
Twenty-three rabbits were given repeated intravenous injections of tracer labelled B.S.A. over periods of 3-4 months. Different dosage schedules were used, but all animals had significant quantities of circulating B.S.A. at all times. The amount of antigen circulating bound to antibody was estimated by (NI-¾SC) precipitate, and most animals showed large amounts of circulating complexes (40-90%) during the stage of rapid antibody production. Twenty-two animals had proteinuria at some time over the period 14-21 days. After this period proteinuria became inconsistent and intermittent, and the animals showed progressively declining antibody production, until this finally negligible, after about 80 days.

Renal biopsies showed minor proliferative changes during the period of proteinuria, but these later disappeared completely. No animals have shown histological or functional evidence of progressive nephritis.


Antigen-antibody reactions known to be capable of producing renal lesions when they occur in vivo fall into two categories: (1) those involving native antibody and foreign antigen; (2) those involving foreign antibody reacting specifically with antigens present in kidney tissue.

If autoantibodies are associated with renal disease their modes of action might be considered in broadly similar fashion. Thus autoantibody directed at a non-renal tissue antigen might give rise to continual formation of soluble complexes, inducing under appropriate conditions a chronic glomerulonephritis; or alternatively, autoantibody specifically reactive with renal glomerular antigens might prove nephrotoxic in the same way as heterologous antikidney antibody.

Although it has been proposed that the renal lesions of systemic lupus erythematosus might arise as a result of the former mechanism, the supporting evidence is scanty. With regard to the occurrence of specific renal autoantibodies, the few reported observations do not include recognition of specific antiglomerular antibodies in patients’ sera.

Recent investigation of sera from cases of chronic active hepatitis have shown that they may contain autoantibodies reactive with a number of tissue-specific antigens, as well as the non-organ specific anti-nuclear and anti-cytoplasmic factors. Some of these tissue-specific antibodies will be described, their incidence in some diseases reported, and their possible significance discussed.


The high incidence and bad prognosis, with poor response to steroid treatment, of children with nephrotic syndrome in Nigeria suggests an incidence of causative diseases different from those in temperate regions. Epidemiological studies have indicated a relationship with plasmodium malariae infection. Histological studies have shown a high incidence of a form of lobular proliferative glomerulonephritis,
possibly suggestive of soluble complex glomerulonephritis. The following immunological studies add support to these concepts:

1. Immunochemically determined differential protein clearance studies show that most of these patients had moderately selective proteinuria which was markedly non-linear on a log-log plot against molecular weight of protein, and Ca

\[ Ca^{2+} G% \]

differed highly significantly \((P = 0.00045\%)\) from a group of British children with the nephrotic syndrome, but a few showed the highly selective proteinuria usually seen in children with the nephrotic syndrome from temperate areas. Preliminary results suggest that only the patients with highly selective proteinuria respond to steroid treatment. If this is confirmed this test will be of considerable value in selecting patients for this treatment, in an area where trial of steroids is dangerous.

Antigenic estimation of the complement component \( B_{1c} \) was normal in all the children studied. Immunoelectrophoresis revealed the altered component \( B_{1a} \) in fresh plasma from the majority of the children with the poorly selective proteinuria, as has been found in acute nephritis and in some patients with progressive proliferative glomerulonephritis, but not in the ones with highly selective proteinuria. This provides further evidence that the disease predominant in children is immunological in nature.

If soluble complex were circulating in these sera one would expect complement components to be incorporated in these complexes. \( B_{1e} \) is normally confined to the Sephadex G.200 middle peak. In sera from some of these patients it was detected in the first (macroglobulin) peak, using antisera absorbed with such material from normal individuals. This suggests that soluble complex circulates in these patients, and provides a possible means of access to the antigen involved. The possible role of this in planning specific treatment of glomerulonephritis will be discussed.

Renal Association (January 11, 1967)

Muldowney, F. P.: Sodium diuresis after relief of obstructive uropathy.

The magnitude and duration of renal sodium loss following relief of partial urinary tract obstruction has been investigated. The majority of cases on external metabolic balance study failed to reduce urinary sodium loss to less than intake within five days of commencing a sodium restricted diet (13-30 mEq. daily). This defect appeared more marked in subjects with obstructive symptoms of more than three months duration (chronic group). In no case, however, did sodium loss proceed to the stage of clinical salt depletion with hypotension. Measurement of total exchangeable sodium (Na\(\text{e}\)) before and after relief of obstruction confirmed the pattern of sodium loss in the chronic group, but no systematic change was seen in acute cases. Initial Na\(\text{e}\) values in the chronic group were significantly raised in six of seven subjects and fell spontaneously to normal levels 1-3 weeks following operation (with the exception of one patient who developed bundle branch block and heart failure). Neither chronic nor acute group showed depression of final Na\(\text{e}\) values below the normal range.

