States as of the closing date of the study, June, 1967. Fifty-three patients have been observed for 2 or more years. Forty-eight patients have died. The survival rate after 1 year on dialysis was 87%. Two and 3 year survival rates were 77.3 and 67.4% respectively. Computed 7 year survival rate is 57.8%. Males and females survived equally well on dialysis.
The group over the age of 46 had a higher fatality rate at the 1, 2, and 3 year intervals; however, cumulative survival rates were not significantly different between the under 45 and over 46 years groups at the 1 year level (p > 0.05). The survival curve describes a constant geometric function with time, indicating that prognosis neither improves nor worsens for the population over a 3-year period on dialysis. This phenomenon is not unique, having been described in a number of other chronic diseases.
Given the premise that these patients represent a population in a fatal situation were it not for the therapy they were receiving, chronic intermittent hemodialysis appears an effective means of prolonging the life of the uremic patient.
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Initial treatment of renal allografts with large intrarenal doses of immuno-suppressive drugs
This report concerns 2-½ years experience with the intrarenal administration of immunosuppressive drugs applied immediately after transplantation for 1 to 3 days. This procedure was carried out in 61 patients who received renal allografts from living donors (52 related and 9 unrelated). Immediately after transplantation, a solution containing 1-2 g of methylprednisolone, 10,000 units of heparin, and 0.5 mg actinomycin D in 1000 ml of physiological saline solution was infused into the graft via a catheter in the renal artery. The patients were maintained indefinitely on oral azathioprine 1.5-2 mg/kg/day and prednisone 0.2-0.5 mg/kg/day starting two days before transplantation. Of 18 rejection crises in the first three months, only one could not be reversed by repeating the immunosuppressive infusion, either intrarenally or systemically. The patient survival rate was 97% and the graft survival rate was 93%. Except for 1 patient, renal function was good as evidenced by creatinine clearance of 45 ml/min or greater, effective renal plasma flow of 250 ml/min or greater, and a serum creatinine of less than 2mg/100 ml.
Authors’ address: Dr. Samuel L. Kountz, Department of Surgery, University California School of Medicine, San Francisco, CA (USA).
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Dialysed egg as nitrogen source in dietary control of chronic renal failure
Homogenized whole fresh eggs, after dialysis for 72 h against distilled water and vacuum freeze-drying, yielded a powder (*K-lov*) which contained 8.4 g of nitrogen/100 g, but was low in potassium and sodium (0.09 and 0.28 mEq/g nitrogen, respectively). The powder which could be flavoured with calcium di-glutamate was given to 6 patients in chronic renal failure in a metabolic unit. Metabolic balance studies showed this diet to be at least as effective as the more familiar Giovanetti-Giordano diet in achieving nitrogen balance. The authors point out that ‘K-lov’ diet is also effective in controlling hyperkalemia when potassium retention is a problem. Reprints from Dr. D.J. Beale, Metabolic Research Unit, East Birmingham Hospital, Birmingham, 9 (England).

Circulating lymphocyte depletion in preparation for renal allotransplantation
The survival of patients who receive renal allografts has improved with the development of expertise in the management of these patients, especially in the use of immunosuppressive drugs. Despite these improved results, patients still die from drug overdosage leading to a critical suppression of humoral defenses and subsequent infection. The ideal recipient preparation by alteration of cellular immunity with maintenance of adequate humoral defenses eludes present day therapy. Suppression of immunologic activity by lymphatic drainage or lymphatic lymphocyte destruction has been attempted by a number of investigators employing a variety of techniques with variable success.
The importance of reinfusing the cell-free lymph for maintenance of adequate levels of lymph and serum proteins was studied. Prolongation of renal allograft survival was obtained solely by means of circulating lymphocyte depletion without seriously affecting the level of circulating immunoglobulins. These results were achieved by depleting the patients of lymphocytes prior to transplantation.
Author’s address: Dr. Jay C. Fish, Department of Surgery, University of Texas Medical Branch, Galveston, TX (USA).

