

PAPERS AND ORIGINALS

Presentation, management, complications, and outcome of acute renal failure in childhood: five years' experience

R COUNAHAN, J S CAMERON, C S OGG, PATRICIA SPURGEON, D G WILLIAMS, ELIZABETH WINDER, C CHANTLER

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Summary

During 1971-5, 72 episodes of acute renal failure were treated in 70 children aged up to 16 years. The commonest causes were renal hypoperfusion (31 cases), haemolytic-uraemic syndrome (12), glomerulonephritis (9), septicaemia (5), and congenital abnormalities (6). Though referral from other hospitals was generally prompt, 10 out of 51 patients had been observed for up to seven days before transfer. Dialysis was used in 44 cases, the most common complications of which were peritonitis in those treated with peritoneal dialysis and acute changes in fluid balance in those treated with haemodialysis.

Altogether 37 patients fully recovered, 10 were discharged with chronically impaired renal function, 17 died, and six entered the dialysis and transplantation programme. The mortality fell from 33% in 1972 to 20% in later years, which was due solely to maintenance dialysis being available. Though all patients with irrevocable kidney failure who were suitable entered the dialysis and transplantation programme, with current financial restrictions we doubt whether we shall be able to find places for all such patients in the future.

Introduction

Acute renal failure (ARF) in childhood has been the subject of several reviews in recent years, but since the report by

Meadow *et al* in 1971¹ on children referred to Guy's Hospital over 18 months for acute dialysis few new facts have been presented; a notable exception was the report on children under 2 years of age treated for ARF at the Hospital for Sick Children, Great Ormond Street.² We have therefore analysed our experience of all children diagnosed as cases of ARF during 1971-5. We excluded those with known chronic renal failure progressing to terminal uraemia and those referred back for regular dialysis after transplant failure. "ARF" refers to acute uraemia whatever the cause.

Patients

During the five-year period 72 episodes of ARF were treated in 70 children aged up to 16 years (tables I and II). Fifty-one patients were referred from other hospitals, seven were referred direct by their general practitioners, and 12 developed ARF while in this hospital. The primary reasons for referral from other hospitals were oliguria or anuria in 25 patients, uraemia or azotaemia in 16, failure of peritoneal dialysis in six, and hypertension in two; one patient had liver failure, and one had ingested ethylene glycol and was expected to develop acute renal failure. In about half the patients the diagnosis on referral was correct, while in the remainder no precise cause for the renal failure was offered. Once renal failure was recognised referral was usually within 24 hours, but 10 patients had been observed for three to seven days before transfer.

TABLE I—Number of cases of ARF in children seen yearly during 1971-5

| | 1971 | 1972 | 1973 | 1974 | 1975 | Total |
|-------------------|------|------|------|------|------|-------|
| No of cases | 9 | 6 | 12 | 25 | 20 | 72 |
| No dialysed | 7 | 3 | 9 | 14 | 11 | 44 |

Evelina Children's Department, Guy's Hospital, London SE1 9RT

R COUNAHAN, MRCP, DCH, honorary lecturer, department of paediatrics
 J S CAMERON, MD, FRCP, professor of renal medicine
 C S OGG, MD, FRCP, renal physician
 PATRICIA SPURGEON, SRN, paediatric ward sister
 D G WILLIAMS, MD, MRCP, consultant physician
 ELIZABETH WINDER, SRN, sister in charge of intermittent dialysis unit
 C CHANTLER, MD, MRCP, consultant paediatrician

TABLE II—Ages of children with ARF

| | -2 | -4 | -6 | -8 | -10 | -12 | -14 | -16 | Total |
|----------------------|----|----|----|----|-----|-----|-----|-----|-------|
| Age in years | 20 | 13 | 6 | 9 | 5 | 10 | 4 | 5 | 72* |
| No of children | | | | | | | | | |

*Two patients had two episodes of ARF.