The pattern of results suggests that (a) partial urinary tract obstruction is associated with sodium retention and (b) relief of obstruction results in reduction of body sodium stores from high to normal levels.

Varia
Hodson, C. J. and Craven, J.D.: The radiological aspects of obstructive atrophy.
The structural changes in the kidney which result from obstruction in the urinary tract are sufficiently peculiar to form a basis for reliable radiologic diagnosis, with a relatively small and uncommon differential diagnosis.
The natural history of these changes, their features and the behaviour of the kidney during their formation will be discussed together with five important aspects: (1) what happens when the obstruction has been removed, (2) the required time of irreversible changes to occur, (3) the effect of temporary obstruction on the growing kidney, (4) a relatively rare atypical response to obstruction which does not, as yet, appear to have been isolated and described, (5) the relationship of severe vesico-ureteric reflux to this problem.

The effects of obstruction of a ureter are more commonly thought of as affecting the size of the renal pelvis and calices rather than the parenchyma of the kidney. Dilatation of these ‘bags’ occurs, but equally important is the reduction in amount of functioning parenchymal tissue and the mechanism by which this occurs.
Acute complete obstruction of a ureter in man is followed by slight dilatation of pelvis and calices, interstitial oedema of the parenchyma, tubular atrophy and focal tubular disruption. (If the condition is bilateral acute uraemia results.) The kidney is not reduced in size, nor is the weight decreased. Dr. Hodson’s experiments of ligature of the ureter in pigs permits the changes in such a process to be followed sequentially. Tubular atrophy and disruption lead to interstitial oedema, low grade inflammatory reaction and fibrosis. Effects on the papillae occur later and may not be related to this initial reaction. The long term effects of such a process have not yet been studied.
Incomplete obstruction of a ureter leads to a slower atrophy of tubules with much less interstitial reaction and insignificant tubular disruption. In time this is associated with glomerular atrophy and considerable shrinkage of parenchyma.
In both these processes the smooth outline of the kidney is retained in the absence of infection. Infection leads to focal greater destruction of renal tissue and scarring.

Second Kanematsu Conference on the Kidney and Australasian Society of Nephrology Combined Meeting
From 29th November to the 2nd of December, 1966, approximately 100 nephrologists met in conference at Sydney Hospital, Sydney, under the auspices of the Keith Kirkland Renal Unit, Medical Research Department, Kanematsu Memorial Institute, Sydney Hospital, and the Post-Graduate Committee in Medicine of the University of Sydney in conjunction with the Australasian Society of Nephrology. The first Kanematsu Conference, held in October, 1963, attracted 70 nephrologists, and the proceedings were published (Bull post-grad. Comm. Med. Univ. Sydney 20: 41-159, 1964). The Second Conference, combined with the Second Scientific Meeting of the Australasian Society of Nephrology, consisted of 23 invited papers on renal physiology, clinical nephrology and renal pharmacology and toxicology, and 20 free communications. Dr. Oliver M. Wrong, Department of Medicine, Postgraduate Medical School of London, was the invited speaker to the Conference, and Professor James R. Robinson, University of Otago School of Physiology, Dunedin, was Australian and New Zealand Post-Graduate Medical Federation Exchange Visitor.

Varia
Papers by invitation on ‘Renal Physiology’ were given on water and solute handling by G. D. Thorburn (intercellular fluid pathways)1, B. D. Stacy (sodium)2, J. A. Young (micro-puncture studies)1, S. Posen (calcium)1, and J. R. Robinson (urea)2; on the nervous control of the renal circulation by P. I. Korner1; and on renal/adrenal hormones by O. M. Wrong (extra-renal actions of aldosterone), G. S. Stokes (renal pressor mechanism)2, and Mary F. Lockett (isolated perfused cat kidneys)2.

Papers by invitation on ‘Clinical Nephrology’ were given on chronic dialysis by J. R. Lawrence and on kidney transplantation by P. R. Knight, Priscilla Kincaid-Smith and R. M. Mitchell2; cases were presented by D. Jeremy, G. F. Murnaghan, J. H. Stewart and P. R. Knight; papers on renal secretion of hydrogen ion were given by J. R. Robinson (normal control)1, O. M. Wrong (renal tubular acidosis)1, A. Z. Györy (citrate utilisation)1 and R. K. Pak Poy (urea stones).