Serotyping for homotransplantation: XIX. Experience with an interhospital scheme of cadaver-kidney sharing and tissue typing
During the first 11 months of an interhospital program of cadaver kidney sharing and tissue typing, 77 possible donors were typed and 47 kidneys from 30 donors were transplanted into 46 recipients. Sixteen transplants were compatible with respect to the five leukocyte antigens considered. There was a tendency to accumulate recipients with few or rare antigens who were difficult to match. When the
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effect of recipient-pool size was studied under a hypothetical situation, 80% of potential transplants were compatible if both donor kidneys were transplanted into two recipients selected from the pool of eight hospitals whereas, only 25% were compatible if the recipients were selected from the ‘donor’ hospital alone. Interhospital cooperation could allow a maximum utilization of cadaver kidneys and rapidly provide data for a critical evaluation of tissue typing in cadaver-organ transplantation.
Author’s address: Dr. Ramon Patel, Department of Surgery, University of California School of Medicine, Los Angeles, CA 90024 (USA).

Oral calcium absorption in patients with renal failure treated by chronic hemodialysis

Oral calcium absorption, measured by a simplified isotopic method, has been assessed in patients undergoing chronic hemodialysis. By comparison with normal subjects, these patients had markedly impaired absorption irrespective of the duration of treatment or the number of dialyses. Responses to vitamin D administration were nil at 25,000 units but the pattern of absorption was successively increased into the low normal range by 50,000 and 100,000 units. It is concluded that dialysis successful by conventional criteria may fail to correct the defect in calcium absorption which accompanies renal failure. The resultant calcium deficiency may be important in the pathogenesis of renal osteodystrophy during dialysis.

Author’s address: Dr. Saul M. Genuth, The Shirley and Maurice Saltzman Institute of Clinical Investigation, Division of Medicine, Mt. Sinai Hospital, Cleveland, OH (USA).

Influence of HL-A incompatibility on cadaveric renal transplantation

The effect of graft incompatibility with respect to antigens of the HL-A system were analyzed in 52 cases of cadaveric renal transplantation followed for a period of between 3 months and 2 years after transplantation. The total number of graft incompatibilities was significantly correlated with the subsequent clinical status of the patients. When incompatibility was limited to one antigen or less, 75% of the patients have had good or moderately good transplant function to the present time. As the number of incompatibilities increased, the proportion of patients whose transplants functioned satisfactorily diminished. Death of the patient or graft failure occurred in all 8 cases in which there were five or more detectable incompatibilities. It is concluded that prospective HL-A antigen typing of donors and recipients should be carried out whenever possible, so that multiple incompatibilities can be avoided.

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The diagnosis of rejection of renal allotransplants in man

The changes in 8 simple laboratory determinations on blood and urine in 20 rejection episodes after renal allotransplantation have been analyzed. The most significant changes were a fall in the 24-hour urinary urea and osmolar excretion; these were also the earliest and most reliable evidence of a rejection episode. Changes in 24-hour urine volume and platelet-count were also significant but were harder to evaluate. In all rejection episodes there was a significant decrease in creatinine clearance which returned to previous levels after treatment. The changes in blood urea, 24-hour urinary protein, and sodium excretion were neither early nor significant.

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Peritoneal sodium transport during hypertonic peritoneal dialysis: Physiologic mechanisms and clinical implications
Hypertonic peritoneal dialysis is frequently utilized to remove excess sodium and water from the body. It is shown that the ultrafiltrate is probably of extracellular origin and is invariably hyponatric to serum. Sodium accompanies the bulk flow of water in varying amounts from patient to patient. Factors that influence the transperitoneal transport of sodium in response to slight diffusion gradients and the solvent drag effect of bulk flow, seem to include peritoneal membrane permeability and the extracellular anionic environment. A method for the proper management of sodium and water removal by hypertonic peritoneal dialysis is described by which hypernatremia, a frequently reported complication may be prevented. The increase in serum sodium concentration results from the proportionally greater removal of extracellular water than sodium and is not dependent on the development of hyperglycemia or sodium diffusion from dialysate to extracellular fluid, as has been previously reported.