TABLE III—Causes, treatment, and outcome of the 72 episodes of ARF

| Cause | No of cases | Mean age (years) | Management | | | | Outcome | | | |
|--|-------------|------------------|------------|----|-------|----|---------|-----|-----|------|
| | | | Con | PD | PD→HD | HD | Rec | CRF | RDT | Dead |
| Renal hypoperfusion (immediately reversible cases) | 31 (14) | 6.5 (6.2) | 14 (14) | 10 | 2 | 5 | 21 (14) | 2 | | 8 |
| Haemolytic-uraemic syndrome | 12 | 3.2 | 3 | 6 | 2 | 1 | 6 | 3 | 1 | 2 |
| Glomerulonephritis | 9 | 6.8 | 5 | 2 | 1 | 1 | 6 | 1 | 1 | 1 |
| Septicaemia or urinary tract infection | 7 | 3.9 | 1 | 3 | | 3 | 3 | | | 4 |
| Congenital abnormality | 6 | 4.0 | 5 | | | 1 | 3 | | | 2 |
| Acute on chronic disease | 5 | 11.2 | | | 3 | 2 | 1 | | 4 | |
| Poisons | 2 | 1.8 | | 2 | | | 2 | | | |
| Total | 72 | 6.4 | 28 | 23 | 8 | 13 | 39 | 10 | 6 | 17 |

Con = Conservative. PD = Peritoneal dialysis. HD = Haemodialysis. Rec = Recovered. CRF = Chronically impaired renal function. RDT = Renal dialysis and transplantation.

Causes of ARF

Table III lists the causes of ARF in the 72 cases. Of the 31 episodes resulting from renal hypoperfusion, 14 were reversed with plasma expanders and diuretics, but 17 failed to respond to this treatment and progressed to established renal failure. The causes of hypoperfusion (with the numbers of cases progressing to established renal failure given in parentheses) were the nephrotic syndrome with hypovolaemia in 10 cases, postoperative in 10 (9), gastroenteritis in 4 (2), bilateral renal venous thrombosis in 2 (2), Reye's syndrome in 2 (2), pyloric stenosis in 1 (1), heart failure (coarctation) in 1, and burns in 1 (1). Nine episodes of ARF resulted from glomerulonephritis, which in two cases was acute proliferative post-streptococcal, in two acute proliferative non-streptococcal, in two mesangiocapillary, in one Henoch-Schönlein, and in one interstitial; in the remaining case the glomerulonephritis occurred with Wegener's granulomatosis.

In five cases ARF resulted from septicaemia, and in two from a urinary tract infection. Of the patients with septicaemia, two had an obvious focus of infection—one in the urinary tract, and the other in the umbilicus—and in these and the two patients with a urinary tract infection the urinary tract was radiographically normal. Congenital abnormalities resulting in ARF were posterior urethral valves (four cases), dysplastic kidneys (one case), and obstruction of vesicoureteric junction in a single kidney (one case). One patient with posterior urethral valves had ARF due to acute retention precipitated by amitriptyline prescribed for enuresis. Two patients known to have chronic renal failure were included since they had a sudden decline in renal function after surgery; this reversed in one.

Assessment

In 24 (47%) of the 51 cases referred from other hospitals the diagnosis was clear from the history or clinical signs, or both, and accompanying investigation results. Useful diagnostic signs were a rash, bruising, an enlarged bladder, and the stigmata of chronic renal failure, especially growth retardation, which was evident in patients presenting in terminal uraemia. In other cases a combination of the following clinical, laboratory, and specialised investigations was necessary.

Clinical—Hydration, blood pressure, and diagnostic signs.

Laboratory—Haemoglobin and platelet and white cell counts; coagulation studies; blood culture; plasma biochemistry; urine sodium, urea, and osmolality; and urine microscopy and culture.

Specialised—Frequent: chest radiography and electrocardiography, intravenous urography (20 cases), micturating cystography (5 cases), renal dynamic scintillography (gammascan) (25 cases), and renal biopsy³ (15 cases); occasional: renal angiography (3 cases) and antegrade and retrograde pyelography.