Papers by invitation on ‘Renal Pharmacology and Toxicology’ were given on testing new drugs by M. J. Rand (pre-clinical aspects)1, on nephrotoxicity by H. H. Pearson (non-fatal phenacetin nephritis)2, A. F. Burry (phenacetin and papillary necrosis) and D. M. le Quesne (antibacterials including merthiolate), and on drug poisoning by E. G. McQueen (new approaches to treatment)1. Free communications accepted for publication were given by O. M. Wrong (colonic metabolism of urea)2, J. R. Blair-West (renin, angiotensin and aldosterone in sodium depletion)2, K. D. G. Edwards (clinical assessment of diuretics)1 and C. Armstrong (ion exchange resins in aspirin poisoning)2.

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2

Accepted for publication by Med. J. Aust.

Kidney Club of the Netherlands (December 1966, Meeting)

Ten Bokkel Huinink, J. A. and van Zeyst, J. A. M.: Hereditary shrunken kidneys. Report of a family in which 9 members suffered from an apparently recessive hereditary nephropathy. Clinically, the course was characterised by hypertension and death in uremia at a relatively early age. Biopsy and post-mortem studies showed widespread arteriosclerosis. Arguments were put forward to consider the vascular renal process as the cause rather than the result of the hypertension.

Troelstra, J. A.: Some aspects of tubular functional disturbances in hereditary disease. General survey and case records. In a patient with Wilson’s disease severe phosphate loss and amino-aciduria improved after penicillamine and diet therapy. Two patients with cystinosis were shown suffering from severe non specific aminoaciduria, phosphaturia and glucosuria. In one of them vitamin D resistant rickets improved with moderate doses of vitamin D and oral phosphate.

(3) Arisz, L.: Differential protein clearances in idiopathic proteinuria. Correlations of clearance determinations with biopsy findings in 43 patients with proteinuria were generally in agreement with the results reported by Hardwicke. All patients with minimal lesions had heavy proteinuria and a ‘selective pattern’. In membranous glomerulonephritis significant correlations were found between the severity of the anatomical lesion and the mean daily protein loss as well as the selectivity of the differential excretion pattern. This tendency for the less severe lesion to cause smaller protein loss and a more selective pattern was also seen in patients with proliferative lesions, though less
significant. Favorable response to steroid therapy correlated better with the ‘selectivity’ of the protein clearances than with the biopsy data.

Fourth Conference of the European Dialysis and Transplantation Association (Paris, June 24-25, 1967)

Review of haemodialysis in Europe. In his annual report Drukker (Amsterdam) recorded that 81 centres were now running ‘chronic programmes’ in Europe and the number of patients on regular haemodialysis had doubled to 621. Although the majority were still using hospital dialysis as an end in itself, one third of the units were now running in conjunction with a transplant programme and six had started home haemodialysis training schemes. There had been a striking fall in mortality in newly accepted patients but even in Kill centres (which includes the majority of those using regular dialysis long term) there was still a 15% mortality in the first 6 months. Prominent among the complications were cannula problems (50% of units now employ long term anticoagulants), neuropathy, pseudogout, metastatic calcification and secondary hyperparathyroidism. Nineteen units reported hepatitis outbreaks involving 45 patients and 26 staff.

Dialysis facilities were under-utilised, the average centre operating at only 2/3 of capacity. The main limitation is staff time—the average patient occupies 60% of one nurse’s full time and 30% of a doctor’s.

Home haemodialysis. Progress reports from the Royal Free (Baillod), Seattle (Rae) and Birmingham (Hilton) and a first report from the National Kidney Centre (Shaldon) gave details of 60 patients already established in the home for up to 3 years. The mortality, at about 1 per 20 patient years, and the morbidity were lower than in hospital dialysis, rehabilitation was faster and diet more liberal (up to 80 g protein per day) owing to unrestricted dialysis time. Schedules of 3-4 nights per week with about 10 h on the machine each time were standard; the burden on the patient was reduced by re-using the dialyser up to 6 times after antiseptic wash-through. A major factor in the success of home haemodialysis has been the reduction in transfusion requirements when blood is no longer given to maintain an arbitrary PCV. Verroust and Crockett (London) reported a total experience of almost 70 patient years without transfusion except to replace acute blood loss or to relieve symptoms which were seldom intolerable unless the PCV fell below 15%. In over 90% of patients an acceptable PCV (average over 20%) could be maintained without regular topping up, though there was often an initial fall in PCV when transfusions were stopped. Great economy in blood sampling and thorough wash-out of good quality KII dialysers were essential for success. Iron therapy was required in some patients who were started on dialysis in the ‘no-transfusion era’.