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Hypertension in end-stage renal disease
Two distinct patterns of response of blood pressure to achievement of dry weight (no clinical evidence of edema and optimal body sodium content and volume of water) antihypertensive drugs and bilateral nephrectomy were documented in 40 unselected patients with end-stage renal disease. Group 1, 35 of 40 patients, was characterized by an excellent response of blood pressure to dry weight and the ability to remain normotensive without antihypertensive drugs as long as dry weight was maintained. Group 2, five of 40 patients, had persistent hypertension in spite of dry weight, a poor response to antihypertensive drugs and a prompt reduction of blood pressure after bilateral nephrectomy. A further important difference between these two groups was seen in the serum renin values obtained at the initiation of therapy. In Group 1 values ranged from 0 to 1.02 Goldblatt Units × 10^-4 per milliliter of serum (mean 0.31) whereas those in Group 2 ranged from 1.88 to 4.60 (mean 3.37). Serum renin levels appear to be of value to predict blood-pressure responses.

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Erythraemia in renal transplantation
Seven cases of erythraemia following successful renal transplantation are described. Four patients developed thrombo-embolic pulmonary complications and two other patients had thrombotic episodes. In the present series, the erythraemia did not appear to be necessarily a bad prognostic sign as far as rejection is concerned. Six of the seven patients were still alive at the time of the report; one six months after the development of erythraemia, three a year later, and one three years afterwards. Two cases had only recently developed this complication. The authors stress that erythraemia is associated with thrombotic complications and suggest that anticoagulation and/or venesection is indicated.

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Intracellular magnesium depletion in chronic renal failure
Skeletal-muscle magnesium, estimated as an index of body magnesium store, was significantly lower (p less than 0.05) in 12 patients with advanced chronic renal failure (most of whom showed hypermagnesemia) than in controls matched for sex and age. There is indirect evidence
that renal insufficiency sets at a new level the control of magnesium gradient across the cell membrane.

Depletion of total-body (intracellular) magnesium was probably due to inadequate intake, as supplied by the modified Giovannetti diet, and impaired absorption, exacerbated by frequent vomiting. Peritoneal dialysis did not contribute greatly to magnesium depletion in the patients. Two patients had clinical features of hypermagnesemia (lethargy, drowsiness, depressed tendon jerks, general flaccidity, relative hypotension and prolonged PR intervals, QRS complexes and QT segments on the electrocardiogram), but no patient had features of magnesium depletion.

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Plasma renin activity, sodium balance, and hypertension in a group of renal transplant recipients

Plasma renin activity was determined 114 times in 13 allograft recipients and related to blood pressure, sodium excretion and allograft rejection. Low renin activity was present in 4 of 5 bilaterally nephrectomized patients before transplantation. Allografted kidneys secreted renin promptly after transplantation with one exception. In 4 of 6 patients with acute tubular necrosis renin was elevated but returned toward base line as renal function improved. In three rejection episodes studied, renin elevation occurred with local cobalt therapy in two episodes, while moderate elevation was noted in the third drug treated episode. Alterations in sodium balance influenced plasma renin activity. Although renin and blood pressure were correlated, changes in renin were seen in individual patients without corresponding changes in blood pressure.

Increased renin activity was observed with allograft rejection, radiation or acute tubular necrosis.

Author’s address: Dr. Tom H. West, Department of Surgery, University of Michigan Medical Center, Ann Arbor, MI (USA).

Immunologic competence in the lymph-dialyzed patient

Lymph dialysis, used in two patients with renal failure, maintained lymphocytes at a number that achieved ‘tolerance’ free of infection, as reflected by the ablation of usual immune responses within protracted periods of time.

When peripheral lymphocyte levels were maintained as high as 700 per cubic millimeter in one patient and as low as 500 per cubic millimeter or less in the other patient, neither demonstrated atopic or delayed hypersensitivity. Both also failed to produce primary or secondary antibody responses to antigen.

Lymph total complement and lymph beta 1C globulin proved to be about Va that of serum levels in the one patient in whom the levels were measured.

Neither lymph nor serum total complement varied much during the clinical course of this patient, but serum beta 1C globulin showed decline to about ¼ its normal value when the lymphocytes in the patient dwindled to less than 500 per cubic millimeter in the depletion period.