Circulatory overload was more common than fluid depletion, and table IV shows their relationship to urine flow. Blood pressure on admission was not closely related to fluid balance, although it was never raised in water- and saline-depleted patients and was normal or raised in overloaded and normally hydrated patients. After restora-

TABLE IV—Water and salt balance on admission in 63 cases

| Balance | No of cases | Inadequate urine flow | Dialysed |
|----------|-------------|-----------------------|----------|
| Overload | 24 | 10 | 18 |
| Normal | 23 | 12 | 15 |
| Depleted | 16 | 3 | 5 |

tion of fluid volume the diuretic response to intravenous frusemide 5 mg/kg was tested when necessary and when there was no acute need for dialysis such as hyperkalaemia. Eight patients had seizures before admission. In three these were associated with hypertension, in two with hypoxaemia, and in the remaining three with hypocalcaemia, Reye's syndrome, and the haemolytic-uraemic syndrome respectively.

The relation between urinary biochemical values and mode of treatment is shown in table V. The highest plasma urea concentration was 97.5 mmol/l (587 mg/100 ml), and 67 patients had concentrations of over 15 mmol/l (90 mg/100 ml). Seven patients were hypernatraemic (>150 mmol (mEq)/l), while nine had plasma sodium concentrations

TABLE V—Urinary biochemical values and mode of treatment

| Treatment | Urine sodium (mmol/l) | | | | Urine : plasma urea ratio | | |
|--------------|-----------------------|-----|-----|-----|---------------------------|------|-----|
| | <10 | <20 | <30 | ≥30 | <5 | 5-10 | >10 |
| Conservative | 6 | 7 | 8 | 9 | 9 | 4 | 6 |
| Dialysis | 1 | 3 | 4 | 15 | 15 | 4 | |
| Total | 7 | 10 | 12 | 24 | 24 | 8 | 6 |

Conversion: SI to traditional units—Urine sodium: 1 mmol/l = 1 mEq/l.

of under 125 mmol (mEq)/l. Ten patients had plasma potassium concentrations higher than 6.5 mmol (mEq)/l, and two had hypokalaemia, one of whom was undergoing peritoneal dialysis, and the other, a patient with the nephrotic syndrome, was in a hypovolaemic crisis. Hypocalcaemia was found in 15 patients, but in only three was it symptomatic. Blood cultures were performed in 36 cases and were positive in six on admission. Dynamic renal scintillography with either ^{99m}Tc-labelled diethylenetriamine penta-acetic acid or ^{99m}Tc-labelled dimercaptosuccinic acid was the most common specialised investigation and was often done repeatedly.

Management

Twenty-eight patients were treated conservatively and 44 were dialysed (table III). Peritoneal dialysis was performed on 31 patients, eight of whom were subsequently transferred to haemodialysis, and 13 had haemodialysis alone. Often there were several indications for dialysis, but circulatory overload was the primary reason in two-thirds of the cases and biochemical disturbance in one-third.

CONSERVATIVE

Conservative treatment consisted in attending to fluid balance, maintaining urine flow with diuretics, and treating infection. In all cases the immediate aim after admission was to establish whether there was adequate renal perfusion. This entailed making a conventional clinical assessment of the fluid and electrolyte balance, the urine biochemistry (see Discussion), and the response to intravenous frusemide. In addition assessment of central venous pressure and also tissue perfusion as judged by central and peripheral temperatures⁴ were extremely useful, especially in children with septicaemia. When

there was poor perfusion despite circulatory expansion vasodilators were given (chlorpromazine 0.1-0.25 mg/kg intravenously), but when these failed early dialysis was started rather than attempts to control the uraemic state by dietary and pharmacological measures. One homogeneous group of eight patients had 10 episodes of hypovolaemia complicating the nephrotic syndrome and had become oliguric and uraemic. These were treated by circulatory expansion with intravenous plasma, diuretics being given concurrently.

Mannitol was not used, and no patient given frusemide developed ototoxicity. When septicaemia was suspected antibiotics were often given blindly until bacteriological results were available. Gentamicin was generally preferred, the dose being determined by the blood level immediately before each injection.