Arterio-venous shunts and fistulae. Infection and clotting remain the major problems of the Quinton-Scribner shunt. Anderson (Edinburgh) found staphylococcus aureus the commonest pathogen in shunt infections and the same organism was usually present in the nares or other carrier sites. Recurrent infection in chronic carriers could sometimes be prevented by regular hexachlorophene bathing and antibiotic nasal cream. Prophylactic antibiotics were ineffective. Kopp (Frankfurt) reported success with a different approach—elimination of skin antiseptics and treatment of the skin with a lanolin ointment.

Varia
thrombosis. Streptokinase proved valuable in removal of such thrombi when used locally in high concentration and covered by systemic steroids to prevent reactions (Anderson, Edinburgh; Kjellstrand, Lund). Subsequent failure of the shunt was much less likely if long term anticoagulants were started at once. A new shunt site, utilising the lateral femoral circumflex vessels, and an all silastic shunt, was described by Höltzenbein (Munster).

The Cimino-Brescia A-V fistula has gained widespread acceptance in centres using blood pumps, particularly those aiming at eventual transplantation, where a local infection may postpone operation and waste a cadaver donor. In the experience of Verberckt (Louvain); Meriel (Toulouse); Dossetor (Montreal and Carmody (Dublin) the fistula was preferred to the shunt by staff and patients who had tried both. Blood flow through the dialyser was slightly lower than with the Quinton-Scribner shunt but the A-V leak between dialyses was greater; Klinkmann (Rostock) recorded cardiac outputs up to 13 l per minute, requiring the revision of one fistula.

Technique of dialysis. Lyman (Menlo Park) described the preparation of block co-polymer membranes with much greater selectivity in the lower molecular weight range than cellulose membranes. Their clinical application was held up by ignorance of the toxic substances in uraemia. Grimsrud (Seattle) and Simpson (Birmingham) showed by studies in test cells that current membrane supports use only a fraction of the potential of our present membranes. Grimsrud described successful clinical trials with his foam-nickel support dialyser which can cut dialysing time by about one third compared with the Kiil, with about half the priming volume. Its excellent performance at low blood flow rates is attractive for pumpless dialysis. The concentric 4-coil kidney (Höltzenbein, Munster) and a parallel coil modification (Nakamoto, Cleveland) had given satisfactory performance in clinical trials; they can be used without a blood pump. The Höltzenbein screening mesh has also been incorporated in a shorter version of the standard twin-coil and Boelaert (Louvain) and Pearson (Newcastle) reported a considerable increase in dialysance and ultrafiltration with a reduction in priming volume. Since these latest dialysers utilise 50 to 80% of the maximum potential of their membrane areas, the search for a more permeable membrane than Cuprophane is at last becoming relevant.

Peritoneal dialysis. Deane (New York) described a new technique for repeated peritoneal dialysis, using an epithelialised track kept open by a prosthesis. Reinsertion of the catheter was a nursing procedure and had been continued for up to 9 months without infection. Lee (Manchester) reported that plasma lactate levels, often raised before dialysis, rose further in many patients treated with commercial dialysis solutions which contain about 40 mEq/l of lactate. He suggested that this may be a cause of some post-dialysis convulsions. Another constituent of current fluids which may have undesirable effects is dextrose, added for its osmotic effect but particularly trouble some in diabetics. Jirka (Prague) showed that dextran could be used in place of dextrose in acute experiments on dogs.

Mirouze (Montpellier) found peritoneal dialysis very useful in acute-on-chronic renal failure, but confirmed the popular view that it is only the last resort therapy for terminal renal failure. Bonomini (Bologna) who used a regime of 50 to 60 h dialysis per week for maintenance therapy found that protein loss was 20-30 g per week. He noted a heavier and less selective loss in patients with chronic glomerulonephritis.

Acute renal failure and intoxications. Luke (Glasgow) used haemodialysis in the most severe 2% of a series of over 1000 cases of barbiturate intoxication and achieved an impressive mortality of under 0.3%. One patient survived a blood phenobarbitone level of 58 mg%.
Jungers (Paris) found that the commonest cause of severe gastro-intestinal haemorrhage complicating acute renal failure was single or multiple acute ulcers, commoner in stomach than duodenum. The haemorrhage was controlled surgically in all 5 patients operated on, with 3 eventual survivals.

Lange (Marburg) noted mild hypoproteinaemia when oliguria recurred during the diuretic phase; a second diuresis followed albumin infusion in 2 patients.