Serum and lymph immune gamma globulins G, M, and A measured in one patient reacted somewhat to an early Corynebacterium sepsis but otherwise varied little during dialysis. All globulin levels were depressed in the depletion period. Lymph values ranged from Vio, immunoglobulin G, to ¼, immunoglobulin M of serum values.
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Significance of the positive crossmatch test in kidney transplantation
Crossmatch tests of the prospective kidney-transplant donor’s lymphocytes with the serum of the
prospective recipient in 225 transplants showed that 8 of 195 with negative crossmatch failed to
function immediately in contrast to 24 of 30 with positive crossmatch (p less than 0.001).
Immediate failure occurred in significantly higher numbers among patients with a higher risk of
having antibodies such as multiparous females and patients receiving secondary transplants. The
effect was not a nonspecific one, for more immediate failures occurred among transplants from
unrelated than among those from related donors. The corresponding frequency of positive
crossmatch was also lower among related donors. The presence of preformed cytotoxic
antibodies against the donor appears to be a strong contraindication for transplantation.

Kidney transplants: Computer display of clinical and laboratory parameters the first 100 days
Data concerning 16 clinical and laboratory parameters from 30 patients who received cadaver
kidney transplants covering the first 100 post-transplant days were arranged and displayed by
computer, for the group as a whole and as several subgroups. Representative examples of the
plots of five day moving averages of daily means made by computer are presented for 7 patients
who had major rejections during the first 100 days and for 15 who survived this period without a
major rejection. Several relationships such as the possibility that a period of maximal rejection
activity occurred around the fifth post-transplant week and that during this time, the leukocyte
count did not move in parallel with the azathioprine dosage are discussed.

Early and late failures of human cadaveric renal allografts
Causes of failure of 85 allografts in a series of 123 cadaver kidney transplantations were
analyzed. Fifty-four failures (62%) occurred during the first three postoperative months, of
which more than half occurred during the first month. Rejection (43.5%) was the most common
cause of failure of an allograft, whereas infection was the most frequent cause of death of the
host. Thrombosis of the renal artery occurred in eight of ten allografts when ABO blood groups
were crossed from non-O-type donor to O-type recipient, but this complication was not seen
when blood groups were crossed from O-type donor to non-O-type recipient. All recipients well
matched by leukocyte antigens, and more than half of

those who were mismatched, had good graft function and minimal rejection episodes. Thy meet
omy and splenectomy made no difference in the incidence of rejection, but appeared to
predispose the patients to fatal infection.
Aseptic necrosis following renal transplantation

Of 27 patients who survived for 6 months or longer following renal homotransplantation, osseous changes developed in ten. Nine of these demonstrated aseptic necrosis of the femoral head, five had involvement of the hips alone, five showed aseptic necrosis at the knee joint, and two had aseptic necrosis of the humeral head. All patients with early necrotic changes were trained to use crutches and were told the dangers of unrestricted activity. Eight of the 10 patients were treated non-operatively. Objective improvement with time, however, was variable and did not occur in most cases.

Author’s address: Dr. R.L. Cruess, Royal Victoria Hospital, Montreal 2, P.Q. (Canada).

Physiologic responses of the transplanted human kidney: Sodium regulation and renin secretion

The denervated, transplanted kidneys of six patients who had received kidneys from live, related donors (one identical twin) were able to maintain normal sodium balance. Peripheral plasma renin activity on a high-salt diet was 354 ± 28 ng of angiotensin II (± SE) in the donors and 291 ± 39 ng per 100 ml in the recipients. Renin activity (low-salt diet) averaged 620 ± 50 ng in the donors and 700 ± 52 ng per 100 ml in the recipients. Aldosterone secretory rates were normal in the patients studied as were exchangeable sodium, potassium and body water. It is concluded that the denervated, transplanted human kidney can maintain clearance comparable with the donor kidney, and sodium regulation and renin secretion as evaluated in this study appear to be normal.

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A soluble glucose polymer for use in renal failure and calorie-deprivation states

‘Caloreen’, a glucose-polymer mixture, composed of 3% glucose, 7% maltose, 5% maltotriose, and 85% polysaccharides is soluble in water, less sweet than 88

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Platelet function in renal failure

Study of the bleeding tendency in uremia in 26 subjects, 10 of whom were bleeding, showed platelet counts and plasma coagulation factors to be normal. There was a significant inverse correlation between the level of serum urea nitrogen and creatinine, and the adhesiveness of the platelets. Platelet adhesiveness was significantly lower in bleeding subjects than in those without bleeding.