PERITONEAL DIALYSIS

Peritoneal dialysis was carried out by conventional means.⁵ With the exclusion of one patient who continued on maintenance dialysis for several months the mean duration of peritoneal dialysis was 11.2 days (range 1-54 days). Thirteen patients were dialysed for seven days or less and only five for more than 14 days. The procedure was technically successful in all but two patients, who continued with haemodialysis for a time because of peritonitis.

Eight patients had trouble-free dialysis, six of them being dialysed for less than a week. The most common complication was peritonitis, which occurred in 13 cases, the evidence for which being bacteriological rather than clinical (table VI). Resolution was usually prompt, although reinfection was common. The one patient who developed candida peritonitis had a candida septicaemia.

TABLE VI—Organisms causing peritonitis during peritoneal dialysis, and treatment given

| Case No | Culture | Day of dialysis | Treatment | Duration of dialysis (days) |
|---------|--|-----------------|------------------|-----------------------------|
| 1 | <i>Pseudomonas</i> | 4 | Gentamicin IP | 18 |
| 2 | <i>Pseudomonas</i> | 10 | Carbenicillin IP | 24 |
| 3 | <i>Escherichia coli</i> | 2 | Gentamicin IM | 8 |
| 4 | <i>Escherichia coli</i> | 3 | Gentamicin IP | 11 |
| 5 | <i>Bacillus</i> sp | 2 | Gentamicin IP | 300 |
| 6 | <i>Escherichia coli</i> , <i>Pseudomonas</i> | 7 | Gentamicin IP | 7 |
| 7 | <i>Pseudomonas</i> | ? | ? | 22 |
| 8 | <i>Escherichia coli</i> , <i>enterococcus</i> | 2 | Gentamicin IP | 12 |
| 9 | <i>Enterobacter</i> | 8 | Gentamicin IP | 54 |
| 10 | <i>Pseudomonas</i> | 2 | Gentamicin IM | 3 |
| 11 | <i>Pseudomonas</i> | 2 | Gentamicin IP | 10 |
| 12 | <i>Candida albicans</i> | 8 | Flucytosine IP | 14 |
| 13 | ? | ? | ? | 14 |

IP = Intraperitoneally. IM = Intramuscularly.

Hyperglycaemia occurred in two patients, one of whom was treated with subcutaneous insulin. Minor complications such as dislodgment or obstruction of the catheter were common and were managed by resiting the cannula.

HAEMODIALYSIS

Four patients treated with haemodialysis were electively transferred from peritoneal dialysis on entering a dialysis and transplantation programme. The other 17 patients, some of whom had had peritoneal dialysis before referral, had haemodialysis because of abdominal surgery (10 cases), failure of peritoneal dialysis (6 cases), and abdominal burns (1 case). Peritoneal dialysis was unsatisfactory in two patients because of peritonitis, and in two others the dialysate did not drain from the abdomen. One child had had many laparotomies; in another, who had undergone heart surgery, the dialysate leaked through the diaphragm into the chest; and a further patient was so hypercatabolic that peritoneal dialysis could not maintain homeostasis.

The mean age of the 17 acutely haemodialysed patients was 8.0 years (range 0.02-15.92 years); three patients were under 3 months of age.⁶ The mean duration of haemodialysis was 13 days (range 1-48 days), and it was usually performed every second day. Access to the circulation was by arteriovenous shunts in the arm in bigger children and in the femoral vessels in infants. Complications were principally

of acute changes in fluid balance. The shunts occasionally clotted but could be cleared with heparinised saline or, if that failed, streptokinase. The circulation distal to the shunts was diminished in some of the smaller children, but this was not injurious to the limb.