Chronic renal failure. Maggiore (Pisa) found that patients with polycystic disease had significantly higher haemoglobin levels than those with the same degree of renal failure from other causes, and that their transfusion requirement on regular dialysis was correspondingly low. Kamp Nielsen (Copenhagen) in a study of 22 patients with severe renal failure (GFR 0-11 ml/min) found evidence of sensory neuropathy, mainly in the lower limbs, in about half. All patients had reduced sensory nerve conduction velocity even in the upper limbs.

The relationship of neuropathy to magnesium metabolism was studied by Kaye (Montreal) and Fleming (Dundee) with conflicting results. Fleming found that nerve conduction times decreased when serum magnesium was restored to normal, but Kaye found a low incidence of clinical neuropathy in the centres with the highest water magnesium content and, by implication, the greatest hypermagnesaemia. The 1-1.5 mEq/l of magnesium which is commonly added to tap water to make dialysis fluid results in a final level of 1.5-2 mEq/l depending on the hardness of the local water. There was agreement that this regularly produced considerable hypermagnesaemia and Fleming suggested omitting magnesium from the bath water since the loss during dialysis was balanced by a positive dietary balance at other times.

Roodvoets (Leiden) found hyperlipaemia in patients on regular dialysis; this increased during dialysis until the serum was milky. The lipaemia and an impaired glucose tolerance were attributed to the recurrent acute glucose load associated with dialysis, but the insulin rise on glucose loading remained intact. Traeger (Lyon) who reported a battery of platelet function tests before and after regular dialysis found no fall in platelet count and an improvement in some of the tests.

Sieberth (Cologne) noted inadequate respiratory compensation for acidosis in patients on regular haemodialysis owing to dysequilibrium between blood and CSF bicarbonate which is not fully corrected between dialysis. Rubini (Los Angeles) found that the rate of accumulation of hydrogen ion was maximum on the day after dialysis and then fell off progressively; he observed the same phenomenon with urea, creatinine and uric acid and suggested a catabolic effect of dialysis as one explanation. An alternative hypothesis was provided by Deane (New York) who found a high extra-renal loss of urea in chronic uraemics which diminished when the blood urea was lowered by dialysis. Scholtz (Berlin) supported this view by showing that urea production rate did not rise after dialysis. He also failed to show any hyperconcentration of urea in cellular water. Both of these studies with labelled urea indicated rapid equilibration throughout the body but the slight delay at the erythrocyte boundary may be important in haemodialysis since Grossman (Frankfurt) found that urea clearance in the twin coil diminished as haematocrit rose.

80

Varia

Renal preservation. Better histological preservation after freezing was reported by Carruthers (Leeds) using a further refinement of Farrants DMSO technique. The laborious task of testing new techniques by re-implantation may be curtailed since Dossetor (Montreal) found several biochemical estimates which correlate well with predicted viability.
Renal transplantation. Nelson (Boston) found the lymphocyte transfer test helpful in excluding unsuitable donors, but slow. The more convenient mixed lymphocyte culture test did not predict graft survival significantly. Albertsen (Aarhus) studied the early post-transplant diuresis and attributed it to excessive solute load, predominantly sodium. A Fanconi-like tubular defect was described by Orlowski (Warsaw) in 4 recipients of cadaver grafts.

By careful selection of cadaver donors Marshall (Melbourne) achieved immediate renal function in 22 of 24 recipients with 20 survivors. In the collected European series reported by Parsons (Leeds) short term survivors were about 60% of those receiving cadaveric grafts and 80% of those with live donors. Mortality in the second year was low at 2 out 30 patients.

About 40% of European patients with failed grafts are now treated by regular dialysis long term or pending retransplantation. The value of such an integration of dialysis and transplant facilities was illustrated by Vantelon (Paris) from the results at Necker. The main problem is the overloading of facilities by patients for whom suitable grafts cannot be found. Traeger (Lyon) suggested selecting only the more favourable patients on the basis of ABO and leucocyte groups. If those with a high chance of finding a suitable match in the first 6 donors are chosen this will leave about half the uraemic population untouched. The need for a hospital dialysis unit streaming its new patients in roughly equal numbers to transplant and home haemodialysis was clearly implied.

First Annual Meeting of the American Society of Nephrology

The first annual Meeting of the American Society of Nephrology was held at Los Angeles, California, October 18-19, 1967. The program included: General Sessions (Membrane transport, Immunologic pathology of renal disease, Renal physiology, Clinical nephrology), Symposia (Chronic dialysis, Mechanism of action of aldosterone, Glomerulo-tubular balance, Renal transplantation, Role of reflux in pyelonephritis, Nature and mechanism of action of the natriuretic third factor) and 80 Free Communications. A more detailed report will be given in a subsequent issue of Nephron.