A prolonged bleeding time was more frequent in the group with bleeding. Abnormal prothrombin consumption was found only in bleeding subjects despite normal numbers of platelets and plasma coagulation factors.

The ingestion of urea in 10 normal volunteers prolonged the bleeding time in 5 and decreased the platelet adhesiveness, which fell to pathologic levels in eight.

These observations suggest a direct effect of urea or one of its metabolites on platelet function.

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Renal transplantation from cadaver donors

Sixteen hospitals cooperate in the supply of cadaver kidneys for renal transplantation. Of these, four have patients maintained by hemodialysis. All patients are tissue typed at the New South Wales Red Cross Blood Transfusion Service and form a common recipient pool. Potential kidney donors are tissue typed and the two recipients of the correct ABO blood group without circulating cytotoxic antibodies and with the best tissue matches are chosen to receive renal allografts. Should the donor die before the results of tissue matching are known, two patients are chosen and tissue typing is completed subsequently. Operations are performed simultaneously in two of the hospitals, and transplantation personnel operate in both hospitals. Both donor kidneys are used whenever possible. Since August, 1967, 54 transplantation operations were performed for 50 patients. Tissue typing was obtained 52 times and results were known before operation 49 times. Twelve patients died, the majority from rejection of the renal allograft and drug toxicity. Thirty-eight patients remain alive, all with functioning allografts. Of these, three required second operations after failure of first allografts. Renal function and rehabilitation of survivors are satisfactory. The incidence of early function of allografts was high, but 12 allografts were destroyed by rejection processes. Since commencement of the programme no patient referred with irreversible renal failure and suitable for renal transplantation has been denied treatment. It is concluded that cooperation between hospitals may enable the treatment of all young and middle-aged patients dying of renal failure by transplantation of kidneys from cadaver donors and the establishment of large recipient pools. Tissue typing can almost always be completed before operation, but further experience is required to evaluate its significance for transplantation from cadaver sources.

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In vivo effectiveness of the antibiotic colistin in preventing growth of pseudomonas aeruginosa

Colistin sulphate was shown to be more effective and more efficient than colistin methane sulphonate in controlling the in vitro multiplication of Pseudomonas aeruginosa [Furtado and Gorrill, 1968]. The next aspect of the investigation was to determine whether administration of
colistin could control in a quantitative and reproducible manner the in vivo survival and multiplication of the organism and the subsequent production of disease by Ps. aeruginosa. The in vivo experimental system described by Gorrill and De Navasquez [1964] was used in the present study (i) to investigate the effect of different concentrations of the two forms of colistin on the in vivo multiplication of Ps. aeruginosa in mouse kidneys during the 5 h after deposition of an intravenous inoculum, and (ii) to determine the role of the antibiotic in preventing or enhancing the production of experimental pyelonephritis. The results show that colistin sulphate is more effective than colistin methane sulphonate when introduced simultaneously with or after inoculation of the infecting organisms. Neither form was nephrotoxic to mice; repeated daily injection of either derivative for 5 days before infection with Ps. aeruginosa did not enhance the rate of production of experimental pyelonephritis. The rate of production of experimental disease was reduced by injection of colistin sulphate 24 h but not 72 h after infection.

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Effects of ethacrynic acid and furosemide on urinary calcium, phosphate and magnesium

Experiments were performed in dogs to determine the effects of Ethacrynic Acid and Furosemide on the renal excretion of calcium, magnesium and phosphate. Both diuretics had a similar action increasing clacium and magnesium excretion, while urinary phosphate remained constant. Plasma concentrations of calcium and magnesium decreased and phosphate rose but no appreciable change occurred when the urinary losses were replaced. Clearance of ultrafilterable calcium paralleled sodium clearance and increased in a greater proportion. A good correlation was found for sodium as related to calcium thus supporting the possibility of a relationship in the renal transport of these two ions. The clearance of ultrafilterable magnesium exceeded the clearance of inulin in some instances demonstrating a secretory mechanism for magnesium.

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