Outcome

Full recovery of renal function and health occurred in 37 patients (53%) after 39 episodes of renal failure. Ten patients (14%) were discharged with chronically impaired renal function, two of whom died several months after admission: both had the haemolytic-uraemic syndrome. Seventeen patients (24%) died, and "renal death" occurred in six others (9%), who entered the dialysis and transplantation programme. Their diagnoses are shown in table VII. Of the 44 patients

TABLE VII—Causes and outcome of irrevocable kidney failure (23 patients)

| Diagnosis | Age (years) | Cause of kidney death | Outcome |
|--------------------------------------|-------------|--|---------|
| Septicaemia | 0.02 | Renal cortical necrosis | Died |
| Renal venous thrombosis | 0.03 | Renal cortical necrosis | " |
| Urethral valves | 0.17 | Mesenteric thrombosis | " |
| Cardiac surgery | 2.42 | Cerebral thrombosis | " |
| Burns | 2.50 | Circulatory failure | " |
| Septicaemia | 2.75 | Circulatory failure | " |
| Haemolytic-uraemic syndrome | 2.75 | Disseminated chickenpox (steroids) | " |
| Glomerulonephritis | 3.92 | Wegener's granulomatosis | " |
| Mesangiocapillary glomerulonephritis | 4.08 | Progressive renal failure | RDT |
| Haemolytic-uraemic syndrome | 6.58 | Terminal renal failure | RDT |
| Haemolytic-uraemic syndrome | 7.33 | Intracranial haemorrhage (heparin) | Died |
| Cardiac surgery | 10.92 | Circulatory failure | " |
| Dysplastic kidneys | 10.25 | Terminal renal failure | " |
| Reflux nephropathy | 10.75 | Terminal renal failure | RDT |
| Acute pyelonephritis | 11.00 | Gram-negative septicaemia (cystoscopy) | Died |
| Reye's syndrome | 11.40 | Bronchopneumonia | " |
| Septicaemia | 11.84 | Circulatory failure | " |
| Mesangiocapillary glomerulonephritis | 12.42 | Appendicitis, terminal renal failure | RDT |
| Renal isograft | 12.66 | Disseminated intravascular coagulation | Died |
| Cardiac surgery | 14.00 | Circulatory failure | " |
| Reflux nephropathy | 14.00 | Terminal renal failure | RDT |
| Henoch-Schönlein nephritis | 14.33 | Terminal renal failure | RDT |
| Cardiac surgery | 15.92 | Circulatory failure | Died |

RDT = Renal dialysis and transplantation.

who were dialysed, 15 (34%) died. Three patients treated conservatively died: one came from abroad in terminal renal failure due to renal dysplasia, one died of cerebral complications after heart surgery, and the third patient had Wegener's granulomatosis. The outcome in all diagnostic groups is shown in table III.

Discussion

An arbitrary upper limit for plasma urea concentration of 10 mmol/l (60 mg/100 ml) may seem unjustifiably low, as it is not uncommon for the urea to rise higher than this, particularly in infants with gastroenteritis or after surgery. Only five patients in our series had plasma urea concentrations below 15 mmol/l (90 mg/100 ml): all were oliguric and gave rise to concern over their renal function.

Referral to the renal unit was usually prompt, though several cases were observed unnecessarily for up to seven days before referral. Generally it is wise to transfer patients early rather than late to a specialised centre. Nowadays patients who prove not to have ARF are immediately transferred back to the referring hospital or sent home, inconvenienced but not, we judge, permanently harmed by the transfer.

The spectrum of diseases seen in our series was similar to that described by Lieberman⁷ in Los Angeles but more varied than in series from other parts of the world.^{8,9} Interestingly no case of the haemolytic-uraemic syndrome was seen in the 18 months before this study.¹ Only one child had ARF as a

consequence of burns. This used to be a frequent contributory cause,¹⁰ but no child treated in the burns unit has developed renal failure since 1970.

On admission many children were extremely ill, and investigation and treatment proceeded simultaneously. Immediate consultation with the paediatric urologists was arranged when urological problems were suspected. The commonest problem was fluid overload and was often the reason for dialysis when oliguria or anuria unresponsive to diuretics was present. Blood pressure was an important guide to acute changes in fluid balance in individual patients in the absence of changes in skin turgor or oedema. It was a less impressive guide, however, in relation to fluid volume at first examination in our patients. Wide variation in renin secretion is a likely reason for this. For example plasma renin activity is raised in the haemolytic-uraemic syndrome, and very low concentrations have been documented by Powell *et al*¹¹ in acute nephritis.

One of the most important and simple investigations, which is little used in routine practice when there is concern about renal function, was the biochemistry of the urine. Conventionally, a urine sodium concentration below 20 mmol (mEq)/l (provided diuretics are not being given) and a urine urea concentration 5-10 times the plasma concentration indicate that the kidney is responding normally to hypoperfusion¹² with avid resorption of sodium and water. Provided the hypoperfusion is corrected renal function should return to normal. When renal failure is established sodium "leakage" due to failure of resorption of sodium occurs and the urine urea is reduced due to poor urine concentration. The data in table V suggest that such sharp demarcation is not possible and that these figures are broad guidelines only. The "incipient" renal failure pattern was seen in all the hypovolaemic nephrotic patients, with urinary sodium concentrations as low as 2 mmol (mEq)/l and urine urea : plasma ratios as high as 30-40. This group was also readily recognised by very high packed cell volumes due to haemoconcentration, and this remains the best guide of intravascular fluid volume in patients with nephrosis, who are often oliguric.

The gammacamera facilitated diagnosis in many children in whom intravenous urography would have been dangerous due to the large osmotic load and possible acidosis. Although the scan so derived may not have been as anatomically precise as an intravenous urogram, the technique was not invasive, could be repeated readily, and did not interfere with fluid and solute balance. Its immediate diagnostic role was to exclude urinary tract obstruction, but also, by computer integration of the radioactivity with area and time, it gave data on renal blood flow, and concentration and excretion of chelate and was a valuable monitor of progress.¹³

Selective angiography was carried out on three patients, including infants, without complication. The procedure was done under general anaesthesia by one experienced consultant. It has been used mainly to allow local perfusion of urokinase into the renal artery in the haemolytic-uraemic syndrome, and some results have already been reported.¹⁴

Two patients who developed peritonitis during peritoneal dialysis needed subsequent haemodialysis, but otherwise peritonitis was rarely symptomatic, was not prevented by systemic antibiotics, and responded promptly to local treatment. This consisted of gentamicin in a dose of x mg/l of dialysate, x being the desired blood level in μ g/ml. One loading dose was also given systemically at the onset of this treatment. Reports of candida peritonitis are few,¹⁵ probably because, as is our experience, it is as readily treated as bacterial peritonitis. A 40% incidence of bacteriological peritonitis is high, however, and should be reduced. Frequent short dialysis of one or two

days and then a rest with catheter removal may be effective.

Though proportionately more patients died after haemodialysis than after peritoneal dialysis, the actual procedure was relatively straightforward and was tolerated well, death being the consequence of very severe disease rather than the mode of treatment. Access to the circulation was difficult in only one infant.

Most patients who died had very severe disease. Drugs (steroids and heparin) contributed to two deaths, and we now use only low-dose heparin in patients with the haemolytic-uraemic syndrome. The patients with burns, who had had their severity underassessed, became profoundly fluid-depleted and died three hours after transfer.

The mortality of patients with ARF in our series fell from 33% in 1972 to 20% in later years. This improvement, however, was due solely to maintenance dialysis being available and does not indicate improved recovery of kidney function. Nevertheless, the outlook for children with renal failure is better than for adults, in whom the mortality remains at about 50%, despite many changes in treatment.¹⁶

All patients with irrevocable kidney failure in this study who were suitable by physical and geographical criteria entered the dialysis and transplantation programme. With current financial restrictions, however, it is doubtful whether places will be available for all suitable patients in the future.

The maximum number of patients treated in any one year was 25 and the maximum number dialysed 14. These numbers seem small for a regional referral centre for ARF and suggest that not only would it be easy for non-specialised units to underestimate the difficulties of ARF and dialysis but that it takes some time for a substantial core of expertise to be obtained. This not only applies to medical staff but is important for nursing staff, an experienced ward sister being especially valuable. Expertise is also gained by those carrying out the specialised investigations, and a close association with the adult renal unit and dialysis and transplantation service has had clear advantages.

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